NEW YORK STATE OF OPPORTUNITY. Workers' Compensation Board

Medical Treatment Guidelines

Hip and Groin Disorders

Effective May 2, 2022

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A. GENERAL GUIDELINES PRINCIPLES

The principles summarized in this section are key to the intended application of the New York State Medical Treatment Guidelines (MTG) and are applicable to all Workers' Compensation Medical Treatment Guidelines.

A.1 Medical Care

Medical care and treatment required as a result of a work-related injury should be focused on restoring functional ability required to meet the patient's daily and work activities with a focus on a return to work, while striving to restore the patient's health to its pre-injury status in so far as is feasible.

A.2 Rendering Of Medical Services

Any medical provider rendering services to a workers' compensation patient must utilize the Treatment Guidelines as provided for with respect to all work-related injuries and/or illnesses.

A.3 Positive Patient Response

Positive results are defined primarily as functional gains which can be objectively measured. Objective functional gains include, but are not limited to, positional tolerances, range of motion, strength, endurance, activities of daily living (ADL), cognition, psychological behavior, and efficiency/velocity measures which can be quantified. Subjective reports of pain and function may be considered and given relative weight when the pain has anatomic and physiologic correlation in proportion to the injury.

A.4 Re-Evaluate Treatment

If a given treatment or modality is not producing positive results within a well-defined timeframe, the provider should either modify or discontinue the treatment regime. The provider should evaluate the efficacy of the treatment or modality 2 to 3 weeks after the initial visit and 3 to 4 weeks thereafter. These timeframes may be slightly longer in the context of conditions that are inherently mental health issues, and shorter for other non-musculoskeletal medical conditions (e.g. pulmonary, dermatologic etc.). Recognition that treatment failure is at times attributable to an incorrect diagnosis a failure to respond should prompt the clinician to reconsider the diagnosis in the event of an unexpected poor response to an otherwise rational intervention.

A.5 Education

Education of the patient and family, as well as the employer, insurer, policy makers and the community should be a primary emphasis in the treatment of work-related injury or illness. Practitioners should develop and implement

effective educational strategies and skills. An education-based paradigm should always start with communication providing reassuring information to the patient. No treatment plan is complete without addressing issues of individual and/or group patient education as a means of facilitating self-management of symptoms and prevention of future injury.

Time Frames

A.6 Acuity

Acute, Subacute and Chronic are generally defined as timeframes for disease stages:

- Acute – Less than one month
- Subacute - One to three month, and
- Chronic - greater than three months.

A.7 Initial Evaluation

Initial evaluation refers to the acute timeframe following an injury and is not used to define when a given physician first evaluates an injured worker (initial encounter) in an office or clinical setting.

A.8 Diagnostic Time Frames

Diagnostic time frames for conducting diagnostic testing commence on the date of injury. Clinical judgment may substantiate the need to accelerate or decelerate the time frames discussed in this document.

A.9 Treatment Time Frames

Treatment time frames for specific interventions commence once treatments have been initiated, not on the date of injury. It is recognized that treatment duration may be impacted by disease process and severity, patient compliance, as well as availability of services. Clinical judgment may substantiate the need to accelerate or decelerate the time frames discussed in this document.

A.10 Delayed Recovery

For those patients who fail to make expected progress 6-12 weeks after an injury and whose subjective symptoms do not correlate with objective signs and tests, reexamination in order to confirm the accuracy of the diagnosis and re-evaluation of the treatment program should be performed. When addressing a clinical issue that is not inherently a mental health issue, assessment for potential barriers to recovery (yellow flags/psychological issues) should be ongoing throughout the care of the patient. At 6-12 weeks, alternate treatment programs, including formal psychological or psychosocial evaluation should be considered. Clinicians must be vigilant for any pre-existing mental health issues or subsequent,

consequential mental health issues that may be impacting recovery. For issues that are clearly and inherently mental health issues from the outset (i.e. when it is evident that there is an underlying, work-related, mental health disorder as part of the claim at issue), referral to a mental health provider can and should occur much sooner. Referrals to mental health providers for the evaluation and management of delayed recovery do not indicate or require the establishment of a psychiatric or psychological condition. The evaluation and management of delayed recovery does not require the establishment of a psychiatric or psychological claim.

Treatment Approaches

A.11 Active Interventions

Active interventions emphasizing patient responsibility, such as therapeutic exercise and/or functional treatment, are generally emphasized over passive modalities, especially as treatment progresses. Generally, passive and palliative interventions are viewed as a means to facilitate progress in an active rehabilitation program with concomitant attainment of objective functional gains.

A.12 Active Therapeutic Exercise Program

Active therapeutic exercise program goals should incorporate patient strength, endurance, flexibility, range of motion, sensory integration, coordination, cognition and behavior (when at issue) and education as clinically indicated. This includes functional application in vocational or community settings.

A.13 Diagnostic Imaging And Testing Procedures

Clinical information obtained by history taking and physical examination should be the basis for selection of imaging procedures and interpretation of results. All diagnostic procedures have characteristic specificities and sensitivities for various diagnoses. Usually, selection of one procedure over others depends upon various factors, which may include: relative diagnostic value; risk/benefit profile of the procedure; availability of technology; a patient's tolerance; and/or the treating practitioner's familiarity with the procedure.

When a diagnostic procedure, in conjunction with clinical information, provides sufficient information to establish an accurate diagnosis, a second diagnostic procedure is not required. However, a subsequent diagnostic procedure including a repeat of the original (same) procedure can be performed, when the specialty physician (e.g. physiatrist, sports medicine physician or other appropriate specialist) radiologist or surgeon documents that the initial study was of inadequate quality to make a diagnosis. Therefore, in such circumstances, a repeat or complementary diagnostic procedure is permissible under the MTG.

It is recognized that repeat imaging studies and other tests may be warranted by the clinical course and/or to follow the progress of treatment in some cases. It may be of value to repeat diagnostic procedures (e.g., imaging studies) during the course of care to reassess or stage the pathology when there is progression of symptoms or findings, prior to surgical interventions and/or therapeutic injections when clinically indicated, and post-operatively to follow the healing process. Regarding serial imaging, (including x-rays, but particularly CT scans), it must be recognized that repeat procedures result in an increase in cumulative radiation dose and associated risks.

A given diagnostic imaging procedure may provide the same or distinctive information as obtained by other procedures. Therefore, prudent choice of procedures(s) for a single diagnostic procedure, a complementary procedure in combination with other procedures(s), or a proper sequential order in multiple procedures will ensure maximum diagnostic accuracy, minimize the likelihood of adverse effect on patients, and promote efficiency by avoiding duplication or redundancy.

A.14 Surgical Interventions

Consideration of surgery should be within the context of expected functional outcome. The concept of "cure" with respect to surgical treatment by itself is generally a misnomer. All operative interventions must be based upon positive correlation of clinical findings, clinical course and imaging and other diagnostic tests. A comprehensive assimilation of these factors must lead to a specific diagnosis with positive identification of pathologic condition(s). For surgery to be performed to treat pain, there must be clear correlation between the pain symptoms and objective evidence of its cause. In all cases, shared decision making with the patient is advised. The patient should be given the opportunity to understand the pros and cons of surgery, potential for rehabilitation as an alternative where applicable, evidence-based outcomes, and specific surgical experience.

A.15 Pre-Authorization

All diagnostic imaging, testing procedures, non-surgical and surgical therapeutic procedures, and other therapeutics within the criteria of the Medical Treatment Guidelines and based on a correct application of the Medical Treatment Guidelines are considered authorized, with the exception of the procedures listed in section 324.3(1)(a) of Title 12 NYCRR. These are not included on the list of pre-authorized procedures. Providers who want to perform one of these procedures must request pre-authorization from the carrier before performing the procedure.

Second or subsequent procedures (the repeat performance of a surgical procedure due to failure of, or incomplete success from the same surgical procedure performed earlier, if the Medical Treatment Guidelines do not specifically address multiple procedures) also require pre-authorization.

A.16 Psychological/Psychiatric Evaluations

In select patients, mental health evaluations are essential to make, secure or confirm a diagnosis. Of course, the extent and duration of evaluations and/or interventions by mental health professionals may vary, particularly based on whether: the underlying clinical issue in the claim is inherently a mental health issue; or there is a mental health issue that is secondary or consequential to the medical injury or illness that is at issue in the claim in question; or there is a pre-existing, unrelated mental health issue that has been made worse by, or is impeding the recovery from (or both) the medical injury or illness that is at issue in the claim in question.

Tests of psychological function or psychometric testing, when indicated, can be a valuable component of the psychological evaluation in identifying associated psychological, personality and psychosocial issues. Although these instruments may suggest a diagnosis, neither screening nor psychometric tests are capable of making a diagnosis. The diagnosis should only be made after careful analysis of all available data, including from a thorough history and clinical interview.
A professional fluent in the primary language of the patient is strongly preferred. When such a provider is not available, services of a professional language interpreter must be provided.

Frequency: When assessing for a pre-existing, unrelated mental health issue that has been made worse by, or is impeding the recovery from (or both) a work-related, medical injury or illness, then a one-time visit for initial psychiatric/psychological encounter should be sufficient, as care would normally be continued by the prior treating provider. If psychometric testing is indicated by findings in the initial encounter, time for such testing should not exceed an additional three hours of professional time. For conditions in which a mental health issue is a central part of the initial claim, or in which there is a mental health issue that is secondary or consequential to the work-related, medical injury or illness, that is part of the claim in question, then more extensive diagnostic and therapeutic interventions may be clinically indicated, and are discussed in detail in the Medical Treatment Guidelines for such mental health conditions.

A.17 Personality/Psychological/Psychosocial Intervention

Following psychosocial evaluation, when intervention is recommended, such intervention should be implemented as soon as possible. This can be used alone

or in conjunction with other treatment modalities. For all psychological/psychiatric interventions, there must be an assessment and treatment plan with measurable behavioral goals, time frames and specific interventions planned**.**

- Time to produce effect: two to eight weeks.
- Optimum duration: six weeks to three months.
- Maximum duration: three to six months.
- Counseling is not intended to delay but rather to enhance functional recovery.

For PTSD Psychological Intervention:

- Optimum duration three to six months.
- Maximum duration: nine to twelve months.

For select patients, longer supervision and treatment may be required, and if further treatment is indicated, documentation of the nature of the psychological factors, as well as projecting a realistic functional prognosis, should be provided by the authorized treating practitioner every four weeks during the first six months of treatment. For treatment expected to last six to twelve months, such documentation should be provided every four to eight weeks. For long-term treatment beyond twelve months, such documentation should be provided every eight to twelve weeks. All parties should strive for ongoing and continuous communications, in order to facilitate seamless, continuous and uninterrupted treatment.

A.18 Functional Capacity Evaluation (FCE)

Functional capacity evaluation is a comprehensive or more restricted evaluation of the various aspects of function as they relate to the patient's ability to return to work. Areas such as endurance, lifting (dynamic and static), postural tolerance, specific range-of-motion, coordination and strength, worker habits, employability, as well as psychosocial, cognitive, and sensory perceptual aspects of competitive employment may be evaluated. Components of this evaluation may include: (a) musculoskeletal screen; (b) cardiovascular profile/aerobic capacity; (c) coordination; (d) lift/carrying analysis; (e) job-specific activity tolerance; (f) maximum voluntary effort; (g) pain assessment/psychological screening; (h) non-material and material handling activities; (i) cognitive and behavioral; (j) visual; and (k) sensory perceptual factors.

In most cases, the question of whether a patient can return to work can be answered without an FCE.

An FCE may be considered at time of MMI, following reasonable prior attempts to return to full duty throughout course of treatment, when the treating physician

is unable to make a clear determination on work status on case closure. An FCE is not indicated early during a treatment regime for any reason including one to support a therapeutic plan.

When an FCE is being used to determine return to a specific job site, the treating physician is responsible for understanding and considering the job duties. FCEs cannot be used in isolation to determine work restrictions. The authorized treating physician must interpret the FCE in light of the individual patient's presentation and medical and personal perceptions. FCEs should not be used as the sole criteria to diagnose malingering.

A.19 Return To Work

For purposes of these guidelines, return to work is defined as any work or duty that the patient is able to perform safely. It may not be the patient's regular work. Ascertaining a return to work status is part of medical care, and should be included in the treatment and rehabilitation plan. It is normally addressed at every outpatient visit. A description of the patient's status and task limitations is part of any treatment plan and should provide the basis for restriction of work activities when warranted. Early return to work should be a prime goal in treating occupational injuries. The emphasis within these guidelines is to move patients along a continuum of care and return to work, since the prognosis of returning an injured worker to work drops progressively the longer the worker has been out of work.

A.20 Job Site Evaluation

The treating physician may communicate with the employer or employer's designee, either in person, by video conference, or by telephone, to obtain information regarding the individual or specific demands of the patient's pre-injury job. This may include a description of the exertional demands of the job, the need for repetitive activities, load lifting, static or awkward postures, environmental exposures, psychological stressors and other factors that would pose a barrier to re-entry, risk of re-injury or disrupt convalescence. When returning to work at the patient's previous job tasks or setting is not feasible, given the clinically determined restrictions on the patient's activities, inquiry should be made about modified duty work settings that align with, the patient's condition in view of proposed work activities/demands in modified duty jobs. It should be noted, that under certain circumstances, more than one job site evaluation may be indicated.

Ideally, the physician would gain the most information from an on-site inspection of the job settings and activities; but it is recognized that this may not be feasible in most cases. If job videos/CDs/DVDs are available from the employer, these can contribute valuable information, as can video conferences, conducted from the worksite and ideally workstation or work area.

Frequency: one or two contacts

- 1st contact: Patient is in a functional state where the patient can perform some work.
- 2nd contact: Patient has advanced to state where the patient is capable of enhanced functional demands in a work environment.

The physician shall document the conversation.

Other

A.21 Guideline Recommendations And Medical Evidence

The Workers' Compensation Board and its Medical Advisory Committee have not independently evaluated or vetted the scientific medical literature used in support of the guidelines, but have relied on the methodology used by the developers of various guidelines utilized and referenced in these Guidelines.

A.22 Experimental/Investigational Treatment

Medical treatment that is experimental/investigational and not approved for any purpose, application or indication by the FDA is not permitted under these Guidelines.

A.23 Injured Workers As Patients

In these Guidelines, injured workers are referred to as patients recognizing that in certain circumstances there is no doctor-patient relationship.

A.24 Scope Of Practice

These Guidelines do not address scope of practice or change the scope of practice.

B. Hip and Groin Disorders

B.1 Overview

The hip and groin disorders described in this section are covered in this guideline. Other prominent disorders, including lumbar radiculopathy and lumbar spinal stenosis (which can present as posterior and lateral hip pain), are not reviewed here in detail but should often be considered in the differential diagnosis of hip pain and hip symptoms (see the *NYS WCB Mid and Low Back Injury Medical Treatment Guidelines* for a discussion of these disorders). Additional diagnostic considerations include inguinal hernias, femoral hernias, atherosclerotic abnormalities, aneurysms, avulsion fractures (especially sartorius, rectus femoris), femoral mononeuritis, tumor, cancer, crystal arthropathies (e.g., gout, pseudogout, hydroxyapatite), and infections including septic arthritis.

B.2 Introduction

B.2.a History Taking and Physical Examination

History taking and physical examination establish the foundation/basis for and dictate subsequent stages of diagnostic and therapeutic procedures. When findings of clinical evaluations and those of other diagnostic procedures are not consistent with each other, the objective clinical findings should have preference. The medical records should reasonably document the following:

History of Present Injury

- Mechanism of injury: This includes details of symptom onset and progression, and symptoms that may arise from postural or functional accommodation to the hip/groin injury;
- Relationship to work: This includes a statement of the probability that the illness or injury is work-related;
- Prior occupational and non-occupational injuries: To the same area including specific prior treatment;
- Ability to perform job duties and activities of daily living; and,
- Exacerbating and alleviating factors for symptoms; not limited to the hip/groin.

Past History

- Past medical history includes, but is not limited to, neoplasm, gout, arthritis, and diabetes;

- Review of systems includes, but is not limited to, symptoms of rheumatologic, neurologic, endocrine, neoplastic, and other systemic diseases. If applicable this should also include GI and GU (noting any incontinence issues) as well as appropriate musculoskeletal areas;

- Smoking history;

- Vocational and recreational pursuits including history of barotrauma;

- Prior imaging studies; and

- Past surgical history.

Physical Examination

Examination of a joint should include the joint below the affected area, including the opposite side for comparison. Physical examination should include accepted tests and exam techniques applicable to the joint or area being examined, including:

- Visual inspection;

- Palpation;

- Range of motion/quality of motion (active and passive) including issues with abnormal internal or external rotation and clicking, popping or catching with range of motion;

- Strength (weakness/atrophy);

- Joint integrity/stability;

- Examination for deformity/displacement including leg length discrepancy;

- If applicable to injury, integrity of distal circulation;

- If applicable, neurological exam (i.e: sensory and motor function, reflexes) as clinically indicated;

- If applicable, assess for testicular tenderness or swelling; and/or

- Assess gait and weight bearing status

B.3 Red Flags

Certain findings, “red flags”, raise suspicion of potentially serious medical conditions. Assessment (history and physical examination) should include evaluation for red flags. In the hip/groin these findings or indicators may include: fracture, dislocations, infection or inflammation, tumors, or systemic rheumatological disorders; and neurological compromise. Further evaluation/consultation or urgent/emergency intervention may be indicated, and the New York Hip/Groin Injury Medical Treatment Guidelines incorporate changes in clinical management triggered by the presence of “red flags.”

Table 1. “Red Flags” for Potentially Serious Conditions Associated with Hip and Groin Pain*

Disorder	Medical History	Physical Examination
Tumor/ Neoplasia	• Severe localized pain (often deep-seated, unrelenting bony pain) • History of cancer (at any point in the lifetime) • Age >50 years • Symptoms consistent with disease in a specific organ system (e.g., cough, change in bowel habit, epigastric pain, early satiety) • Constitutional symptoms, such as recent unexplained weight loss, fatigue • Pain that continues at night or at rest	• Pallor, reduced blood pressure, diffuse weakness • Tenderness over bony landmarks and percussion tenderness (other than greater trochanteric pain syndrome or groin strain) • New mass or tenderness • Abnormal pulmonary examination (crackles, wheezes, rhonchi, decreased breath sounds) • New findings at a distant site to the original complaints
Infection	• Constitutional symptoms, such as recent fever, chills, or unexplained weight loss • Recent bacterial infection (e.g. urinary tract infection) • History of recurring infections treated with antibiotics (e.g., repeated urinary tract infections) • Foreign travel with exposure potential • Insect bites	• Fever, tachycardia, tachypnea, hypotension • Elevated white blood cell count (may be decreased in elderly or immunocompromised) • Shift in the white blood cell differential towards immature cells (“left shift”) • Abnormal urinalysis • Abnormal body part examination (e.g., pulmonary) • Tenderness over bony landmarks
Progressive Neurologic Deficit	• Severe spine or extremity pain • Progressive numbness or weakness • Complaints of new clumsiness of gait	• Significant and progressive dermatomal and/or myotomal (motor) involvement • Evidence of cauda equina • Hyperreflexia or other evidence of myelopathy
Rheumatologic Disease	• Diffuse arthralgias • Prior arthropathy • Skin changes, lesions, or ulcers • Fatigue, malaise • Subtle mental status changes	• Polyarticular joint effusions (usually with warmth) • Radiographic abnormalities consistent with erosive or degenerative pathology • Elevated sedimentation rate (ESR) or C-reactive protein (CRP)

		• Hematuria, proteinuria • Other specific abnormalities as appropriate (e.g., ANA, RF, anti-DNA, C3, anti-Ro, anti-La, oral ulcers, pulmonary abnormalities, ophthalmological involvement, dermal abnormalities)
Testicular Torsion	• Acute onset testicular and groin pain	• Tenderness • Loss of blood flow on ultrasound
Ectopic Pregnancy	• Acute onset lower abdominal or groin pain	• Pregnancy test • Vaginal ultrasound

*This list is not meant to be comprehensive; rather, it is a review of the more common suggestive historical and examination findings.

B.4 Diagnostic Testing and Testing Procedures

One diagnostic imaging procedure may provide the same or distinctive information as obtained by other procedures. Therefore, prudent choice of procedure(s) for a single diagnostic procedure, a complementary procedure in combination with other procedures(s), or a proper sequential order in multiple procedures will ensure maximum diagnostic accuracy, minimize adverse effect to patients and promote cost effectiveness by avoiding duplication or redundancy.

All diagnostic imaging procedures have a significant percentage of specificity and sensitivity for various diagnoses. None is specifically characteristic of a certain diagnosis. Clinical information obtained by history taking and physical examination should be the basis for selection and interpretation of imaging procedure results.

When a diagnostic procedure, in conjunction with clinical information, provides sufficient information to establish an accurate diagnosis, the second diagnostic procedure will be redundant if it is performed only for diagnostic purposes. At the same time, a subsequent diagnostic procedure (that may be a repeat of the same procedure, when the rehabilitation physician, radiologist or surgeon documents that the study was of inadequate quality to make a diagnosis) can be a complementary diagnostic procedure if the first or preceding procedures, in conjunction with clinical information, cannot provide an accurate diagnosis. Usually, preference of a procedure over others depends upon availability, a patient's tolerance, and/or the treating practitioner's familiarity with the procedure.

It is recognized that repeat imaging studies and other tests may be warranted by the clinical course and to follow the progress of treatment in some cases. It may be of value to repeat diagnostic procedures (e.g. imaging studies) during the course of care to reassess or stage the pathology when there is progression of symptoms or findings, prior to surgical interventions and therapeutic injections when warranted, and post-operatively to follow the healing process. Regarding CT examinations, it must be recognized that repeat procedures result in an increase in cumulative radiation dose and associated risks.

When indicated, the following studies can be utilized for further evaluation of Hip and Groin injuries, based upon the mechanism of injury, symptoms, and patient history.

B.5 Diagnostic Criteria and Differential Diagnosis

The history, physical examination, and radiographs will effectively diagnose most hip disorders. If the diagnosis of a hip and groin disorder remains unclear, magnetic resonance imaging (MRI; with or without gadolinium) is generally the imaging method used to diagnose most other intraarticular and extraarticular pathologies. Other imaging techniques include ultrasound, computed tomography (CT) imaging, postoperative radiography, and magnetic resonance and CT arthrography.

The treating provider performing an initial evaluation of a patient with hip or groin pain should seek a discrete explanatory diagnosis. A review of systems that also involve the knee, spine, abdomen, and genitourinary tract is necessary. The examination of a patient with hip or groin pain generally needs to focus on the hip joint and include relevant neighboring structures similar to the review of systems. Potentially serious disorders include infections, tumors, or systemic rheumatological disorders.

Table 2. Diagnostic Criteria for Non-"Red Flag" Conditions

Probable Diagnosis or Injury	Symptoms	Signs	Tests and Results
Hip Osteoarthrosis	Nonradiating hip pain. Morning stiffness or stiffness on standing after sitting <1 hour. Sleep disturbance sometimes present; mood disturbance usually not present. Often other affected joints.	Range of motion (ROM) generally reduced, especially hip internal rotation. May be normal when mild.	Radiographs usually ordered to help secure diagnosis. Other diagnostic tests only if targeting the specific body part and there is a potential for meaningful intervention.
Hip Dislocation	Inability to bear weight. Acute onset associated with forceful event or accident. Recurrent problem if congenital.	Unable to bear weight. Lower extremity shortened and externally rotated.	Hip radiographs usually ordered. Other testing usually not necessary.
Hip Fracture	Fall or motor vehicle collision. Severe pain. Unable to bear weight.	Unable to bear weight. Lower extremity shortened and externally rotated.	Radiographs required. Other testing usually not necessary in acute treatment setting.
Labral Tears	Nonradiating groin pain with ROM. Typically provoked with specific, predictable activities, such as specific position(s). May have buckling, clicking, catching.	Variable findings; pain reproducible on ROM. Extent of ROM often restricted. Pain reproduced with hip ROM into extension from flexion. Pain with hyperflexion, internal rotation, and	Radiographs are often ordered. MRI is sometimes ordered, and MR arthrography is often helpful.

	Pain may be worse with pivoting and walking.	adduction (impingement position) is present in most cases. Pain and/or click may also be reproduced with the labral stress test and/or with resisted straight leg raise.	
Hip Osteonecrosis	Nonradiating hip pain. History of systemic factors (e.g., diabetes mellitus, alcohol).	Reduced ROM and pain with passive ROM usually present. May have pain with weight bearing. May be unable to bear weight if osseous collapse has occurred.	Radiographs required. MRI and CT may be ordered for further evaluation of the femoral head. Bone scans are sometimes ordered, particularly for evaluation of other joints.
Femoroacetabular Impingement	Nonradiating groin pain. Pain is often positional and worse with activity. Pain with hip flexion and internal rotation.	Decreased internal rotation and adduction with hip flexed to 90 degrees. Positive impingement test (pain with passive adduction and gradually internally rotating the flexed hip).	Radiographs usually ordered. MRI and MR arthrography helpful.
Gluteus Medius Tears	Nonradiating hip pain. May have weakness, especially with more acute tears.	Abnormal gait with inability to stabilize pelvis. Tender over greater trochanter. ROM usually reduced. Qualitative muscle strength weakness.	Radiographs usually ordered. MR helpful.
Greater Trochanteric Pain Syndrome	Nonradiating hip pain. Pain increased when lying on the affected side or stair climbing. Pain worse with activity.	Tender to palpation over the greater trochanter. Pain with hip ROM. Extent of ROM usually normal. Antalgic gait sometimes present and increased pain with stair climbing.	Radiographs sometimes ordered. Other testing usually not required for short-term and mild cases. MRI sometimes helpful.
Groin Strains	Focal pain in the muscle-tendon junction affected. May have epidydimal pain if inguinal area is involved. Pain in the adductor if an adductor strain, and generally history of very forceful use for adductor strain.	Patients avoid use or movement. Focal tenderness at affected myotendinous junction. Muscular defect if complete rupture, usually with hematoma at rupture site. Reduced qualitative strength.	No testing usually ordered.
Hip Dysplasia	May be asymptomatic other than with dislocation or instability. Pain is in groin and may have symptoms with specific positions.	Pain reproduced with impingement sign. Pain reproduced with hip hyperextension or placing hip in the FABER position. Increased ROM of both hips may be present, but affected hip has altered motion, often limited by pain.	Radiographs are usually ordered and often sufficient for diagnostic purposes.

Hip Instability	Dislocation may have occurred. May have subjective weakness.	ROM may be increased and findings present for ligamentous laxity. Increased hip external rotation (in extension during log roll or in flexion such as the FABER maneuver).	Radiographs are usually ordered. MRI may be helpful.
Ligamentum Teres Ruptures	May be asymptomatic or have experienced pain if there was a ligament tear with a discrete traumatic event. Event usually involved exaggerated adduction and external rotation or abduction.	Exam is usually normal in the absence of other findings. May accompany osteoarthrosis; thus, those exam findings may be present.	Radiographs are usually ordered. MRI may be helpful.

Adapted from Rondinelli RD (Ed.). *Guides to the Evaluation of Permanent Impairment, Sixth Edition*. Chicago, Ill: AMA Press; 2008; and Sanders SH, Harden RN, Vicente PJ. Evidence-based clinical practice guidelines for interdisciplinary rehabilitation of chronic nonmalignant pain syndrome patients. *Pain Prac*. 2005;5(4):303-15.

C. Conditions

This Guideline covers the following conditions:

C.1 Hip Osteoarthrosis

C.2 Hip Osteonecrosis

C.3 Hip Fractures

C.4 Prevention of Venous Thromboembolic Disease

C.5 Pre / Post-Operative Rehabilitation, including Hip Arthroplasty and Hip Fractures

C.6 Femoroacetabular Impingement, Hip Impingement or Labral Tears

C.7 Glueteus Medius Tendinosis and Tears, Greater Trochanteric Pain Syndrome and Trochanteric Bursitis

C.8 Hamstring and Hip Flexor Strains

C.9 Groin Strains and Adductor-Related Groin Pain

C.10 Meralgia Paresthetica

C.11 Lower Abdominal Strains

C.12 Epididymo-Orchitis

C.1 Hip Osteoarthrosis

C.1.a Related Terms

- Arthritis
- Arthropathy
- Arthrosis
- Degenerative Arthritis
- Degenerative Arthrosis
- Degenerative Joint Disease
- Non-inflammatory Arthritis
- Osteoarthritis
- Osteoarthrosis
- Rheumatism

C.1.b Introduction

Hip degenerative joint disease (DJD) is most commonly caused by osteoarthrosis (OA). Although *osteoarthritis* is the more common name for this entity, *osteoarthrosis* is considered to be more technically precise because classic inflammation is absent.

OA may develop in only one joint after a significant traumatic injury such as fracture, in which case it is often delayed by many years.

The common pathway for hip OA involves sufficient destruction of the joint by various causes that may be indistinguishable on radiograph. Thus, the correct interpretation of findings consistent with possible OA on radiograph is usually degenerative joint disease, but not osteoarthrosis.

C.1.c Diagnostic Studies

C.1.c.i Antibodies to Assist in Diagnosing Hip Pain, Including Differentiating Inflammatory Rheumatic Disorders From Hip Osteoarthrosis

Recommended – in select patients with acute, subacute, chronic or postoperative hip pain.

Indications: Undiagnosed patients with either systemic arthropathies and/or peripheral neuropathies, or patients with incomplete evaluations. Diagnostic testing should generally include sedimentation rate. Other tests may include rheumatoid factor, antinuclear antibody level, and others.

Rationale: Rheumatoid panels are helpful in select circumstances to confirm inflammatory arthritides and are thus recommended for use among those with symptoms suggestive of possible rheumatoid disorders.

Evidence for use of antibodies to assist in diagnosing hip pain

C.1.c.ii C-Reactive Protein to Assist in Diagnosing Hip Pain, Including Differentiating Inflammatory Rheumatic Disorders From Hip Osteoarthrosis

Recommended - in select patients with acute, subacute, chronic or postoperative hip pain.

Indications: Used as a non-specific inflammatory indicator. Undiagnosed patients with either systemic arthropathies and/or peripheral neuropathies, or patients with incomplete evaluations. Diagnostic testing should generally include sedimentation rate, which is also non-specific. Other tests may include rheumatoid factor and antinuclear antibody level.

Rationale: Rheumatoid panels are helpful in select circumstances to confirm inflammatory arthritides and are thus recommended for use among those with symptoms suggestive of possible rheumatoid disorders.

Evidence for use of C-Reactive protein to assist in diagnosing hip pain

C.1.c.iii Erythrocyte Sedimentation Rate to Assist in Diagnosing Hip Pain, Including Differentiating Inflammatory Rheumatic Disorders From Hip Osteoarthrosis

Recommended – in select patients with acute, subacute, chronic or postoperative hip pain.

Indications: Used as a non-specfic indicator of inflammation. Undiagnosed patients with either systemic arthropathies and/or peripheral neuropathies, or patients with incomplete evaluations. Diagnostic testing should generally include sedimentation rate. Other tests may include rheumatoid factor, antinuclear antibody level, and others.

Rationale: Rheumatoid panels are helpful in select circumstances to confirm inflammatory arthritides and are thus recommended for use among those with symptoms suggestive of possible rheumatoid disorders.

Evidence for use of erythrocyte sedimentation rate to assist in diagnosing hip pain

C.1.c.iv Other Non-Specific Inflammatory Markers to Assist in Diagnosing Hip Pain, Including Differentiating Inflammatory Rheumatic Disorders from Hip Osteoarthrosis

Recommended – to assist in diagnosing acute, subacute, chronic and postoperative hip pain.

Indications: Undiagnosed patients with either systemic arthropathies and/or peripheral neuropathies, or patients with incomplete evaluations. Diagnostic testing should generally include sedimentation rate. Other tests may include rheumatoid factor, antinuclear antibody level, and others.

Rationale: Rheumatoid panels are helpful in select circumstances to confirm inflammatory arthritides and are thus recommended for use among those with symptoms suggestive of possible rheumatoid disorders.

Evidence for use of other non-specific inflammatory markers to assist in diagnosing hip pain

Evidence for the Use of Antibodies, C-Reactive Protein, Erythrocyte Sedimentation Rate, Other Non-Specific Inflammatory Markers

C.1.c.v Arthroscopic Examinations Have Been Used Primarily for Treatable Hip Disorders and Have Been Used to Diagnose Hip Osteoarthritis

Not Recommended – to solely diagnosis hip oseoarthritis.

Rationale: The diagnosis of hip OA is generally straightforward and does not necessitate or benefit from arthroscopy. Thus, arthroscopy is not recommended as a routine diagnostic procedure.

Evidence for use of arthroscopic examination to diagnosis hip osteoarthritis

C.1.c.vi Bone Scanning to Assist in the Diagnosis of Osteonecrosis, Neoplasms, or Other Conditions with Increased Polyosthotic Bone Metabolism

Recommended – in select patients with acute, subacute or chronic hip pain to assist in the diagnosis of suspected metastases, primary bone tumors, infected bone

(osteomyelitis), inflammatory arthropathies, or trauma (ie. occult fractures)

Indications: Patients with hip pain with suspicion of osteonecrosis, suspected metastases, primary bone tumors, infected bone (osteomyelitis), inflammatory arthropathies, or trauma (ie. occult fractures).

Frequency/Dose/Duration: One evaluation. A second evaluation may be indicated with a significant change in symptoms, generally after more than three months.

Rationale: Bone scanning may be a helpful diagnostic test to evaluate suspected metastases, primary bone tumors, infected bone. (osteomyelitis), inflammatory arthropathies, or trauma (e.g., occult fractures). Bone scanning is generally not indicated for evaluation of hip OA. It may be helpful in patients with suspected early AVN, but without x-ray changes. In patients where the diagnosis is felt to be secure, there is not an indication for bone scanning because it does not alter treatment or management.

Evidence for use of bone scans to diagnosis early osteonecrosis

C.1.c.vii Computerized Tomography Scans for Routine Diagnosis of Hip OA

Not Recommended – for diagnosis of hip OA.

C.1.c.viii Computerized Tomography for Evaluation of Recurrent Post-Arthroplasty Dislocations

Recommended – to evaluate recurrent/chronic post-arthroplasty dislocations.

Indications: Recurrent dislocations after arthroplasty. Patients with a need for imaging but with contraindicatations for MRI.

Benefits: Imaging to help explain dislocations and plan treatment.

Frequency/Dose/Duration: One evaluation. A second evaluation is rarely needed.

Rationale: Computerized tomography is considered to be superior to MRI for imaging of most hip abnormalities where advanced imaging of calcified structures is required. A contrast

CT is recommended for select use of recurrent dislocations after arthroplasty.

Evidence for use of CT scans to evaluate recurrent post-arthroplasty dislocations

C.1.c.ix Helical Computerized Tomography (CT Scan) for Advanced Imaging of Bony Structures

Recommended – for select patients with acute, subacute, or chronic hip pain for whom advanced imaging of bony structure is thought to be potentially helpful. Helical CT is also recommended for patients who need advanced imaging, but have contraindications for MRI**.**

Indications: Patients with acute, subacute, or chronic hip pain who need advanced bony structure imaging. Patients needing advanced imaging, but with contraindications for MRI (e.g., implanted ferrous metal hardware) are also candidates.

Frequency/Dose/Duration: One evaluation. A second evaluation is rarely needed.

Rationale: Helical CT scanning has been largely replaced by MRI. However, it has been thought to be superior to MRI for evaluating subchondral fractures, although a definitive study has not been reported. In addition, for patients who have contraindications for MRI (e.g., implanted ferrous metal hardware) but require evaluation of AVN, helical CT is recommended.

Evidence for use of helical CT for advanced imaging of bony structures

C.1.c.x Local Anesthetic Injections for Hip Pain Diagnosis

Recommended – to assist in diagnosising the cause of hip pain.

Indications: Moderate to severe hip pain of uncertain cause.

Frequency/Dose/Duration: One injection. A second evaluation is rarely needed. Intraarticular hip injections with anesthetic agents are generally thought to be better if performed with a glucocorticosteroid as it generally accomplishes both diagnostic and therapeutic purposes simultaneously, although occasionally a simple anesthetic injection may be helpful in select cases.

Rationale: Local anesthetic injections for diagnostic purposes are helpful for confirming a diagnostic impression, although there are no quality studies evaluating these injections for purposes of evaluating hip pain (for therapeutic injections, see Injections).

Evidence for use of local anesthetic injections for hip pain diagnosis

C.1.c.xi Electromyography, Including Nerve Conduction Studies, Have Been Used to Confirm Diagnostic Impressions of Other Peripheral Nerve Entrapments, Including the Lateral Femoral Cutaneous Nerve to the Thigh (Meralgia Paresthetica)

Recommended – in select patients to assist in the diagnosis of subacute or chronic pheripheral nerve entrapments, including lateral cutaneous nerve to thigh (meralgia paresthetica).

Indications: Patients with subacute or chronic paresthesias with or without pain, particularly if the diagnosis is unclear. Generally, should not be obtained for symptoms of under three weeks duration.

Frequency/Dose/Duration: Generally, only obtained at presentation. If a diagnosis remains unclear, symptoms progress, or months have passed re-assessment may be indicated.

Rationale: Electrodiagnostic studies may assist in confirming peripheral nerve entrapments, such as the lateral cutaneous nerve to the thigh.

Evidence for the Use of Electromyography/Nerve Conduction

C.1.c.xii Magnetic Resonance Imaging is Used as a Test for Select Hip Joint Problems

MRI is considered the imaging test of choice for soft tissues,it is the gold standard for evaluating osteonecrosis after x-rays.

Not Recommended – for routine evaluation of acute, subacute or chronic hip joint pathology, including degenerative joint disease.

Recommended - for select hip joint pathology, particularly involving concerns regarding soft tissue pathology or with symptoms lasting more than three months.

Rationale: MRI findings consistent with OA are likely to be particularly helpful for soft tissue abnormalities. MRI has been suggested for the evaluation of patients with symptoms lasting more than 3 months. Because there are concerns that MRI is inferior to MR arthrography, particularly for evaluating the labrum, MRI without arthrography is recommended for evaluating the joint but not the labrum. MRI is not recommended for routine hip imaging, but it is recommended for select hip joint pathology, particularly involving concerns regarding soft tissue pathology.

Evidence for use of MRI for evaluation of hip joint pathology

C.1.c.xiii Radiographs (X-Rays) to Diagnosis Hip Osteoarthritis

<u>Recommended</u> – to assist in diagnosing hip osteoarthritis.

Indications: Nearly all patients with hip pain thought to potentially have hip OA.

Frequency/Dose/Duration: Generally, only obtained once at presentation.

Rationale: X-rays are helpful for the evaluation of hip OA and to diagnose hip OA.

Evidence for use of radiographs to diagnosis hip osteoarthritis

C.1.c.xiv Ultrasound to Diagnose Hip OA

<u>Not Recommended</u> – to diagnose hip OA.

Rationale: There is no clear indication for the use of ultrasound to evaluate osteoarthrosis.

Evidence for use of ultrasound to diagnose hip OA

C.1.d Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.1.d.i Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for Treatment of Acute, Subacute, or Chronic Hip OA

Recommended - for treatment of acute, subacute or chronic hip OA.

Indications - For acute, subacute or chronic hip OA, NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration: As needed use may be reasonable for many patients.

Indications for Discontinuation: Resolution of hip OA pain, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.1.d.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended - concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

Indications: For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration: Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy, between the agents for prevention of gastrointestinal bleeding.

Indications for Discontinuation: Intolerance, development of adverse effects, or discontinuation of NSAID.

C.1.d.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Recommended - Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin.

C.1.d.iv Acetaminophen for Treatment of Hip OA Pain

Recommended - for treatment of hip OA pain, particularly in patients with contraindications for NSAIDs.

Indications: All patients with hip OA pain, including acute, subacute or chronic.

Dose/Frequency: Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation: Resolution of pain, adverse effects or intolerance.

C.1.d.v Topical NSAIDs for Treatment of Acute, Subacute or Chronic Hip OA

Recommended - for acute, subacute or chronic hip OA.

Indications: For most patients, oral medications are recommended. However, for those with contraindications for oral NSAIDs or intolerance, topical NSAIDs may be a reasonable alternative.

Frequency/Dose/Duration: Per manufacturer's recommendations.

Indications for Discontinuation: Resolution of hip OA pain, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.1.d.vi Norepinephrine Inhibiting Anti-depressants

Not Recommended - for the treatment of pain associated with hip osteoarthrosis.

C.1.d.vii Selective Serotonin Reuptake Inhibitors (SSRIs)

Not Recommended - for treatment of pain associated with hip osteoarthrosis.

C.1.d.viii Anti-Convulsant Agents for Hip OA

Not Recommended – for hip OA pain patients.

C.1.d.ix Gabapentin for Peri-Operative Pain Relief and Opioid-Sparing After Total Hip Arthroplasty.

Recommended - for treatment of perioperative pain and to reduce the need for opioids post operatively.

Indications: Perioperative use, e.g., arthroplasty.

Frequency/Dose/Duration: Limited use to immediate peri-operative period, usually a few days.

Indications for Discontinuation: Completion of course, sufficient recovery, resolution of pain, intolerance, adverse effects.

C.1.d.x Opioids for Acute, Subacute, or Chronic Hip Pain

Not Recommended - for acute, subacute, or chronic hip pain.

C.1.d.xi Skeletal Muscle Relaxants

Not Recommended - for acute and subacute, moderate to severe hip pain.

Evidence for the use of Skeletal Muscle Relaxants

C.1.d.xii Capsicum

Recommended - for short-term treatment of acute or subacute hip pain as well as for acute exacerbations of chonic hip pain as a counterirritant.

Indications: Temporary flare ups of chronic hip pain or acute or subacute hip pain.

Frequency/Dose/Duration: Duration of use for patients with chronic pain is limited to an acute flare-up period, generally lasting no more than 2 weeks. Caution should be exerted to avoid application near the genitals.

Indications for Discontinuation: Resolution of pain, completion of a course, intolerance, other adverse effects.

Evidence for the use of Capsicum

C.1.d.xiii Lidocaine Patches

Not Recommended - to treat hip OA pain.

Evidence for the Use of Lidocaine Patches

C.1.d.xiv Eutectic Mixture of Local Anesthestics (EMLA)

Not Recommended - to treat hip OA Pain.

C.1.d.xv Glucosamine Sulfate, Chondroitin Sulfate and/or Methylsulfonylmethane

Not Recommended – for the treatment of hip osteoarthrosis.

Evidence for the Use of Glucosamine

C.1.d.xv Complementary or Alternative Treatments or Dietary Supplements

Not Recommended – for the treatment of hip osteoarthrosis.

C.1.e Treatments

C.1.e.i Cryotherapy / Heat

C.1.e.i.a Cryotherapy

Recommended - for Acute, Subacute, or Chronic hip OA, as well as for hip arthroplasty and surgery patients.

Frequency/Duration: Approximately three to five self-applications per day as needed.

Indications for Discontinuation: Resolution, adverse effects, non-compliance.

C.1.e.i.b Heat Therapy

Recommended - for acute, subacute or chronic hip OA.

Frequency/Duration: Approximately three to five self-applications per day as needed.

Indications for Discontinuation: Resolution, adverse effects, non-compliance.

C.1.e.i.c Diathermy

Not Recommended - for the treatment of hip osteoarthrosis or for patients with acute, subacute or chronic hip pain.

C.1.e.i.d Infrared Therapy

Not Recommended for treatment of hip osteoarthrosis or for patients with acute, subacute or chronic hip pain**.**

C.1.e.i.e Ultrasound Treatment

Not Recommended for treatment of hip osteoarthrosis or for patients with acute, subacute or chronic hip pain.

C.1.e.i.f Low Level Laser Therapy

Not Recommended - for the treatment of osteoarthrosis or acute, subacute or chronic hip pain.

C.1.e.i.g Self-Application of Heat Therapy

Recommended - for the treatment of osteoarthrosis

Indications: Hip OA and patients desiring to use non-medicinal treatments. Others may benefit as well.

Frequency/Dose/Duration: Applications may be periodic or continuous. Applications should be home-based as there is no evidence for efficacy of provider-based heat treatments. Primary emphasis should generally be on functional restoration program elements, rather than on passive treatments in patients with chronic pain.

Indications for Discontinuation: Intolerance, increased pain, development of a burn, other adverse event.

Evidence for the use of low-tech heat therapy

C.1.f Rehabilitation

Rehabilitation (supervised formal therapy) required as a result of a work-related injury should be focused on restoring functional ability required to meet the patient's daily and work activities and return to work; striving to restore the injured worker to pre-injury status in so far as is feasible.

Active therapy requires an internal effort by the patient to complete a specific exercise or task. Passive therapy are those interventions not requiring the exertion of effort on the part of the patient, but rather are dependent on modalities delivered by a therapist. Generally passive interventions are viewed as a means to facilitate progress in an active therapy program with concomitant attainment of objective functional gains. Active interventions should be emphasized over passive interventions.

The patient should be instructed to continue both active and passive therapies at home as an extension of the treatment process in order to maintain improvement levels.

Assistive devices may be included as an adjunctive measure incorporated into the rehabilitation plan to facilitate functional gains.

C.1.f.i Therapeutic Exercises – Physical / Occupational Therapy

Recommended - strengthening exercises for treatment of hip OA.

Frequency/Dose/Duration –Total numbers of visits may be as few as two to three for patients with mild functional deficits or up to 12 to 15 with more severe deficits with documentation of ongoing objective functional improvement.

When there are ongoing functional deficits, more than 12 to 15 visits may be indicated if there is documentation of functional improvement towards specific objective functional goals (e.g., range of motion, advancing ability to perform work activities). As part of the rehabilitation plan a home exercise program should be developed and performed in conjunction with the therapy.

C.1.f.ii Walking Aid: Cane / Crutches / Walker

Recommended – for select moderate to severe acute hip or groin pain or subacute and chronic hip or groin pain.

Indications: Disabling, moderate to severe chronic hip OA where risks of increasing debility are outweighed by device use that increases mobility.

Benefits: Improve mobility, walking distance.

Indications for Discontinuation: Resolution (e.g., post-operative recovery).

Rationale: For acute injuries, crutches and canes may be helpful during the recovery and/or rehabilitative phase to increase functional status (e.g., from wheelchair to walker to cane). For chronic hip pain, crutches may paradoxically increase disability through debility. In those circumstances, institution or maintenance of advice for use of crutches or canes should be carefully considered against potential risks.

Evidence for use of Canes and Crutches

C.1.f.iii Orthotics, Shoe Insoles and Shoe Lifts

Recommended – for patients with significant leg discrepancy and hip pain felt to be a consequence of that discrepancy.

Indications: Significant leg length discrepancy (usually at least 2cm), with hip pain or another adverse health attribute thought to be related to the discrepant length.

Indications for Discontinuation: Lack of efficacy.

Rationale: They are recommended for select patients with significant leg length discrepancies felt to be producing or contributing to symptoms.

Evidence: for Orthotics, Shoe Insoles and Shoe Lifts

C.1.f.iv Magnets and Magnetic Stimulation

Not Recommended -for treatment of osteoarthrosis or acute, subacute or chronic hip pain.

C.1.f.v Manipulation or Mobilization

Not Recommended for treatment of hip osteoarthrosis.

Evidence for the Use of Manipulation or Mobilization

C.1.f.vi Massage

Not Recommended – for treatment of hip osteoarthrosis.

Evidence for the use of Massage

C.1.f.vii Reflexology

Not Recommended - for treatment of hip osteoarthrosis or acute, subacute or chronic hip pain.

Evidence for the Use of Reflexology

C.1.f.viii Electrical Therapies

Not Recommended - for the treatment of hip osteoarthrosis or acute, subacute or chronic hip pain.

Evidence for the Use of Electrical Stimulation Therapies

Not Recommended - for hip osteoarthrosis or acute, subacute or chronic hip pain.

Evidence for the Use of Transcutaneous Electrical Stimulation (TENS)

C.1.f.ix Acupuncture

Recommended -- for select patients in the treatment of chronic osteoarthrosis of the hip as an adjunct to more efficacious treatments.
Indications: Moderate to severe chronic osteoarthrosis of the hip. Prior treatments should include NSAIDs, weight loss, and exercise including a graded walking program and strengthening exercises.

Frequency/Dose/Duration: A limited course of six appointments with a clear objective and functional goals to be achieved. Additional appointments would require documented functional benefits, lack of plateau in measures and probability of obtaining further benefits. Additional sets of six appointments should only occur based on documented incremental functional gain.

Indications for Discontinuation:
Resolution, intolerance, non-compliance including non-compliance with aerobic and strengthening exercises.

Evidence for the Use of Acupuncture

C.1.f.x Pre-Operative Exercise

Recommended – for patients who exhibit evidence of weakness or unsteady gait. Flexibility components may be reasonable in those without fixed deficits.

Indications: All arthroplasty patients may benefit, but particularly those with weakness or unsteady gait. Also particularly helpful for those needing supervised encouragement.
Benefits: Improved speed of post-operative recovery. Potential for improved long-term results.

Frequency/Dose/Duration: One pre-operative course. Two or three follow-up appointments for adherence and additional exercise instruction may be needed for select patients. Patients with severe deficits may require two to three appointments a week for four to six weeks in advance of arthroplasty. Those with minimal deficits may benefit from a single appointment to teach programmatic elements for a self-directed program.

Indications for Discontinuation: Achievement of program goals, resolution of strength or gait deficits, intolerance or non-compliance.

Evidence for the Use of Pre- and Post-Operative Rehabilitation Programs

C.1.f.xi Post-Operative Exercise and/or Rehabilitation Program

Recommended – for hip arthroplasty surgery patients.

Frequency/Dose/Duration: Duration based primarily on progress. Two or three times weekly in outpatient settings gradually tapered as home exercises are instituted and the patient's recovery advances. Courses of up to three months in more severe cases may be required.

Indications for Discontinuation: Attainment of goals, achievement of plateau, non-compliance.

Evidence for the Use of Post-Operative Exercise and/or Rehabilitation Programs

C.1.f.xii Late Post Operative Exercise Program After Arthroplasty or Hip Fracture

Recommended - for patients who exhibit significant evidence of weakness or unsteady gait.

Indications: Ongoing significant deficits in function, gait, strength, and activity level beyond 3 months post-operatively.

Indications for Discontinuation: Lack of progressive functional gain.

Evidence for the Use of Late Post-Operative Exercises

C.1.g Injection Therapy

C.1.g.i Intraarticular Glucocorticosteroid Injections

Recommended - for the treatment of hip osteoarthrosis.

Indications: Hip OA pain where control with NSAID(s), acetaminophen, weight loss and exercise is unsatisfactory.

Frequency/Dose/Duration: An injection should be adminstered and the results evaluated.

Indications for Discontinuation: Generally one injection is performed. A second injection may be considered if there is improvement (increased function and decreased pain) that is incomplete.

Evidence for the Use of Intraarticular Glucocorticosteroid Injections

C.1.g.ii Intraarticular Hip Viscosupplementation Injections

Not Recommended - for the treatment of hip osteoarthrosis.

Evidence for the Use of Intraarticular Hip Viscosupplementation Injections

C.1.g.iii Intraarticular Platelet-Rich Plasma Injections

Not Recommended - for the treatment of hip osteoarthrosis.

Evidence for the Use of Platelet-Rich Plasma

C.1.g.iv Prolotherapy Injections

Not Recommended - for treatment of acute, subacute or chronic hip pain.

Evidence for the use of Prolotherapy

C.1.g.v Botulinum Injections

Not Recommended - for hip osteoarthrosis or other hip disorders.

Evidence for the use of Botulinum Injections

C.1.g.vi Glucosamine Sulfate Intra-Muscular Injections

Not Recommended - for the treatment of hip osteoarthrosis.

Evidence for the use of glucosamine sulfate intra-muscular injections

C.1.g.vii Glucosamine Sulfate Intra-Articular Injections

Not Recommended - for the treatment of hip osteoarthrosis.

Evidence for use of glucosamine sulfate intra-articular injections

C.1.h Surgery

C.1.h.i Hip Arthroplasty

Recommended - for severe arthritides, osteonecrosis with collapse or insufficient response to non-operative treatment, or substantially symptomatic hip dysplasia.

Evidence for the Use of Hip Arthroplasty

C.1.h.ii Osteotomy

Recommended - for the treatment of hip osteoarthrosis in select patients.

Indications: Indications include significant alignment abnormalities, dysplasia, osteonecrosis, nonunion of femoral neck fracture, slipped capital femoral epiphyses, and cox vara. Generally performed on younger patients in preference to arthroplasty.

Rationale: For selective patients in the absence of other proven treatment for many of these advanced conditions.

Evidence for the Use of Osteotomy

C.1.h.iii Post Operative Exercise and Rehabilitation Program

Recommended - for hip arthroplasty surgery patients.

C.1.h.iv Post Operative Assistive Devices- Walking aid, ADL Adaptive equipment (e.g. long-handled reacher or shoe horn or sock aid, elevated toilet seat).

Recommended - as needed post-operatively.

C.1.h.v Treatment of Infected Prosthesis

Recommended - an infected prosthesis is a serious outcome that usually requires surgical debridement, drainage and appropriate antibiotics. Treatment frequently necessitates prolonged IV antibiotics and may require removal of implanted hardware.

C.1.h.vi Treatment of Dislocations

Recommended – referral back to the treating surgeon, as appropriate, to reduce dislocation and incidence of recurrence.

C.2 Hip Osteonecrosis

C.2.a Related Terms

- Osteonecrosis
- Avascular Necrosis (AVN)
- Aseptic Necrosis
- Ischemic Bone Necrosis
- Ischemic Bone Death

C.2.b Introduction

Osteonecrosis (aka, avascular necrosis) involves bone death.

Some cases are considered occupational disorders, particularly in the setting of dysbarism (atmospheric compression/decompression) workers including divers and other workers in compressed air atmospheres who experience impaired blood supply to the femur due to nitrogen gas in the blood during excessively rapid decompression. Major trauma is another reported cause.

Significant, discrete trauma is thought to be a risk factor. However, nontraumatic job physical factors are controversial. Treatment is primarily based on alleviating the exposure(s) thought to be responsible. A surgical "coring" procdedure, vascularized and unvascularized bone grafting, and osteotomy are sometimes utilized. Severe cases may require arthroplasty.

C.2.c Diagnostic Studies

Initial Assessment

The history, physical, and radiographs effectively diagnose most hip disorders. Review of systems and examinations also should involve the knee, spine, abdomen, and genitourinary tract. Osteonecrosis is most commonly diagnosed on imaging studies. If the diagnosis of hip pain remains unclear after radiographs, magnetic resonance imaging (MRI with or without gadolinium etc.) is generally the imaging of choice.

The criteria presented below is an overview of the clinical thought process for evaluation of hip osteonecrosis.

Diagnostic Criteria for Non-Red-Flag Conditions

Probable Diagnosis or Injury	Symptoms	Signs	Tests and Results
Osteonecrosis	Non-radiating hip pain. History of systemic factors (e.g., diabetes mellitus, alcohol)	Reduced ROM and pain with passive ROM usually present. May have pain with weight bearing. May be unable to bear weight if osseous collapse has occurred.	Radiographs required. MRI and CT may be ordered for further evaluation of the femoral head.

C.2.c.i Bone Scanning with SPECT

Recommended – for select use in patients with acute, subacute, or chronic pain to assist in the diagnosis of osteonecrosis and other conditions with increased polyosthotic bone metabolism, particulary when more than one joint needs evaluation.

Indication / Rationale: Bone scanning is helpful to identify areas of increased bone metabolism; thus its primary use is for osteonecrosis cases.

Frequency/Dose/Duration: One evaluation.

Evidence for the Use of Bone Scans

C.2.c.ii CT for Evaluating Osteonecrosis

Recommended - for evaluating patients with osteonecrosis, including patients who need advanced imaging, but have contraindications for MRI or where helical CT is unavailable.

Indications: Hip pain thought to be from osteonecrosis, but with contraindications for MRI.

Frequency/Dose/Duration: Generally, one evaluation. A second may be needed if there is a significant clinical change or to evaluate progress/resolution.

Rationale: Computerized tomography is considered superior to MRI for imaging of most hip abnormalities where advanced imaging of calcified structures is required. For osteonecrosis, there is no clear preference of CT over MRI. However, helical CT is generally thought to be preferable to CT for identification of fracturing and thus use of CT is limited, including those settings without helical CT.

Evidence for the Use of Computerized Tomography (CT) Scan

C.2.c.iii Helical CT for Evaluating Osteonecrosis

Recommended – for evaluating patients with osteonecrosis who have contraindications for MRI.

Indications: Hip pain thought to be from osteonecrosis, especially with concerns about fracturing and collapse. Also indicated for those needing evaluation of osteonecrosis but with contraindications for MRI.

Frequency/Dose/Duration: Generally, one evaluation. A second may be needed if there is a significant clinical change or for evaluating progress/resolution.

Rationale: Helical CT is considered superior to MRI for imaging of most hip abnormalities where advanced imaging of calcified structures is required. For osteonecrosis, there is no clear preference of CT over MRI. Helical CT is thought to be better than CT at identifying fracturing and is therefore recommended for select use.

Evidence for use of Helical CT

C.2.c.iv MRI for Diagnosing Osteonecrosis

Recommended – for subacute or chronic hip pain thought to be due to osteonecrosis particularly when the diagnosis is unclear or if additional diagnostic evaluation and/or staging is needed.

Frequency/Dose/Duration: Generally one evaluation. A second may be needed if there is a significant clinical change or need to evaluate progress/resolution.

Rationale: Helical computerized tomography is considered superior to MRI for imaging bone collapse. MRI is considered superior for imaging bone marrow edema, which is inversely correlated with prognosis. Thus, both tests have their advantages.

Evidence for the Use of Magnetic Resonance Imaging (MRI)

C.2.c.v X-Rays for Diagnosing Osteonecrosis

Recommended – for all patients thought to have osteonocrosis.

Frequency/Dose/Duration: Periodically obtaining x-rays to follow the course of the disease is customary.

Rationale: X-rays are helpful to evaluate most patients with hip pain, both to diagnose and to assist with the differential diagnostic possibilities. Early stage osteonecrosis x-rays may be normal or show slight osteopenia. A high index of suspicion is necessary.

Evidence for the Use of X-rays/Radiographs

C.2.c.vi Ultrasound for Osteonecrosis

Not Recommended – for diagnosing osteonecrosis.

C.2.d Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.2.d.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs) for Treatment of Acute, Subacute, or Chronic Osteonecrosis

Recommended - for treatment of acute, subacute, or chronic osteonecrosis *Indications* – For acute, subacute, or chronic osteonecrosis, NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration: As needed use may be reasonable for many patients.

Indications for Discontinuation: Resolution of osteonecrosis, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.2.d.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended – for concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

*Indication*s: For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration: Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation: Intolerance, development of adverse effects, or discontinuation of NSAID.

C.2.d.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin.

C.2.d.iv Aetaminophen for Treatment of Osteonecrosis Pain

Recommended - for treatment of osteonecrosis pain, particularly in patients with contraindications for NSAIDs.

Indications: All patients with osteonecrosis pain, including acute, subacute, chronic, and post-operative.

Dose/Frequency: Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation: Resolution of pain, adverse effects or intolerance.

C.2.d.v Opioids

Recommended – for limited use (maximum of seven days) as adjunctive therapy for NSAIDs.

Indications – For pain management, a brief prescription of opioids as adjuncts to more efficacious treatments (especially NSAIDs, acetaminophen) is often required, especially nocturnally.

Frequency/Duration - Prescribed as needed throughout the day, then later only at night, before weaning off completely.

Rationale for Recommendation – some patients have insufficient pain relief with NSAIDs, thus judicious use of opioids may be helpful, particularly for nocturnal use. Opioids are recommended for brief, select use, primarily used at night to achieve sleep.

C.2.d.vi Bisphosphonates

Not Recommended – for treatment of osteonecrosis.

C.2.d.vii Anti-Convulsant Agents (including Topriamate)

Not Recommended for treatment of pain associated with osteonecrosis.

C.2.d.viii Gabapentin and Pregabalin

Not Recommended for pain associated with osteonecrosis.

Evidence for use of gabapentin and pregabalin for osteonecrosis

C.2.d.ix Glucocorticosteroids

Not Recommended – for the treatment of osteonecrosis.

Evidence for use of glococorticosteroids for treatment of osteonecrosis

C.2.e Treatments

The early treatment focus for mild to moderate cases of osteonecrosis is to identify and treat reversible risk factors. Reduction or elimination of activities that significantly provoke symptoms including avoidance of dysbaric exposures is recommended. Moderately severe or severe cases generally receive prompt surgical treatment, especially if collapse has occurred.

C.2.e.i Initial Care

Assessing disease severity is the first step for osteonecrosis evaluation. Elimination of decompression atmospheres is a prominent early intervention. Nonprescription analgesics may provide sufficient pain relief for most patients with hip pain from osteonecrosis. If either the condition is progressing and/or disease severity is more advanced, surgical intervention is indicated.

The primary activity of concern for acute and subacute cases of osteonecrosis is de/compression. Patients with osteonecrosis should not generally undergo any de/compression atmospheres until the condition is resolved. High force and/or high impact force (e.g., jumping) should generally be precluded in patients presenting with osteonecrosis (especially those with more severe disease at risk of collapse) until the condition is either substantially improved or resolved. Regardless of phase of the osteonecrosis (acute, subacute, chronic), adherence to decompression tables is highly advisable.

C.2.e.ii Surgery

C.2.e.ii.a Core Decompression Surgery

Recommended – for the treatment of osteonecrosis.

Indications: Patients with generally moderate to severe osteonecrosis either (i) not responding to risk factor modification and/or (ii) felt to be at risk of collapse and further delay while treating risk factors or with hyperbaric oxygen is felt to be too risky.

Evidence for the Use of Core Decompression

C.2.e.ii.b Arthroplasty for Osteonecrosis

Recommended – for the treatment of osteonecrosis with collapse or severe disease unresponsive to non-operative treatment.

Indications: Patients with collapse of the femoral head are immediate candidates for arthroplasty. Additional candidates include those with severe osteonecrosis who are: (i) unresponsive to risk factor modification, and/or (ii) felt to be at risk of immediate collapse.

Rationale: Once the head of the femur collapses, the treatment is usually arthroplasty.

Evidence for the Use of Arthroplasty Surgery

C.2.f Other Treatments

C.2.f.i Dysbaric Exposures or Other Symptom-Providing Activities or Other Risk Factors

Recommended – reduction or elimination of activities that are significant risks for osteonecrosis, including avoidance of dysbaric exposures.

C.2.f.ii Non-Weight Bearing Activities

Not Recommended – for patients with osteonecrosis.

C.2.f.iii Hyperbaric Oxygen

Recommended – for treatment of osteonecrosis.

Indications: Osteonecrosis Ficat Stage 2. It may be reasonable to attempt HBO in patients with more severe osteonecrosis.

Frequency/Dose/Duration: Up to 30 treatments.

Indications for Discontinuation: Completion of course, intolerance, clinical resolution, osteonecrosis collapse.

Evidence for the Use of Hyperbaric Oxygen

C.3 Hip Fractures

C.3.a Overview

Hip fractures include both frank and stress fractures. Occupational fractures most commonly result from falls or motor vehicle accidents. Stress fractures most typically involve repeated applications of unaccustomed force over a relatively short interval of hours to days. These are usually treated with elimination of the offending exposure and observation. Physical therapy to address movement system impairments, such as muscle performance and motor patterns, may assist in reducing forces on the affected site.

C.3.b Related Terms

- Fracture
- Stress Fracture
- Hip Fracture
- Femoral Fracture
- Femoral Neck Fracture
- Intracapsular Fracture
- Intertrochanteric Fracture
- Subtrochanteric Fracture
- Acetabular Fracture

C.3.c Initial Assessment

The initial evaluation of a patient with potential occupational hip fracture is generally straightforward as the history, mechanism of injury and inability to use the hip provide strong diagnostic evidence. Review of systems that also involve the knee, spine, abdomen, and genitourinary tract is necessary.

C.3.d Diagnostic Criteria

The criteria presented below is an overview of the clinical thought process for evaluation of typical occupational hip fractures.

Diagnostic Criteria for Non-red-flag Conditions

Hip Fracture	Fall or motor vehicle accident. Severe pain. Unable to bear weight.	Unable to bear weight. Lower extremity shortened and externally rotated.	X-rays required. Bone scan or CT scan may be indicated after plain film if there is a high index of suspicion of fracture

C.3.e Diagnostic Studies

C.3.e.i Bone Scan

Recommended – for use in select patient with acute, subacute or chronic hip pain to assist in the diagnosis of fractures.

Indications: Patients with hip fractures also with suspicion of osteonecrosis, Paget's disease, neoplasm, or other increased polyosthotic bone metabolism.

Frequency/Dose/Duration: One scan. Rarely, a second scan may be indicated after passage of at least three months and a clinically meaningful change in symptoms and signs that beget a material change in the diagnosis.

Rationale: Bone scanning may be a helpful diagnostic test to evaluate trauma (e.g., occult fractures). Bone scanning is generally not indicated for evaluation of hip OA. In patients where the diagnosis is felt to be secure, there is not an indication for bone scanning as it does not alter treatment or management.

Evidence for the use of Bone Scans

C.3.e.ii Computerized Tomography (CT)

Recommended - for evaluating hip fracture patients with concerns for osteonecrosis or following traumatic dislocations or arthroplasty-associated recurrent dislocations. CT is also recommended for patients who need advanced imaging but have contraindications for MRI.

Indications: Hip fracture patients with pain from osteonecrosis with suspicion of subchondral fracture(s), increased polyosthotic bone metabolism, or traumatic hip dislocations, particularly when acetabular or femoral head fracture fragments are sought; arthroplasty-associated recurrent hip dislocations to evaluate the rotational alignment (anteversion) of the

acetabular and femoral components; patients with contraindications for MRI.

Frequency/Dose/Duration: One evaluation. A second evaluation is rarely needed.

Rationale: Computerized tomography is considered superior to MRI for imaging of most hip abnormalities where advanced imaging of calcified structures is required.

Evidence for the use of Computerized Tomography (CT)

C.3.e.iii Helical CT Scan

Recommended – for select patients for evaluating hip fractures thought to potentially have osteonecrosis or have need for advanced bone imaging, but who have contraindications for MRI (implanted hardware).

Indications: Patients with hip fracture who are thought to have osteonecrosis, or have need of advanced bone imaging, but who have contraindications for MRI. Helical CT is generally helpful for vascular concerns, reduces motion artifact and speeds scanning time.

Frequency/Dose/Duration: One evaluation. A second evaluation is rarely needed.

Rationale: Helical CT scanning has been largely replaced by MRI. However, it has been thought to be superior to MRI for evaluating subchondral fractures. In addition, there are patients who have contraindications for MRI (e.g., implanted ferrous metal hardware), and in those patients who require evaluation of AVN, helical CT is recommended.

Evidence for the use of Helical CT for Evaluating Hip Fracture with suspected Osteonecrosis

C.3.e.iv Magnetic Resonance Imaging (MRI)

Recommended - for select hip fracture patients who also have subacute or chronic hip pain with consideration of accompanying soft tissue pathology or other diagnostic concerns.

Indications: Patients with subacute or chronic hip pain who need imaging surrounding soft tissues, including evaluating periarticular structures or masses (generally not indicated for acute hip pain as radiographs usually suffice).

Frequency/Dose/Duration: Generally, only one examination should be required. A second evaluation is rarely needed.

Rationale: MRI has been suggested for evaluations of patients with symptoms over 3 months.

Evidence for the Use of Magnetic Resonance Imaging (MRI)

C.3.e.v Radiographs

Recommended – for evaluating hip fractures.

Indications: All patients with potential hip fractures. Also in the absence of red flags with moderate to severe hip pain lasting at least a few weeks, and/or limited range of motion.

Frequency/Dose/Duration: Obtaining x-rays once is generally sufficient. For patients with chronic or progressive hip pain, it may be reasonable to obtain a second set of x-rays, particularly if symptoms change.

Evidence for the Use of Radiography (X-ray) for evaluating hip fractures

C.3.e.vi Ultrasound

Not Recommended – for evaluating hip fracture patients.

Evidence for the Use of Ultrasound (US) for evaluating hip fracture patients

C.3.f Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.3.f.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of pain associated with hip fracture.

Indications: For treatment of pain associated with hip fractures, NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration: As needed use may be reasonable for many patients.

Indications for Discontinuation - Resolution of pain, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.3.f.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended - concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk for gastrointestinal bleeding.

*Indication*s – For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration – Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation – Intolerance, development of adverse effects, or discontinuation of NSAID.

C.3.f.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease

prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin.

C.3.f.iv Acetaminophen for Treatment of Hip Pain

Recommended - for treatment of pain associated with hip fracture, particularly in patients with contraindications for NSAIDs.

Indications: All patients with hip fracture pain, including acute, subacute, chronic, and post-operative.

Dose/Frequency: Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation: Resolution of pain, adverse effects or intolerance.

C.3.f.v Bisphosphonates

Recommended – for select patients with osteopenia-related hip fractures.

Indications: Patients with hip fractures thought to be due to osteoporosis or osteopenia to prevent additional fractures.

Benefits: Increased bone mineral density. Reduced risk of secondary fractures.

Frequency/Dose/Duration: As per manufacturer recommendations.

Evidence for the Use of Bisphosphonates

C.3.f.vi Calcitonin

Not Recommended – for hip fracture patients.

Evidence for the Use of Calcitonin

C.3.f.vii Opioids

Recommended - for treatment of select patients with post-operative hip fractures.

Indications – For post-operative hip fractures, a brief course of a few days to not more than one week of an opioid is recommended for treatment. Opioids may be helpful for brief nocturnal use after surgery. For other hip fracture patients, opioids are not recommended. Most patients should attempt pain control with NSAIDs/acetaminophen prior to opioids. Discontinuation of opioids as early as possible is recommended.

Frequency/Dose/Duration – Generally, patients require no more than a few days to not more than one week of treatment with opioids for most hip surgeries.

Indications for Discontinuation – Resolution of hip fracture pain, sufficient control with other medications, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.3.g Treatments

C.3.g.i Hot and Cold Therapies

C.3.g.i.a Cryotherapy for Acute, Subacute, Chronic, or Post-operative Hip Pain

Recommended - for acute, subacute, chronic, or post-operative hip pain.

Indications – All patients with hip pain.

Frequency/Duration – Approximately three to five self-applications per day as needed.

Indications for Discontinuation – Resolution, adverse effects, non-compliance.

C.3.g.i.b Heat Therapy for Acute, Subacute, Chronic, or Post-operative Hip Pain

Recommended - for acute, subacute, chronic, or post-operative hip pain**.**

Indications – All patients with hip pain.

Frequency/Duration – Approximately three to five self-applications per day as needed.

Indications for Discontinuation – Resolution, adverse effects, non-compliance.

C.3.g.ii Surgery

C.3.g.ii.a Surgical Intervention for Hip Fracture

Recommended – as soon as the patient is medically stable.

Indications: Hip fractures.

Rationale: There are many different surgical approaches and products used for fixation. The type of surgical treatment (e.g., pin, screw, nail) or non-operative management is deferred to the treating surgeon.

Evidence for the Use of Surgical Treatment for Hip Fractures

C.3.g.ii.b Arthroplasty for Hip Fractures

Recommended – especially for patients with displaced femoral neck and subcapital fractures.

Evidence for the Use of Total Hip Arthroplasty

C.3.g.ii.c Hemiarthroplasty

Recommended – for patients with displaced femoral neck and subcapital fractures.

Indications: Hip fractures, especially displaced femoral neck and subcapital fractures.

Evidence for the Use of Hemiarthroplasty

C.3.g.ii.d Systemic Antibiotics

Recommended – for patients undergoing hip surgery; typically one day use.

Evidence for the Use of Antibiotics for Hip Surgery

Recommended – for patient undergoing hip surgery, especially with prothesis.

Indications: Systemic prophylatic antibiotics are considered mandatory and have been long utilized.

Benefits: Reduced risk of joint or prosthetic infection.

Evidence for the Use of Antibiotics

Recommended – for wound infection management (post operative complications).

Indications: For management of post operative complications and for recurrent infections.

C.3.g.ii.e Treatment of Infected Prosthesis

Recommended - an infected prosthesis is a serious outcome that usually requires surgical debridement, drainage and appropriate antibiotics. Treatment frequently necessitates prolonged IV antibiotics and may require removal of implanted hardware.

C.3.g.ii.f Treatment of Dislocations

Recommended – referral back to the treating surgeon, as appropriate, to reduce dislocation and incidence of recurrence.

C.3.h Other

C.3.h.i Acupuncture

Recommended – after hip arthroplasty procedures.

Indications: Hip arthroplasty patients.

Frequency/Dose/Duration: Up to three post-operative days.

Rationale: Two quality trials demonstrated efficacy of acupuncture *for hip arthroplasty patients, including reducing opioid needs.*

Evidence for the Use of Acupuncture for Hip Arthroplasty

C.4 Prevention of Venous Thromboembolic Disease

C.4.a Introduction

Venous thromboembolic disease (VTED) is a high-risk complication among post-operative hip or knee arthroplasty patients resulting in morbidity and mortality.

C.4.b Medications

C.4.b.i Low-Molecular Weight Heparin

Recommended – for prevention of venous thromboembolic disease.

Indications: Post-operative arthroplasty patients, hip fracture patients and other major hip surgery patients, particularly those with either prolonged inactivity or prolonged reduced or sedentary activity levels. Patients with prior reactions to LMWH should generally receive other treatments first.

Frequency/Dose/Duration: There is no consensus on duration of treatment, and individualization based on activity level appears indicated.

Indications for Discontinuation: Development of major complication (e.g., major bleeding) or other adverse effect.

Rationale: Generally, major bleeding is the most significant adverse effect of most of the medications used to prevent VTED.

Evidence for the Use of Low-Molecular Weight Heparin

C.4.b.ii Factor Xa Inhibitors

Recommended – for the prevention of venous thromboembolic disease.

Indications: Post-operative arthroplasty patients, hip fracture patients, or other major hip surgery patients, particularly those with prolonged inactivity or prolonged reduced or sedentary activity levels. Patients with prior reactions should generally receive other treatments first. Patients with renal failure or renal insufficiency should generally receive a different medication due to renal excretion of this compound.

Evidence for the Use of Factor Xa Inhibitors

C.4.b.iii Warfarin and Heparin

Recommended – for prevention of venous thromboembolic disease.

Indications: Post-operative arthroplasty patients, hip fracture patients and other major hip surgery patients.

Harms: Increased risk of bleeding. Risk of intracranial and gastrointestinal bleeds of particular concern, however, somewhat less concerning than some other treatment options as the treatment is more readily reversible than with low molecular weight heparins or Factor Xa inhibitors.

Frequency/Dose/Duration: Subcutaneous injections of Heparin, which can be titrated to the activated partial thromboplastin time (aPTT). Warfarin dose titrated to International Normalized Ratio (INR).

Evidence for the Use of Warfarin and Heparin

C.4.b.iv Aspirin

Recommended – for the prevention of deep venous thrombosis.

Indications: Post-operative arthroplasty patients, hip fracture patients and other major hip surgery patients, generally after cessation of other treatments such as LMWH, heparin, or other anticoagulants.

Evidence for the Use of Aspirin

C.4.c Treatments

C.4.c.i Devices

C.4.c.i.a Compression Stockings

Recommended – for prevention of Venous Thromboembolic Disease.

Indications: All post-operative hip surgery patients (e.g., hip fractures, hip arthroplasties, or any other patients thought at increased risk of VTED in the post-operative period).

Indications for Discontinuation: One-month post-operative and/or resumption of all normal activities and activity levels. Use beyond four weeks is indicated for those who have not resumed normal activities.

Evidence for the Use of Compression Stockings

C.4.c.i.b Lower Extremity Pumps

Recommended – for prevention of venous thromboembolic disease.

Indications: Post-operative major hip surgical patients (e.g., hip fractures, hip arthroplasties, or any other patients thought at increased risk of VTED in the post-operative period).

Frequency/Dose/Duration: Devices include foot pumps, foot plus calf pumps, entire lower extremity intermittent compression devices and various other combinations.

Indications for Discontinuation: Discontinuation is generally recommended by 14 days unless there are continuing ongoing issues, such as delayed rehabilitation and ambulation, that result in a judgment of increased risk.

Evidence for the Use of Lower Extremity Pumps

C.5 Pre- and Post-Operative Rehabilitation, Including Hip Arthroplasty and Hip Fractures

C.5.a Introduction

Although there is probably overlap with characteristics and needs of arthroplasty patients, mobilization and exercises after hip fracture may differ somewhat and are considered separately below.

C.5.b Treatments

Therapy

Rehabilitation (supervised formal therapy) required as a result of a work-related injury should be focused on restoring functional ability required to

meet the patient's daily and work activities and return to work; striving to restore the injured worker to pre-injury status in so far as is feasible.

Active therapy requires an internal effort by the patient to complete a specific exercise or task. Passive therapy are those interventions not requiring the exertion of effort on the part of the patient, but rather are dependent on modalities delivered by a therapist. Generally passive interventions are viewed as a means to facilitate progress in an active therapy program with concomitant attainment of objective functional gains. Active interventions should be emphasized over passive interventions.

The patient should be instructed to continue both active and passive therapies at home as an extension of the treatment process in order to maintain improvement levels.

Assistive devices may be included as an adjunctive measure incorporated into the rehabilitation plan to facilitate functional gains.

C.5.b.i Post-Operative Exercise and Rehabiliation Program

Recommended – for hip fracture patients.

Indications: All hip fracture patients. Programs need to be individualized, based on factors such as preoperative condition, bone quality, immediate surgical results, contraindications, and other medical conditions.

Frequency/Dose/Duration –Total numbers of visits may be as few as two to three for patients with mild functional deficits or up to 12 to 15 with more severe deficits with documentation of ongoing objective functional improvement.

When there are ongoing functional deficits, more than 12 to 15 visits may be indicated if there is documentation of functional improvement towards specific objective functional goals (e.g., range of motion, advancing ability to perform work activities). As part of the rehabilitation plan a home exercise program should be developed and performed in conjunction with the therapy.

Evidence for the Use of Post-Operative Exercise and Rehabilitation

C.6 Femoracetabular Impingement, "Hip Impingement" or Labral Tears

C.6.a Introduction

The criteria presented below is an overview of the clinical thought process for evaluation of femoroacetabular impingement or labral tears.

Diagnostic Criteria for Non-Red Flag Conditions

Labral Tears	Nonradiating groin pain with ROM. Typically provoked with specific, predictable activities, such as specific position(s). May have buckling, clicking, catching. Pain may be worse with pivoting and walking.	Variable findings; pain reproducible on ROM. Extent of ROM often restricted. Pain reproduced with hip into extension from flexion. Pain with hyperflexion, internal rotation, and adduction (impingement position) is present in most cases. Pain and/or click may also be reproduced with the labral stress test and/or with resisted straight leg raise.	Radiographs are often ordered. MRI is sometimes ordered, and MR arthrography is often helpful.
Femoroacetabular Impingement	Nonradiating groin pain. Pain is often positional and worse with activity. Pain with hip flexion and internal rotation.	Decreased internal rotation and adduction with hip flexed to 90 degrees. Positive impingement test (pain with passive adduction and gradually internally rotating the flexed hip).	Radiographs usually ordered. MRI and MR arthrography helpful.

C.6.b Diagnostic Studies

C.6.b.i MR Arthrogram

Recommended – for diagnosing femoracetabular impingement or labral tears in patients with subacute or chronic hip pain.

Indications: Patients with subacute or chronic hip pain and symptoms or clinical suspicion of femoroacetabular impingement, labral tears, or other hip joint concerns.

Frequency/Dose/Duration: Generally one arthrogram is needed.

Rationale: MRA is helpful in evaluating and confirming femoroacetabular impingement or labral tears. Enhanced MR

arthrogram allows better labral evaluation and is recommended for diagnosing femoroacetabular impingement compared to other imaging procedures.

Evidence for MR Arthrogram to diagnose femoroacetabular impingement

C.6.b.ii MRI

Recommended – in select patients with subacute or chronic lateral hip pain when there is diagnostic uncertainty as to the etiology and to assist in making an accurate diagnosis.

C.6.b.iii Ultrasound

Recommended – for evaluating patients with femoroacetabular impingement or labral tears.

Indications: Patients with hip pain thought to be from impingement or labral tears. Generally arthrogram and MRI is/are the preferred diagnostic tests, yet selective use of ultrasound may be helpful.

Frequency/Dose/Duration: Generally only once.

Rationale: Ultrasound may be helpful in evaluating and confirming femoroacetabular impingement or labral tears and is thus recommended.

C.6.c Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.6.c.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of labral tears and femoroacetabular impingement.

Indications – labral tears and femoroacetabular impingement, NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration – As needed use may be reasonable for many patients.

Indications for Discontinuation – Resolution of labral tears and femoroacetabular impingement, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.6.c.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended – concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

*Indication*s – For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration - Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation – Intolerance, development of adverse effects, or discontinuation of NSAID.

C.6.c.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease

prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or ejight hours before the daily aspirin.

C.6.c.iv Acetaminophen for Treatment of Femoroacetabular Impingement or Labral Tears

Recommended - for treatment of labral tears and femoroacetabular impingement, particularly in patients with contraindications for NSAIDs.

Indications – All patients with femoroacetabular impingement painor labral tears, including acute, subacute, chronic, and post-operative.

Dose/Frequency – Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation – Resolution of pain, adverse effects or intolerance.

Rationale for Recommendations - For most patients, generic ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Second-line medications should include one of the other generic medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative for these patients, although most evidence suggests acetaminophen is modestly less effective for arthrosis patients. There is evidence that NSAIDs are as effective for relief of pain as opioids (and tramadol) and less impairing.

C.6.c.v Opioids

Opioids are rarely used for treatment of patients with femoroacetabular impingement or labral tears.

Recommended - for short term (less than one week) for patients with femoroacetabular impingement or labral tears.

Rationale for Recommendations - Opioids cause significant adverse effects – poor tolerance, constipation, drowsiness, clouded judgment, memory loss, and potential misuse or dependence have been reported in up to 35% of patients. Before prescribing opioids, patients should be informed of these potential adverse effects and cautioned against operating motor vehicles or machinery. Opioids do not appear to be more effective than safer analgesics for managing most

musculoskeletal symptoms; they should only be used if needed for severe pain.

Recommended - for select treatment of patients with post-operative femoroacetabular impingement or labral tears.

Indications – For post-operative femoroacetabular impingement or labral tears, a brief course of a few days to not more than one week of an opioid is recommended for treatment. Opioids may be helpful for brief nocturnal use after surgery. Most patients should attempt pain control with NSAIDs/acetaminophen prior to opioids. Discontinuation of opioids as early as possible is recommended.

Frequency/Dose/Duration – Generally, patients require no more than a few days to not more than one week.

Indications for Discontinuation – Resolution of pain, sufficient control with other medications, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.6.d Treatments

C.6.d.i Rehabilitation Programs

Rehabilitation (supervised formal therapy) required as a result of a work-related injury should be focused on restoring functional ability required to meet the patient's daily and work activities and return to work; striving to restore the injured worker to pre-injury status in so far as is feasible.

Active therapy requires an internal effort by the patient to complete a specific exercise or task. Passive therapy are those interventions not requiring the exertion of effort on the part of the patient, but rather are dependent on modalities delivered by a therapist. Generally passive interventions are viewed as a means to facilitate progress in an active therapy program with concomitant attainment of objective functional gains. Active interventions should be emphasized over passive interventions.

The patient should be instructed to continue both active and passive therapies at home as an extension of the treatment process in order to maintain improvement levels.

Assistive devices may be included as an adjunctive measure incorporated into the rehabilitation plan to facilitate functional gains.

C.6.d.i.a Therapeutic Exercise - Physical or Occupational Therapy

Recommended – for femoroacetabular impingement or labral tears, particularly post-operatively and to address any strength deficits.

Frequency/Dose/Duration –Total numbers of visits may be as few as two to three for patients with mild functional deficits or up to 12 to 15 with more severe deficits with documentation of ongoing objective functional improvement.

When there are ongoing functional deficits, more than 12 to 15 visits may be indicated if there is documentation of functional improvement towards specific objective functional goals (e.g., range of motion, advancing ability to perform work activities). As part of the rehabilitation plan a home exercise program should be developed and performed in conjunction with the therapy.

Indications for Discontinuation – Improved function and reduced pain, post-operative healing, intolerance, lack of efficacy or non-compliance.

C.6.d.ii Injection Therapy

C.6.d.ii.a Local Glucocorticosteroid Injections

Recommended – for treatment of hip impingement or labral tears in select patients.

Indications: Hip impingement or labral tears generally not resolving over a period of a few weeks of treatment with activity modification and NSAIDs.

Frequency/Dose/Duration: Generally one injection is performed. A second injection may be considered if there is improvement (increased function and decreased pain) that is incomplete.

Evidence for use of local glucocorticosteroid injections for hip impingement

C.6.d.iii Surgery

C.6.d.iii.a Arthroscopy

Recommended – to diagnose and treat patients with hip pain if there is a suspicion of labral tear, intraarticular body, femoracetabular impingement, or there are other subacute or chronic mechanical symptoms for patients who failed conservative management are are thought to be best treated with arthroscopy.

Indications: Patients with hip pain with suspicion of labral tear, intraarticular body, femoroacetabular impingement, or other subacute or chronic mechanical symptoms.

Rationale: Arthroscopy of the hip is increasingly utilized to treat several hip disorders, especially ones with mechanical symptoms. Symptomatic labral tears and removal of foreign bodies have been reported as successfully treated. Femoroacetabular impingement is also a potential indication.

Evidence for Arthroscopy to diagnose and treatment patients with hip pain.

C.6.d.iii.b Surgical Repair

Recommended – for hip impingement or labral tear cases that fail conservative management and either fail arthroscopic repair and/or are throught to be best treated with an open approach.

Indications/Rationale: Patients with hip pain with suspicion of labral tear, intraarticular body, femoroacetabular impingement, or other subacute or chronic mechanical symptoms that are thought to be best treated with an open approach.

Evidence for Open surgical repair is recommended for "hip impingement" or labral tear cases

C.6.d.iv Other

C.6.d.iv.a Walking Aid: Cane / Crutches / Walker

Recommended – for select patients with moderate to severe femoroacetabular impingement or labral tears.

Indications: Disabling, moderate to severe femoroacetabular impingement or labral tears where risks of increasing debility are outweighed by device use that increases mobility.

Indications for Discontinuation: Resolution (e.g., post-operative recovery).

Rationale: For acute injuries, crutches and canes may be helpful during the recovery and/or rehabilitative phase to increase functional status (e.g., from wheelchair to walker to cane). For chronic hip pain, crutches may paradoxically increase disability through debility. In those circumstances, institution or maintenance of advice for use of crutches or canes should be carefully considered against potential risks.

Evidence for use of Canes and Crutches

C.7 Gluteus Medius Tendinosis and Tears ("Rotator Cuff of the Hip") Greater Trochanteric Pain Syndome and Trochanteric Bursitis

C.7.a Introduction

The criteria presented below is an overview of the clinical thought process for evaluation of Gluteus Medius Tendinosis and Tears ("Rotator Cuff of the Hip"), Greater Trochanteric Pain Syndrome and Trochanteric Bursistis.

Diagnostic Criteria for Non-Red-Flag Conditions

Gluteus Medius Tears	Nonradiating hip pain. May have weakness, especially with more acute tears.	Abnormal gait with inability to stabilize pelvis. Tender over greater trochanter. ROM usually reduced. Qualitative muscle strength weakness.	Radiographs usually ordered. MRA/MRI helpful.
Greater Trochanteric Pain Syndrome	Nonradiating hip pain. Pain increased when lying on the affected side or stair	Tender to palpation over the greater trochanter. Pain with hip ROM. Extent of ROM usually	Radiographs sometimes ordered. Other testing usually

	climbing. Pain worse with activity.	normal. Antalgic gait sometimes present and increased pain with stair climbing.	not required for short-term and mild cases. MRI sometimes helpful.

C.7.b Diagnostic Studies

C.7.b.i MR Arthogram

Recommended – to diagnose gluteus medius tendinosis or tears, and for greater trochanteric pain syndrome in patients with subacute or chronic hip pain.

Indications: Patients with subacute or chronic hip pain and symptoms or clinical suspicion of gluteus medius tendinosis or tears, and for greater trochanteric pain syndrome patients. It is a consideration as well in those with trochanteric bursitis, especially if it does not resolve readily.

Frequency/Dose/Duration: Generally only one arthrogram is needed.

Rationale: MR arthrograms appear helpful in evaluating and confirming gluteus medius tendinosis or tears, or greater trochanteric pain syndrome. As compared to other imaging procedures, enhanced MR arthrogram allows better labral evaluation and is recommended for diagnosing gluteus medius tendinosis or tears, or trochanteric bursitis. It is likely the best imaging procedure available for these patients and is recommended for select use.

Evidence for use of MR to diagnose gluteus medius tendinosis or tears, and for greater trochanteric pain syndrome

C.7.b.ii MRI

Recommended – in select patients with subacute or chronic lateral hip pain where there is diagnostic uncertainty as to the etiology and to assist in making an accurate diagnosis.

C.7.b.iii Ultrasound

Recommended – for evaluating patients with gluteus medius tendinopathies, greater trochanteric bursitis, and greater trochanteric pain syndrome/lateral hip pain.

Indications: Patients with hip pain thought to be from these disorders. Generally, arthrogram and MRI is/are the preferred diagnostic tests, yet selective use of ultrasound may be helpful.

Frequency/Dose/Duration: Generally only once.

Rationale: Ultrasound appears helpful in evaluating and confirming gluteus medius tendinopathies and is thus recommended.

Evidence for the Use of Diagnostic Tests for Trochanteric Bursitis or Greater Trochanteric Pain Syndrome

C.7.c Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.7.c.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain.

Indications – gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain, NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration – As needed use may be reasonable for many patients.

Indications for Discontinuation – Resolution of gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.7.c.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended – concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

Indications – For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of

prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration - Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation – Intolerance, development of adverse effects, or discontinuation of NSAID.

C.7.c.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin.

C.7.c.iv Acetaminophen

Recommended - for treatment of gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain, particularly in patients with contraindications for NSAIDs.

Indications – All patients with gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain, including acute, subacute, chronic, and post-operative.

Dose/Frequency – Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation – Resolution of pain, adverse effects or intolerance.

C.7.c.v Opioids

Opioids are rarely used for treatment of patients with gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain. They are more frequently used briefly in the immediate post-operative period.

Not Recommended - for gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain.

Rationale for Recommendations - Opioids cause significant adverse effects – poor tolerance, constipation, drowsiness, clouded judgment, memory loss, and potential misuse or dependence have been reported in up to 35% of patients. Before prescribing opioids, patients should be informed of these potential adverse effects and cautioned against operating motor vehicles or machinery. Opioids do not appear to be more effective than safer analgesics for managing most musculoskeletal symptoms; they should only be used if needed for severe pain or for a short time (not more than one week) in the post-operative period.

Recommended - for select treatment of patients with post-operative gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain.

Indications – For post-operative gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric, a brief course of a few days to not more than one week of an opioid is recommended for treatment. Opioids may be helpful for brief nocturnal use after surgery. Most patients should attempt pain control with NSAIDs/acetaminophen prior to opioids. Discontinuation of opioids as early as possible is recommended.

Frequency/Dose/Duration – Generally, patients require no more than a few days to not more than one week, of treatment with opioids for most epicondylar surgeries.

Indications for Discontinuation – Resolution of pain, sufficient control with other medications, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.7.d Treatments

C.7.d.i Rehabilitation

Therapeutic Exercise - Physical or Occupational Therapy

Recommended - for greater trochanteric pain syndrome, trochanteric bursitis and gluteus medus tendinosis and tears,

particularly to address any strength deficits in the lateral hip musculature.

Frequency/Dose/Duration –Total numbers of visits may be as few as two to three for patients with mild functional deficits or up to 12 to 15 with more severe deficits with documentation of ongoing objective functional improvement.

When there are ongoing functional deficits, more than 12 to 15 visits may be indicated if there is documentation of functional improvement towards specific objective functional goals (e.g., range of motion, advancing ability to perform work activities). As part of the rehabilitation plan a home exercise program should be developed and performed in conjunction with the therapy.

Indications for Discontinuation – Resolution, post-operative healing, intolerance, lack of efficacy or non-compliance.

C.7.d.ii Injection Therapy

C.7.d.ii.a Glucocorticosteroid Injections

Recommended – as a treatment option for acute, subacute or chronic trochanteric bursitis, greater trochanteric pain syndrome and gluteus medius tears with accompanying clinical bursitis.

Indications: Symptoms of trochanteric bursitis of at least a couple weeks with prior treatment that has included NSAIDs or acetaminophen and avoidance of aggravating activities.

Frequency/Dose/Duration: Maximum of three injections. Each injection should be scheduled separately and the effects of each evaluated before additional injections are scheduled rather than scheduling a series of three injections. The most tender location is recommended to be targeted. Fluoroscopic guidance is not necessary for an initial injection, although it is a more reasonable option for a second injection especially if the first injection is unsatisfactory. Glococorticosteroid injections provide an option for treatment, particularly after inadequate results from NSAID trials, exercise or other conservative interventions.

Evidence Glucocorticosteroid Injections for Acute, Subacute, or Chronic Trochanteric Bursitis

C.7.d.iii Surgery

C.7.d.iii.a Surgical Repair

Recommended – for gluteus medius tears that are not-responsive to medical management.

Indications/Rationale: Tears of the gluteus medius tendon with accompanying pain and/or functional deficits felt amenable to surgical treatment. Generally, at least 3 weeks of non-operative treatment is advisable to ascertain whether the function and pain will sufficiently recover without need for surgery.

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Evidence for Surgical Repair of Gluteus Medius Tears

C.7.d.iii.b Post Operative Therapeutic Exercises – Physical / Occupational Therapy

Recommended – for patients with surgical repair of gluteus medius tears.

Indications: Programs need to be individualized, based on factors such as preoperative condition, bone quality, immediate surgical results, contraindications, and other medical conditions.

Frequency/Dose/Duration: Duration based primarily on progress; two or three times weekly for four to six weeks in an outpatient setting gradually tapered as home exercises are instituted and the patient's recovery advances.

Evidence for the Use of Post-Operative Exercise and Rehabilitation

C.8 Hamstring and Hip Flexor Strains

C.8.a Introduction

Hamstring and hip flexor strains are thought to be true muscular strains (i.e., disrupted myotendinous junctions). The examination findings are tenderness usually at either the muscle origin or insertion with swelling or

large ecchymoses in more severe cases. Some cases involve complete ruptures and require surgical repair. Clinical tests are generally not necessary. Treatments may include NSAIDs, heat or cold, ace wraps, work limitations, therapy, and progressive agility, and trunk stabilization.

C.8.b Diagnostic Studies

C.8.b.i Ultrasound

Recommended – for diagnosing hamstring strains and tears and hip flexor strains.

Indications: Patients with hamstring strains, tears and hip flexor strains that are generally at least moderate in severity. Mild strains generally resolve with appropriate treatment and without need for diagnostic testing.

Frequency/Dose/Duration: Once.

Rationale: Ultrasound may be helpful in evaluating and confirming these diagnoses and is thus recommended.

C.8.b.ii MRI

Recommended – to diagnose hamstring or hip flexor strains in select more severe cases.

Indications: Severe and select cases of moderately-severe strains in which there is consideration for surgical repair.

Rationale: Can help to assess degree of severity in more severe cases which helps define surgical eligibility. Thus, MRI is recommended.

Evidence for X-Rays or MRI to Diagnosis Hamstring Strains and Tears

C.8.c Treatments

C.8.c.i Cryotherapy/Heat

Hot or Cold or Ace Wrap Therapies

Recommended – for treatment of hamstring or hip flexor strains.

Indications: Most patients with sufficient pain from hamstring or hip flexor strains needing treatment and medication, especially in the acute and peri-operative stages.

Frequency/Dose/Duration: Generally tailored according to severity and patient preferences.

Evidence for Ice or Heat or Wraps for Treatment of Hamstring or Hip Flexor Strains

C.8.c.ii Rehabilitation Therapy

Rehabilitation required as a result of a work-related injury should be focused on restoring functional ability required to meet the patient's daily and work activities and return to work; striving to restore the injured worker to pre-injury status in so far as is feasible.

Active therapy requires an internal effort by the individual to complete a specific exercise or task. This form of therapy requires supervision from a therapist such as verbal, visual and/or tactile instruction(s). At times, the therapist may help stabilize the patient or guide the movement pattern, but the energy required to complete the task is predominately executed by the patient. Patient should be instructed to continue active therapies at home as an extension of the treatment process in order to maintain improvement levels.

Active interventions should be emphasized over passive interventions. Passive interventions, those not requiring the exertion of effort on the part of the patient, but rather dependent on modalities delivered by a therapist. Generally passive interventions are viewed as a means to facilitate progress in an active therapy program with concomitant attainment of objective functional gains.

Assistive devices may be included as an adjunctive measure incorporated into the rehabilitation plan to facilitate functional gains.

C.8.c.ii.a Therapeutic Exercise - Physical or Occupational Therapy

Recommended - for greater hamstring and hip flexor strains, particularly to address any strength deficits in the lateral hip musculature.

Frequency/Dose/Duration – Exercises are generally individualized and increased over time. Many therapists combine exercises with other treatment

modalities. Stretching exercises are frequently included and progress to strengthening exercises. Frequency of visits is usually individualized based on severity of the disorder, prior response to treatment, and job functions. Two to three visits per week for two weeks are often used to initiate an exercise program. Total numbers of visits may be as few as 2 to 3 for mild patients or up to 12 to 15 with documenation of objective functional improvement.

As part of the rehabilitation plan, patients should be instructed to continue both active and passive therapy, at home as an extension of the treatment process in order to maintain improvement.

Indications for Discontinuation – Resolution of symptoms, post-operative healing, intolerance, lack of efficacy or non-compliance.

C.8.c.iii Injection Therapy

C.8.c.iii.a Intraarticular Glucocorticosteroid Injections

Recommended - for the treatment of hamstring or hip flexor strains.

Indications: for hamstring or hip flexor strains where control with NSAID(s), acetaminophen, weight loss and exercise is unsatisfactory.

Frequency/Dose/Duration: A single injection should be admistered and the results evaluated.

Indications for Discontinuation: Generally one injection is performed. A second injection may be considered if there is improvement (increased function and decreased pain) that is incomplete.

Evidence for the Use of Intraarticular Glucocorticosteroid Injections

C.8.c.iii.b Intraarticular Hip Viscosupplementation Injections

Not Recommended - for the treatment of hamstring or hip flexor strains.

Evidence for the Use of Intraarticular Hip Viscosupplementation Injections

C.8.c.iii.c Intraarticular Platelet-Rich Plasma Injections

Not Recommended - for the treatment of hamstring or hip flexor strains.

Evidence for the Use of Platelet-Rich Plasma

C.8.c.iii.d Prolotherapy Injections

Not Recommended - for treatment of hamstring or hip flexor strains.

Evidence for the use of Prolotherapy

C.8.c.iii.e Botulinum Injections

Not Recommended - for hamstring or hip flexor strains.

Evidence for the use of Botulinum Injections

C.8.c.iii.f Glucosamine Sulfate Intra-Muscular Injections

Not Recommended - for the treatment of hamstring or hip flexor strains.

Evidence for the use of glucosamine sulfate intra-muscular injections

C.8.c.iii.g Glucosamine Sulfate Intra-Articular Injections

Not Recommended - for the treatment of hamstring or hip flexor strains.

Evidence for use of glucosamine sulfate intra-articular injections

C.8.c.iv Surgery

Surgical Repair

Recommended – for treatment of large or complete hamstring or hip flexor strains in select patients.

Indications/Rationale: Large or complete tears of the hamstrings or hip flexor strains with functional deficits felt amenable to surgical treatment. Generally large or complete hamstrings tears require surgical repair to facilitate recovery.

C.8.c.v Other

C.8.c.v.a Bed Rest

Not Recommended – for treatment of hamstring or hip flexor strains.

Evidence for Bed Rest for Treatment of Hamstring or Hip Flexor Strains

C.8.c.v.b Walking Aid: Cane / Crutches / Walker

Recommended – for select moderate to severe hamstring or hip flexor strains.

Indications: Disabling, moderate to severe hamstring or hip flexor strains where risks of increasing debility are outweighed by device use that increases mobility.

Indications for Discontinuation: Resolution (e.g., post-operative recovery).

Rationale: For acute injuries, crutches and canes may be helpful during the recovery and/or rehabilitative phase to increase functional status (e.g., from wheelchair to walker to cane).

Evidence for use of Canes and Crutches

C.8.c.v.c Electrical Therapies

Not Recommended - for the treatment of hamstring or hip flexor strains.

Evidence for the Use of Electrical Stimulation Therapies

C.8.c.v.d Transcutaneous Electrical Stimulation (TENS)

Not Recommended - for hamstring or hip flexor strains.

Evidence for the Use of Transcutaneous Electrical Stimulation (TENS)

C.9 Groin Strains and Adductor-Related Groin Pain

C.9.a Introduction

Groin strains are generally thought to be true strains with disrupted myotendinous junction(s) that involve the adductor muscles in the upper thigh. Clinical tests are generally not necessary, although in the more severe cases, evaluation with x-rays and/or MRI are recommended for evaluation of the underlying bony structure as well as the degree of muscle tear as rare cases may require surgery.

C.9.b Diagnostic Studies

C.9.b.i Ultrasound

Recommended – for evaluating groin strains or adductor-related groin pain.

Indications: Patients with groin strains or adductor-related groin pain that are generally at least moderate in severity. Mild strains generally resolve with appropriate treatment and without need for diagnostic testing.

Frequency/Dose/Duration: Generally only once.

Rationale: Ultrasound appears helpful in evaluating and confirming these diagnoses and is thus recommended.

Evidence for the Use of Diagnostic Tests for Groin Strains or Adductor-related Groin Pain

C.9.b.ii X-Rays or MRI

Recommended – to diagnose groin strains or adductor-related groin pain in more severe cases.

Indications: Severe and select cases of moderately-severe strains in which there is consideration for surgical repair.

Rationale: X-rays aid avulsion fracture diagnosis and MRI aids the diagnosis of strain/tear severity. These tests help assess degree of severity in more severe cases which helps define surgical eligibility.

Evidence X-rays or MRI to Diagnose Groin Strains or Adductor-related Groin Pain

C.9.c Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.9.c.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of groin strains or adductor-related groin pain.

Indications – NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration – As needed use may be reasonable for many patients.

Indications for Discontinuation – Resolution of symptoms, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.9.c.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended – concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

*Indication*s – For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration - Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation – Intolerance, development of adverse effects, or discontinuation of NSAID.

C.9.c.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin.

C.9.c.iv Acetaminophen

Recommended - for treatment of groin strains or adductor-related groin pain, particularly in patients with contraindications for NSAIDs.
Indications – All patients with groin strains or adductor-related groin pain.

Dose/Frequency – Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation – Resolution of pain, adverse effects or intolerance.

C.9.d Treatments

C.9.d.i Hot and Cold Therapies

C.9.d.i.a Cryotherapy

Recommended - for groin strains or adductor-related groin pain.

Indications – All patients with groin strains or adductor-related groin pain.

Frequency/Duration – Approximately 3 to 5 self-applications per day as needed.

Indications for Discontinuation – Resolution, adverse effects, non-compliance.

C.9.d.i.b Heat Therapy

Recommended - groin strains or adductor-related groin pain

Indications – All patients with groin strains or adductor-related groin pain.

Frequency/Duration – Approximately three to five self-applications per day as needed.

Indications for Discontinuation – Resolution, adverse effects, non-compliance.

C.9.d.ii Rehabilitation

Rehabilitation Programs

Recommended – for treatment of groin strains or adductor-related groin pain.

Indications: Most patients may benefit from a course of therapy, but particularly those with strength deficits and/or significant functional impairments. Thus, groin strains and/or adductor-related groin pain generally at least moderate in severity. Mild cases usually resolve with elimination of exposure(s), NSAIDs and time.

Frequency/Dose/Duration –Total numbers of visits may be as few as two to three for patients with mild functional deficits or up to 12 to 15 with more severe deficits with documentation of ongoing objective functional improvement.

When there are ongoing functional deficits, more than 12 to 15 visits may be indicated if there is documentation of functional improvement towards specific objective functional goals (e.g., range of motion, advancing ability to perform work activities). As part of the rehabilitation plan a home exercise program should be developed and performed in conjunction with the therapy.

Rationale: Rehabilitation required as a result of a work-related injury should be focused on restoring functional ability required to meet the patient's daily and work activities and return to work;

striving to restore the injured worker to pre-injury status in so far as is feasible.

Evidence for the Use of Treatments for Groin Strains or Adductor-related Groin Pain

C.9.d.iii Other

C.9.d.iii.a Bed Rest

Not Recommended – for the treatment of groin strains or adductor-related groin pain.

Evidence Bed Rest for Treatment of Groin Strains or Adductor-related Groin Pain

C.10 Meralgia Paresthetica

C.10.a Introduction

Meralgia paresthetica is a peripheral entrapment neuropathy of the lateral femoral cutaneous nerve, a sensory nerve supplying the upper lateral aspects of the thigh. Although a nerve entrapment may occur at any point along the nerve, the condition is most commonly from localized pressure in the area of the inguinal ligament. In an occupational setting, it has been attributed to pressure from tight, heavy tool belts or military armor. Onset may be relatively acute (e.g., after one night's sleep) or insidious. Other causes include trauma, scarring from prior trauma or surgery, and insults from systemic rheumatological disorders. Symptoms involve tingling and numbness in the distribution of the nerve. Pain may be absent, mild, or (rarely) severe. There is no muscle weakness.

C.10.b Diagnostic Studies

C.10.b.i Magnetic Resonance Neurography

Recommended – for the diagnosis of meralgia paresthetica.

Indications: Most cases are diagnosed clinically and successfully treated empirically, thus requiring no testing. Testing is advised however before surgery both to secure the diagnosis and more precisely identify the location of entrapment for the operative approach.

Rationale: The diagnosis is usually made on clinical grounds and imaging is generally not indicated. For patients in whom there is either a considerable question about the accuracy of the diagnosis, or for whom surgery is contemplated, a nerve conduction study is recommended to confirm the diagnosis and localize the entrapment.

Evidence for use of Magnetic Resonance Neurography for the Diagnosis of Meralgia Paresthetica

C.10.b.ii Nerve Conduction Study

Recommended – to confirm the diagnosis of meralgia paresthetica and localize the entrapment.

Indications: Most cases are diagnosed clinically and successfully treated empirically, thus requiring no testing. Testing is advised however before surgery both to secure the diagnosis and more precisely identify the location of entrapment for the operative approach.

Frequency/Dose/Duration: Once. Should generally not be ordered until symptoms have persisted for at least three weeks to allow sufficient time for electrical findings to develop.

Rationale: The diagnosis is usually made on clinical grounds and imaging is generally not indicated. For patients in whom there is either a considerable question about the accuracy of the diagnosis, or for whom surgery is contemplated, a nerve conduction study is recommended to confirm the diagnosis and localize the entrapment.

Evidence for use of Nerve Conduction Study to Confirm Diagnosis of Meralgia Paresthetica and Localize Entrapment

C.10.c Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.10.c.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of meralgia paresthetica.

Indications: NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration: As needed use may be reasonable for many patients.

Indications for Discontinuation: Resolution of meralgia paresthetica, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.10.c.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended – concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high of gastrointestinal bleeding.

Indications: For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration: Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation: Intolerance, development of adverse effects, or discontinuation of NSAID.

C.10.c.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease

prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or eight hours before the daily aspirin.

C.10.c.iv Acetaminophen for Treatment of Meralgia Paresthetica

Recommended - for treatment of meralgia paresthetica, particularly in patients with contraindications for NSAIDs.

Indications: All patients with meralgia paresthetica pain, including acute, subacute, chronic, and post-operative.

Dose/Frequency: Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation: Resolution of pain, adverse effects or intolerance.

C.10.c.v Topical Lidocaine

Not Recommended – for the treatment of meralgia paresthetica.

C.10.d Treatments

C.10.d.i Hot and Cold Therapies

C.10.d.i.a Cryotherapy

Recommended - meralgia paresthetica.

Indications: All patients with meralgia paresthetica.

Frequency/Duration: Approximately three to five self-applications per day as needed.

Indications for Discontinuation: Resolution, adverse effects, non-compliance.

C.10.d.i.b Heat Therapy

Recommended - meralgia paresthetica.

Indications: All patients with meralgia paresthetica.

Frequency/Duration: Approximately three to five self-applications per day as needed.

Indications for Discontinuation: Resolution, adverse effects, non-compliance.

C.10.d.ii Injection Therapy

C.10.d.ii.a Glucocorticosteroid Injections

Recommended – for the treatment of meralgia paresthetica if more conservative treatments are not efficacious.

Indications: Meralgia paresthetica sufficiently severe and not responding to other more conservative, non-invasive treatments.

Frequency/Dose/Duration: One injection. A second injection is not warranted if there is sufficient recovery from the first.

Evidence for use of Glucocorticosteroid Injections for Treatment of Meralgia Paresthetica

C.10.d.iii Surgery

C.10.d.iii.a Surgical Release

Recommended – for treatment of select patients with meralgia paresthetica.

Indications: Patients who both have continued symptoms unresponsive to the above treatments and in whom symptoms are sufficiently severe to warrant invasive treatment. Should have diagnosis and site of entrapment confirmed by either Nerve conduction study or MR neurography.

Rationale: For patients in whom there is either a considerable question about the accuracy of the diagnosis, or for whom surgery is contemplated, a nerve conduction study or MR neurography is recommended to confirm the diagnosis and localize the entrapment. Surgical release is rarely needed, but for those who both have continued symptoms unresponsive to the above and in whom the symptoms are sufficiently severe to warrant invasive treatment, surgical release is recommended.

Evidence for Surgical Release for Treatment of Meralgia Paresthetica

C.10.d.iv Other

C.10.d.iv.a Spinal Cord Stimulator

Not Recommended – for treatment of patients with meralgia paresthetica.

Evidence for use of Spinal Cord Stimulator for Treatment of Meralgia Paresthetica

C.11 Lower Abdominal Strains

C.11.a Introduction

Lower abdominal strains are frequent occurrences in occupational populations that involve heavy lifting. Patients should be evaluated for hernias and referred for consideration of surgical repair if found.

C.11.b Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.11.b.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of lower abdominal strains.

Indications: NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration: As needed use may be reasonable for many patients.

Indications for Discontinuation: Resolution of lower abdominal strains, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.11.b.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding

Recommended – concommminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

*Indication*s: For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration: Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding

Indications for Discontinuation: Intolerance, development of adverse effects, or discontinuation of NSAID.

C.11.b.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or eight hours before the daily aspirin.

C.11.b.iv Acetaminophen for Treatment of Lower Abdominal Strains

Recommended - for treatment of lower abdominal strains, particularly in patients with contraindications for NSAIDs.

Indications: All patients with lower abdominal strains, including acute, subacute, chronic, and post-operative.

Dose/Frequency: Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation: Resolution of pain, adverse effects or intolerance.

C.11.c Treatments

C.11.c.i Hot and Cold Therapies

C.11.c.i.a Cryotherapy

Recommended - lower abdominal strains.

Indications – All patients with lower abdominal strains.

Frequency/Duration – Approximately three to five self-applications per day as needed.

Indications for Discontinuation – Resolution, adverse effects, non-compliance.

C.11.c.i.b Heat Therapy

Recommended - lower abdominal strains.

Indications – All patients with lower abdominal strains.

Frequency/Duration – Approximately three to five self-applications per day as needed.

Indications for Discontinuation – Resolution, adverse effects, non-compliance.

C.11.d Rehabilitation

Rehabilitation

Recommended – for treatment of lower abdominal strains.

Indications: Most patients may benefit from a course of therapy, but particularly those with strength deficits and/or significant functional impairments. Exercise is able to address functional deficits and is thus recommended for lower abdominal strains at least moderate in severity.

Mild cases usually resolve with elimination of exposure(s), NSAIDs and time.

Frequency/Dose/Duration –Total numbers of visits may be as few as two to three for patients with mild functional deficits or up to 12 to 15 with more severe deficits with documentation of ongoing objective functional improvement.

When there are ongoing functional deficits, more than 12 to 15 visits may be indicated if there is documentation of functional improvement towards specific objective functional goals (e.g., range of motion, advancing ability to perform work activities). As part of the rehabilitation plan a home exercise program should be developed and performed in conjunction with the therapy.

C.12 Epididymo-Orchitis

C.12.a Introduction

The vast majority of cases of epididymitis or combined epididymito-orchitis have infectious origins.

There is a small, but not insignicant minority of patients who report a history of a heavy lift or strain that precipitated the symptoms, thus giving rise to the possibility that this entity may sometimes be an occupational disease or injury outside of the obvious setting of direct work-related trauma. Patients with a clinical course that does not resolve should be evaluated by a urologist.

Patients should be evaluated for testicular torsion (a surgical emergency), tumor and genitourinary infections. Those with evidence suggesting any of these conditions should be referred to a primary health care provider or urologist.

C.12.b Medications

For most patients, ibuprofen, naproxen, or other older generation NSAIDs are recommended as first-line medications. Acetaminophen (or the analog paracetamol) may be a reasonable alternative to NSAIDs for patients who are not candidates for NSAIDs, although most evidence suggests acetaminophen is modestly less effective. There is evidence that NSAIDs are as effective for relief of pain as opioids (including tramadol) and less impairing.

C.12.b.i Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Recommended - for treatment of epididymo-orchitis.

Indications – epididymo-orchitis, NSAIDs are recommended for treatment. Over-the-counter (OTC) agents may suffice and should be tried first.

Frequency/Duration – As needed use may be reasonable for many patients.

Indications for Discontinuation – Resolution of epididymo-orchitis, lack of efficacy, or development of adverse effects that necessitate discontinuation.

C.12.b.ii NSAIDs for Patients at High Risk of Gastrointestinal Bleeding.

Recommended – concomminent use of cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers, and proton pump inhibitors for patients at high risk of gastrointestinal bleeding.

*Indication*s – For patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, elderly, diabetics, and cigarette smokers.

Frequency/Dose/Duration - Proton pump inhibitors, misoprostol, sucralfate, H2 blockers recommended. Dose and frequency per manufacturer. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding.

Indications for Discontinuation – Intolerance, development of adverse effects, or discontinuation of NSAID.

C.12.b.iii NSAIDs for Patients at Risk for Cardiovascular Adverse Effects

Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should have the risks and benefits of NSAID therapy for pain discussed.

Recommended - Acetaminophen or aspirin as the first-line therapy appear to be the safest regarding cardiovascular adverse effects.

Recommended - If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-

dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or eight hours before the daily aspirin.

C.12.b.iv Acetaminophen

Recommended - for treatment of epididymo-orchitis, particularly in patients with contraindications for NSAIDs.

Indications – All patients with epididymo-orchitis pain, including acute, subacute, chronic, and post-operative.

Dose/Frequency – Per manufacturer's recommendations; may be utilized on an as-needed basis. There is evidence of hepatic toxicity when exceeding four gm/day.

Indications for Discontinuation – Resolution of pain, adverse effects or intolerance.

C.12.c Treatments

C.12.c.i Rehabilitation

Not Recommended – for the treatment of epididymo-orchitis.

C.12.c.ii Bed Rest

Not Recommended – for treatment of epididymitis or epididymo-orchitis.

C.12.c.iii Ice or Intermittent Elevation

Not Recommended – for treatment of epididymitis or epididymo-orchitis.

Evidence for the use of Ice or Intermittent Elevation for Treatment of Epididymitis or Epididymo-orchitis

Appendix 1 – Evidence Tables

Evidence for use of antibodies to assist in diagnosing hip pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: C-Reactive Protein, CRP, Erythrocyte Sedimentation Rate, ESR, ESP, Inflammatory Markers; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 16 articles in PubMed, 429 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1690 in Google Scholar, and 10 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 6 articles considered for inclusion, 3 diagnostic studies and 2 systematic studies met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: antibodies; hip osteoarthritis, hip degenerative joint disease, hip osteoarthrosis, hip degenerative arthritis; sensitivity, specificity, predictive value of tests, gold-standard, accurate, accuracy, precision, precise, test. We found and reviewed 8 articles in PubMed, 12 in Scopus, 0 in CINAHL, 26 in Cochrane Library, 2430 in Google Scholar, and 0 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for use of C-Reactive protein to assist in diagnosing hip pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: C-Reactive Protein, CRP, Erythrocyte Sedimentation Rate, ESR, ESP, Inflammatory Markers; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 16 articles in PubMed, 429 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1690 in Google Scholar, and 10 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 6 articles considered for inclusion, 3 diagnostic studies and 2 systematic studies met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: antibodies; hip osteoarthritis, hip degenerative joint disease, hip osteoarthrosis, hip degenerative arthritis; sensitivity, specificity, predictive value of tests, gold-standard, accurate, accuracy, precision, precise, test. We found and reviewed 8 articles in PubMed, 12 in Scopus, 0 in CINAHL, 26 in Cochrane Library, 2430 in Google Scholar, and 0 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for use of erythrocyte sedimentation rate to assist in diagnosing hip pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: C-Reactive Protein, CRP, Erythrocyte Sedimentation Rate, ESR, ESP, Inflammatory Markers; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; diagnostic, diagnosis, sensitivity, specificity, positive

predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 16 articles in PubMed, 429 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1690 in Google Scholar, and 10 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 6 articles considered for inclusion, 3 diagnostic studies and 2 systematic studies met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: antibodies; hip osteoarthritis, hip degenerative joint disease, hip osteoarthrosis, hip degenerative arthritis; sensitivity, specificity, predictive value of tests, gold-standard, accurate, accuracy, precision, precise, test. We found and reviewed 8 articles in PubMed, 12 in Scopus, 0 in CINAHL, 26 in Cochrane Library, 2430 in Google Scholar, and 0 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for use of other non-specific inflammatory markers to assist in diagnosing hip pain
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: C-Reactive Protein, CRP, Erythrocyte Sedimentation Rate, ESR, ESP, Inflammatory Markers; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 16 articles in PubMed, 429 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1690 in Google Scholar, and 10 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 6 articles considered for inclusion, 3 diagnostic studies and 2 systematic studies met the inclusion criteria. A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: antibodies; hip osteoarthritis, hip degenerative joint disease, hip osteoarthrosis, hip degenerative arthritis; sensitivity, specificity, predictive value of tests, gold-standard, accurate, accuracy, precision, precise, test. We found and reviewed 8 articles in PubMed, 12 in Scopus, 0 in CINAHL, 26 in Cochrane Library, 2430 in Google Scholar, and 0 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Antibodies, C-Reactive Protein, Erythrocyte Sedimentation Rate, Other Non-Specific Inflammatory Markers

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/ Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Conrozier 2000 (score =5.0)	C-reactive protein	Diagnostic	No mention of sponsorship or COI.	N = 78 patients with symptomatic hip OA and who fulfilled the ACR criteria for hip	Mean age: 65 years; 21 males, 24 females	Rheumatoid arthritis, hip osteoarthritis	Serum levels of YKL-40 and C-reactive protein in patients with hip OA (N=45) vs.	Mean standard error of YKL-40 level was 90.3 ng/ml in patients with	Serum YKL-40 was higher in hip OA patients. Correlation between YKL-40 and CRP suggests that YKL-40	Data suggest serum YKL-40 was significantly higher in hip OA patients and

				OA or control patients			healthy control patients (N=33)	hip OA vs 66.9 in the control (p=0.03). Mean CRP level was 2.93 mg/l in OA and 1.41 mg/l in control (p = 0.006). In patients with OA YKL-40 and CRP serum levels correlate (r_s = 0.42, p = 0.01). No such correlation in the control.	may be a marker of OA-related joint inflammation.	correlated with CRP.
Garnero 2005 (score =4.5)	C-reactive protein, biomarkers	Diagnostic	Sponsored by a grant from NEGMA-LERADS Laboratories. No mention of COI.	N = 376 patients with hip OA. Inclusion criteria: presence of symptomatic disease, as defined by the presence of daily hip pain for at least one month during the past 2	Mean age: 62.4 ± 7.0 years; 152 males, 224 females	Hip osteoarthritis	Ten different molecular markers were compared: S-PINP, U-CTX-I, U-CTX-II, S-COMP, S-PIIINP, S-HA, S-YKL-40, S-CRP, S-MMP1, S-MMP3. Patients were categorized into tertiles of levels of molecula	Five principal components accounted for 65% of the total variance. Urinary CTX-II correlated with joint pain (r = 0.13, p = 0.0095), joint space	Data suggest evidence of different pathophysiological processes involved in hip OA. CTX-II showed most consistent association with the symptoms and signs of OA.	Data suggest CTX-II most associated with hip OA pathophysiology.

				months, and a Lequesne algofunctional index of at least 3 points.			r markers.	width (r = -.20, p < 0.0001), and presence of bone sclerosis (r = 0.15, p = 0.007). Patients with U-CTX-II and/or S-CRP in the 2 highest tertiles (n =336) had an average pain VAS score of 45.3 mm, while patients in the lowest tertile of the same (n =40) had a score of 35.5 mm (p = 0.003).		
Jung 2004 (score =4.5)	C-reactive protein, biomarkers	Diagnostic	No mention of sponsorship or COI.	N = 136 patients with radiological and clinical manifestation of OA of either the hip or knee	Mean Age: 64.6 years; 62 males, 74 females	Hip or knee osteoarthritis.	Group 1: Urine samples specific for a human collagen type-II C-telopeptide (Ctx-II) in patients	Mean CTx-II in the urine level of patients with OA was 527 ng/mmol creatini	Urine CTx-II in those with severe OA compared with a control suggests collagen type II derived fragments	Data suggest urine CTx-II concentrations are significantly higher in those with severe OA compared

				or control patients.			with hip or knee OA patients (N=88) vs Group 2: Urinary Ctx-II samples in healthy controlpatients (N=48)	ne vs 190 ng/mmol creatinine in control (p < 0.001).	may be markers for OA.	to healthy controls.

Evidence for use of arthroscopic examination to diagnose hip osteoarthritis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: arthroscopy, arthroscopic examination; hip osteoarthritis, hip degenerative joint disease, hip osteoarthritis, hip degenerative arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 19 articles in PubMed, 13 in Scopus, 8 in CINAHL, 5 in Cochrane Library, 101 in Google Scholar, and 0 from other sources. We considered for inclusion 3 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 4 articles considered for inclusion, 3 diagnostic studies and 0 systematic studies met the inclusion criteria.

Evidence for the Use of Arthroscopic Examinations

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Dougados 1999 (Score= 4.5)	Hip arthroplasty/ hip osteoarthritis	Prospective cohort	No mention of sponsorship or COI.	N=506 patients had diagnosis of hip osteoarthritis.	Age range: 50-75 years; 304 females; 202 males.	Hip osteoarthritis	Patients with hip OA were referred to total hip arthroplasty surgery (n=106) vs. Patients with hip OA without hip surgery (n=400).	Pain VAS last value for THA intervention group: 71±24, for no THA group: 36±27 (p<0.0001). Mean change of pain VAS during study for THA group: +5±22, for no THA group: -9±21 (p<0.0001).	"[T]HA could be considered as a valid outcome measure in OA. However, further studies should be conducted in other countries with different health care systems to evaluate the inter-country reliability of this measurement."	Data suggest joint space width change is predictive of THA.
Baber 1998 (Score= 4.0)	Diagnostic arthroscopy/ hip osteoarthritis	Diagnostic longitudinal case series	Authors declared no sponsorship or COI	N=328 patients had hip arthroscopy.	Mean age: 36 years; 210 female, 118 males.	Osteoarthritis or osteochondral defects	Osteoarthritis preoperative diagnosis (n=174) vs. Diagnosis of "idiopathic hip pain" (n=154).	Arthroscopy identified abnormality in 124 (81%) idiopathic hip pain patients. Arthroscopy identified different abnormality in 52	"Arthroscopy of the hip is considered to be of value in assessing and treating the adult patient with pain in the hip of uncertain cause."	Data suggest arthroscopy changed the diagnosis in 53% of the study population from "idiopathic hip pain" to osteochondral defects, torn labra, loose bodies,

								(30%) preoperative diagnosis patients.		OA, and others.
Mei-Dan 2016 (Score=4.0)	Hip resurfacing arthroplasty	Case series	Sponsored by Smith & Nephew. COI: authors reported potential conflict of interest that O.M-D has received funding from Smith & Nephew.	N=68 patients had subsequent hip arthroscopy.	Mean age: 58 years; 26 males, 42 females.	Symptomatic hip-resurfaced arthroplasty	Patients who received a diagnosis before undergoing hip arthroscopy (n=41) vs. patients who underwent hip arthroscopy without an established diagnosis (n=27).	WOMAC score improved from 7 to 2 among patients who were diagnosed before hip arthroscopy ($p<0.001$). WOMAC score worsened from 15 to 21 among patients who received hip arthroscopy without an established diagnosis ($p=0.002$).	"Hip arthroscopy is a safe surgical treatment option for those patients with a painful hip resurfacing arthroplasty. Having an accurate diagnosis before hip arthroscopy improves the likelihood a good outcome."	This subgroup analysis of a large study lacked standardized symptom and diagnostic outcome scoring for hip resurfacing. Data suggest that women are more likely to require post-resurfacing hip arthroscopy; population started with twice as many women as men.

Evidence for use of bone scans to diagnosis early osteonecrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: bone scans, bone scintigraphy, arthroscopy, arthroscopic examination; hip osteoarthritis, hip degenerative joint disease, hip osteoarthritis, hip degenerative arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 19 articles in PubMed, 567 in Scopus, 4 in CINAHL, 39 in Cochrane Library, 17,000 in Google Scholar (only went through first 100), and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus,

0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for use of CT scans to evaluate recurrent post-arthroplasty dislocations

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: computerized tomography, x-ray computer tomography, cone-beam computed tomography, spiral cone-beam computed tomography, spiral computer tomography, emission-computed single-photon tomography, emission-computer tomography; hip osteoarthritis, arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 80 articles in PubMed, 838 in Scopus (Went through first 100), 39 in CINAHL, 32 in Cochrane Library, 3560 in Google Scholar, and 1 from other sources. We considered for inclusion 5 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 6 articles considered for inclusion, 3 diagnostic studies and 0 systematic studies met the inclusion criteria.

Evidence for the Use of Computed Tomography (CT) Scan

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Turmezei 2014a (score=5.0)	Computerized tomography	Diagnostic	Sponsored by the Arthritis Research UK Research Progression award, the Cambridge NIHR Biomedical Research Centre, and the Evelyn Trust Clinical Training Fellowship award. No COI.	N=456 hips from 230 female volunteers.	0 males, 230 females; Mean age 66±17.	All participants in the study were female healthy volunteers who were free of hip fracture, metastatic bone disease, and unilateral metabolic bone disease.	Compared CT scans of all participants for osteoarthritis features.	Frequency (%) of no osteophyte, possible osteophyte, single osteophyte <5mm, definite osteophyte >5mm: 82 (18), 136 (29.8), 209 (45.8), 29 (6.4). Frequency (%) of no subchondral cyst, possible subchondral cyst, single subchondral cyst <5mm, definite subchondral cyst >5mm: 348 (76.3), 36	"[F]inally, we believe that feature severity mapping has the potential to develop in several important roles for the assessment of hip osteoarthritis, including phenotyping and sensitive 3D disease representation."	Data suggest CT mapping may provide benefits for assessing hip OA and localizing osteophytes.

								(7.9), 40 (8.8), 32 (7). Frequency (%) of joint space width (JSW) >4.5mm, JSW 2.5mm-4.5mm, JSW of 1.5mm-2.5mm, JSW <1.5mm: 0 (0), 1 (0.2), 77 (16.9), 378 (82.9).		
Turmezei 2014b (score= 5.0)	Computerized tomography	Diagnostic	Sponsored by the Arthritis Research UK Research Progression award, the Cambridge NIHR Biomedical Research Centre, and the Evelyn Trust Clinical Training Fellowship award. No COI.	N=30 females from the cohort mentioned above.	0 males, 30 females; Mean age 66±17.	Participants were selected from the cohort mentioned above by the author and had a range of osteoarthritis imaging features from absent to severe.	CT scans vs Kellgren & Lawrence (K&L) grading and minimum JSW measurement in digitally reconstructed radiographs (DRR).	Intra-observer weighted kappa-statistic (95% CI), first author vs self for osteophyte score, cyst score, JSW score, Ct composite score, CT grade, DRR K&L grade: 0.78 (0.51-1.00), 1.00 (0.91-1.00), 0.63 (0.35-0.90), 0.65 (0.36-0.94), 0.74 (0.47-1.00), 0.84 (0.57-1.00). Intra-observer weighted kappa-statistic (95% CI), other vs self for osteophyte score, cyst score, JSW score, Ct	"CT grading of hip osteoarthritis has substantial reliability. Sensitivity was increased when CT features of osteoarthritis were assigned a composite score (0-7) that also performed well as a diagnostic test, but at the cost of reliability."	Data suggest that the new CT grading system for hip OA may be superior to the established Kellgren & Lawrence system, but the results need to be validated.

								composite score, CT grade, DRR K&L grade: 0.87 (0.68-1.00), 0.85 (0.75-0.94), 0.23 (0.00-0.69), 0.64 (0.37-0.91), 0.74 (0.53-0.95), 0.57 (0.40-0.74). Inter-observer weighted kappa-statistic (95% CI), author vs other for Osteophyte score, cyst score, JSW score, Ct composite score, CT grade, DRR K&L grade: 0.62 (0.39-0.86), 1.00 (0.91-1.00), 0.28 (0.00-0.62), 0.58 (0.29-0.87), 0.75 (0.48-1.00), 0.63 (0.37-0.90).		
Turmezei 2016 (score=5.0)	Computerized tomography	Diagnostic	Sponsored by the Arthritis Research UK Research Progression award, the Cambridge NIHR Biomedical Researc	N=203 healthy female volunteers.	0 males, 203 females; mean age 65±18.	All participants in the study were female healthy volunteers who were free of hip fracture, metastatic bone disease, and unilatera	Cortical bone thickness utilizing CT scans vs Kellgren & Lawrence grade, minimum joint space width (JSW), and CT osteophyte score.	There was 25% significantly thicker cortical bone for each increase in K&L grade at superolateral and anterior femoral head-neck junction. There was up to 7% significantl	"CBM applied to the proximal femur in clinical CT imaging data identified significant structural changes in peri-articular cortical bone thickness that were associated	Data suggest that quantitative 3D analysis of the proximal femur can detect cortical bone change correlating to the structural

			h Centre, and the Evelyn Trust Clinical Training Fellowship award. No COI.			l metabolic bone disease.		y thicker cortical bone for each unit increase in osteophyte load score circumferentially.	with worse radiological hip osteoarthritis, particularly at the superolateral head–neck junction."	changes in hip OA.

Evidence for use of helical CT for advanced imaging of bony structures

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: helical computerized axial tomography scan, helical CAT scan, helical CT scan, computerized tomography, X-Ray computed tomography, cone-beam computed tomography, spiral cone-beam computed tomography, spiral computed tomography, emission-computed single-photon tomography, emission-computed tomography; hip osteoarthritis, hip degenerative joint disease, hip osteoarthritis, hip degenerative arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 80 articles in PubMed, 849 in Scopus (reviewed the first 100), 39 in CINAHL, 32 in Cochrane Library, 3650 in Google Scholar, and 0 from other sources. We considered for inclusion 5 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 0 randomized trials and 4 systematic studies met the inclusion criteria.

Evidence for use of local anesthetic injections for hip pain diagnosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Local anesthetic injections, local anesthetic, local anesthesia; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 7 articles in PubMed, 178 in Scopus, 98 in CINAHL, 7 in Cochrane Library, 1030 in Google Scholar (Went through first 100), and 9 from other sources. We considered for inclusion 3 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 3 from other sources. Of the 9 articles considered for inclusion, 6 diagnostic studies and 0 systematic studies met the inclusion criteria.

Evidence for the Use of Local Anesthetic Injections for Hip Pain Diagnosis

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:

Deshmukh, 2010 (score=6.5)	Local Anesthetic Injection	Diagnostic	No sponsorship or COI.	N=204 patients with Hip OA	Mean age: 65.4 years; 76 men, 128 females.	Hip Osteoarthritis	Patients with positive response from hip injections (n=152) vs patients with negative response from hip injections (n=52)	Calculations derived a sensitivity [TP(true positive)/ (TP + FN(false negative)] of 91.5%, a specificity [TN/(TN + FP)] and a positive predictive value [TP/(TP + FP)] of 100% each, and a negative predictive value [TN/(TN + FN)] of 84.6%.	"[R]esults support the role of a diagnostic hip injection in confirming origin of pain from an arthritic process in the hip joint. It is a valuable tool to differentiate knee pain originating from the hip from that originating from the knee and also to distinguish other sources of hip pain, most notably the lumbar spine."	Data suggest diagnostic injection in being useful as a diagnostic tool to differentiate the source of a typical hip pain.
Dorleijn, 2014 (score=5.5)	Local Anesthetic Injection	Diagnostic Meta-Analysis	No Sponsors hips. COI, one or more of the authors have receive or will receive benefits for personal or professional use.	N=351 patients with Hip OA	Mean age: 58.2 years; No mention of sex distribution.	Hip osteoarthritis	Complete pain relief vs. partial pain relief vs. no pain relief.	Positive response to the diagnostic hip injection estimates of 0.97 (95% CI 0.87, 0.99) for sensitivi	"[F]or clinical practice, no recommendation can be made regarding the use of hip injections for diagnosing hip OA. High quality, accurately	Study data are not supportive of local anesthetic injections

								ty and of 0.91 (95% CI 0.83, 0.95) for specificity for predicting pain relief after subsequent therapy including THA. This relates to a positive likelihood ratio (LR+) of 10.6 (95% CI 5.6, 20.1) and a negative likelihood ratio (LR−) of 0.04 (95% CI 0.01, 0.15).	reported studies are needed to provide better evidence on the diagnostic role of hip injection."	
Faraj, 2003 (score= 5.5)	Local Anesthetic Injection	Diagnostic	No sponsorship, No COI.	N= 47 patients with hip joint pain.	Mean age; 57 years; 20 males, 27 females.	Identify the source of pain in patients with coxarthrosis but ill-defined clinical and radiologi	Patients given intracticular injection of 0 5% bupivacaine only (n=24). Vs.	Patients with positive response (patients who had complete or significa	"Our result support the earlier studies, that there is a role for local anesthetic injection in identifying the source of pain in patients	At 10 year, data suggest intra-articular bupivacaine may be used in diagnosing coaxthro

						cal features.	Patients injected with local anesthetics (0.5% Bupivacaine hydrochloride) and local steroid (Triamcinolone acetate) (n=23).	nt relief of pain following) (n=24). Patients with negative response (Injection resulted in no change of symptoms) (n=21).	who have coxarthrosis wit borderline clinical and radiological features and an associated low back spondylosis …"	sis versus referred thigh pain.
Ashok, 2009 (score= 5.0)	Local Anesthetic Injection	Diagnostic	No sponsorship, No COI.	N= 48 patients with hip OA and symptoms of Spine pathology	Mean age: 66 years; 21 males, 27 females.	Hip and spinal pain.	Injection carried out by senior author under strict aseptic precautions. Injections was done on the right hip (n= 25) and the left hip (n=23).	After post injection, 37 of the 48 patients had a positive response and 11 had negative response (3 reported a light relief and 8 patients had no relief of pain).	"A fluoroscopically guided local anaesthetic hip injection is a useful diagnostic test in identifying the source of pain in patients with concurrent hip and spine symptoms. "	Data suggest hip injection may have diagnostic value in distinguishing hip versus spinal pain.
Crawford, 1998 (score= 4.5)	Local Anesthetic Injection	Diagnostic	No sponsorship, No COI.	N= 42 patients with hip OA	No mention of age or sex of	Hip arthroplasty.	Group 1 (n=17): patients with history of osteoarth	Thirty tree of the 42 patients had	"We believed that the injection of local anaesthetic	Data suggest value from the use of intra

					patients.		ritis of the hip but had minimal radiological changes. Group 2 (n=15): patients who had concomitant spinal and hip pathology. Group 3 (n= 2): patients who had Paget's disease and secondary osteoarthritis. Group 4 (n=8): patients with unseal pain patterns and three gained reliefs from injection.	complete pain relief after injection, 8 had no relief and 1 patients had minimal pain relief.	into the hip is a reliable test, with low morbidity. In difficult cases it will aid in the clarification of the cause of pain which possibly arises from the hip."	articular anesthetic in distinguishing hip pain etiology.
Yoong, 2011 (score 4.0)	Local Anesthetic Injection	Diagnostic	No sponsorship. COI, Mrs Verna Hamilton and Mrs Joan Bryant for their help in data collection and maintain	N= 138 Patients with OA	Mean age: 68 years; 94 males, 64 females.	Diagnostic hip injection for possible osteoarthritis.	Patient with complete relief after diagnostic injection. (n=71) Vs. Patients with partial	Total of 54/58 patients (93%, 95% CI: 84–97%) with good post-operative result after hip replace	"[C]omplete relief of hip pain following intracapsular injection of local anaesthetic is associated with good surgical outcome	Data suggest U.S guided local anesthetic hip join injection may be useful in confirming hip pathology.

			ing the hip arthroplasty database.				pain relief after diagnostic injection (n=18) Vs. Patients with no pain relief after diagnostic injection (n=49)	ment following a relief of pain after diagnostic injection. Five of eight (63%, 95% CI: 31–86%) had a good post-operative outcome. Forty-four of 49 (90%, 95% CI: 78–96%) patients who had no response to diagnostic injection did not undergo arthroplasty surgery.	following joint replacement."	

Evidence for the use of electromyography, including nerve conduction studies

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Electromyography, nerve conduction; hip osteoarthritis, hip joint degenerative disease, hip degenerative arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 5 articles in PubMed, 52 in Scopus, 2 in CINAHL, 23 in Cochrane Library, 1,300 in Google Scholar, and 0 from other sources. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 2 diagnostic studies and 0 systematic studies met the inclus

ion criteria.

Evidence for the Use of Electromyography/Nerve Conduction

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Dwyer, 2014 (Score=5.5)	Electromyography, Nerve Conduction	Comparison Study	Sponsored by University of Kentucky Department of Orthopedics grant. No COI.	N=30 patients with hip osteoarthritis.	Mean Age; 57.7 years; no mention of gender in groups.	Muscle activity of gluteus medius muscle during function in patients with unilateral hip osteoarthritis.	Patients with Hip OA (n=13) performing step tasks (3 times for each limb for a total of six trials.), force platform, and gait. Vs. Control Group (n=17) performing step tasks (3 times for each limb for a total of six trials), force platform , and gait.	Increased gluteus medius muscle SEMG amplitudes in participants with hip OA for the involved limb muscle during step up initiated with that limb (+13.7% [3.1%, 24.4%]; P = 0.025) and for the uninvolved limb muscle during step up initiated with both the involved (+23.4% [13.1%, 33.8%]; P < 0.001) and uninvolved (+10.6% [4.4%, 21.5%];	"Based on the results of this study, significantly greater gluteus medius muscle amplitudes existed bilaterally during gait and step tasks for patients with end-stage hip joint OA compared to healthy controls…"	Data suggest any strengthening of gluteal muscles may assess in neuromuscular control thus improving strength in hip OA.

								P = 0.027) limb when compared to the control group.		
Schmidt, 2016 (score=4.5)	Electromyography, Nerve Conduction	Comparison Study	Sponsored by voluntary participation and the Central Innovation Program for small and medium sized enterprises of the Federal Ministry for Economic Affairs and Energy for funding (KF3218301SK3). No COI.	N=34 Patients with Hip OA	Mean age: 63.3 years; 20 males, 14 females.	Comparing greater muscle activity asymmetry between patients with unilateral hip osteoarthritis and patients with non – affected limbs.	Patients with unilateral hip osteoarthritis (OA) (n=17) Vs. Control Patients that are healthy with non-affected limbs.(n=17)	Patient with Hip OA approximately was 5 mm shorter than the non-affected limb (LLD = 4.7 _ 3.7 mm; p = 0.020). Control group: No difference between the left and right limb (p = 0.893). Walking speed of healthy controls (0.95 _ 0.08 m/s) did not differ (p = 0.179) from that in the patient group (1.01 _ 0.13 m/s)	"Our data show that hip OA patients display altered activation patterns of proximal and distal lower limb muscles. In particular, in those muscles of the non-affected limb that experience greater ground reaction forces (TA, GM) and those of the affected limb that stabilize the hip [48] during the stance phase. The continuous GM muscle activity may provide additional ankle joint stability throughout	Data suggest that hip OA patients exhibit changed activation patterns of proximal and distal lower limb muscle.

									the complete stance phase…"	

Evidence for use of MRI for evaluation of hip joint pathology
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: magnetic resonance imaging, MRI; hip osteoarthritis, hip denegerative joint disease, hip arthrosis, hip degenerative arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 93 articles in PubMed, 948 in Scopus, 39 in CINAHL, 100 in Cochrane Library, 24,600 in Google Scholar, and 0 from other sources. We considered for inclusion 17 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 11 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for the Use of Magnetic Resonance Imaging

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Roemer 2011 (Score=7.5)	MRI/hip osteoarthritis	diagnostic	Sponsored by Australia Research Council Future Fellowship. One or more of the authors have received or will receive benefits for personal or professional use.	N=52 patients with chronic hip pain.	Mean age: 63.5 ± 9.5 years; 14 males, 28 females.	Hip osteoarthritis	MRI detected lesions vs. radiographic Kellgren-Lawrence grading scheme.	Reliability for all features was intra-reader from 0.69 synovitis to 0.85 cartilage, inter-reader from 0.48 labral integrity, and 0.85 BMLs. MRI detected features and Jellgren-Lawrence grade	"MRI-based semiquantitative assessment of the hip shows adequate reliability. Presence of more severe MRI-detected intraarticular pathology shows a strong association with radiographic OA. The	Data suggest the presence of severe MRI intra-articular pathology shows a high degree of correlation with hip OA.

								indicated strong correlation (p for trend: .26).	results suggest possible associations between MRI-detected pathology and clinical symptoms."	
Leydet-Quilici 2010 (score=7.0)	MRI/hip osteoarthritis	Diagnostic	Sponsored by Marseille University Hospital, France. No COI.	N = 23 patients with advanced hip OA scheduled to undergo surgical hip replacements.	Mean age: 63.9 years; 12 males, 19 females.	Hip osteoarthritis	Normal bone marrow vs subchondral cyst (n=13) vs edema-like (n=23) vs necrosis-like (n=17) vs necrosis (n=8) MR patterns.	Edema-like at MRI vs histological BME (K:0.77; CI 95%: 0.61-0.91). Necrosis-like vs histological bone marrow fibrosis (K:0.49; CI 95%: 0.28-0.69) Necrosis-like vs bone marrow necrosis (K:0.24; CI 95%: 0.01-0.47). MRI cystic bone marrow vs histological pseuydocysts (K:0.58; CI 95%: 0.32-0.78). MRI necrosis vs histological bone marrow necrosis (K:0.28; CI	"In advanced hip OA, the so-called "BME" MR lesion corresponds to a combination of edema, fibrosis, and necrosis at histopathology. When the classical "BME" is more specifically separated into edema-like and necrosis-like MR patterns, MR Imaging and histological findings show substantial agreement, with edema-like MR pattern mainly corresponding to histological edema.	Data suggest MRI and histological findings are highly correlated in advanced hip OA.

								95%: 0.03-0.52). Normal hematopoietic and fatty marrow at MRI vs histological normal bone tissue (K:0.9; CI 95%: 0.73-1).		
Xu 2013 (score=6.5)	MRI/hip osteoarthritis	Diagnostic	No mention of sponsorship. COI: The third author is the President of Boston Imaging Core Lab (BICL), LLC and is a consultant to Genzyme, Stryker, Merck Serono, Novartis and Astra Zeneca. The 4th author is supported by an Australia Research Council (ARC) Future Fellowship	N = 44 patients referred to a secondary orthopedic center for evaluation of chronic hip pain.	Mean age: 63.3 ± 9.5 years; 20 males, 24 females.	Hip osteoarthritis	Radiography performance vs MRI performance.	Intra and inter observer agreement of scoring for cartilage: 73.3%, and 73.3%. Subchondral cysts: 92.4% and 92.9%. Osteophytes: 66.6% and 62.2%. Bone attrition: 100% and 93.3%. The AUC of radiography for detecting overall diffuse cartilage damage, marginal osteophytes, subchondral cysts and bone attrition was 0.76,	"Diagnostic performance of radiography is good for bone attrition, fair for marginal osteophytes and cartilage damage, but poor for subchondral cysts."	Data suggest radiography in OA defects is relatively good for bone attrition, fair for detection of osteophytes and cartilaginous damage but marginal for detection of subchondral cysts.

			and receives research or institutional support from ARC, NIH, and NHMRC. The senior author is CMO of BICL and is a consultant to Merck Serono and National Institute of Health. The 7th author is part of the Management Team of BICL (European Operation)					0.78, 0.67, and 0.82,		
Kumar 2013 (Score=6.0)	Hip osteoarthritis/ MRI	Diagnostic	No mention of sponsorship. The authors declared no conflict of interest.	N=85 patients with cartilage defects.	Mean age: 47 years; 44 males, 41 females.	Hip radiographic osteoarthritis	Control group with Kellgren-Lawrence scored 0,1 (n=55) vs. mild-moderate hip radiographic osteoarthritis with Kellgren-Lawrence	Worse Kellgren-Lawrence score was associated with increasing severity of femoral cartilage defects (p=0.002), subchondral cyst (p-0.005), acetabular	"Acetabular cartilage defects, but not femoral cartilage defects or ROA, were associated with greater self-reported pain and disability. BMELs and subchondral cysts were	Data suggest acetabular cartilage defects were more closely associated with self-reported pain and BMEIs and subchondral cysts correlated more to self-reported

							scored 2,3 (n=30).	cartilage defects (p=0.001), and no significant association with the numbers of these defects.	related to greater hip related self-reported pain and disability. None of the radiographic or MRI features was related to physical function."	pain and disability of the hip.
Lee 2014 (score=6.0)	MRI/hip osteoarthritis	Diagnostic	Sponsored by a grant from NIH-NIAMS. No mention of COI.	N = 98 subjects that received MRI's and radiographs of the hip.	Mean age: 44 ± 13 years; 52 males, 48 females.	Hip osteoarthritis.	SHOMRI vs radiographic assessment with KL classifications, OARSI scores, HOOS and ROM evaluations.	ICCs of intra- and inter reader per feature were ICC > 0.9. Intra-reader kappa values were between 0.65 and 0.79. Inter-reader kappa values were between 0.55 and 0.79. Percent agreement for intra-reader ranged from 70.5% to 98.4% and 66.3% to 99.0% for inter-reader reproducibility. The eight MRI features had a correlation with KL	"SHOMRI demonstrated moderate to excellent reproducibility and significant correlation with radiographic gradings and clinical parameters."	Data suggest the MRI (SHOMRI) demonstrates significant correlation to both clinical and radiological findings in hip OA and may be used as an additional non-invasive tool for diagnostic purposes.

								classification (P range < 0.001-0.03). SHOMRI bone marrow edema pattern and subchondral cysts scores showed a correlation with all three HOOS subscales (P range < 0.001-0.01).		
Kumar 2015 (score=6.0)	MRI/hip osteoarthritis	Diagnostic	Sponsored by a grant from NIH-NIAMS. No mention of COI.	N = 66 patients with radiographic hip OA, a Kellgren-Lawrence grade of two or three at the hip in weight-bearing anterior-posterior radiographs. Control subjects had a KL grade of zero or one and without history of diagnosed OA or hip injury.	Mean age: 51.6 years; 38 males, 28 females.	Hip osteoarthritis.	Patients with hip OA (n=36) vs patients without hip OA (n=30) using the OARSI guidelines.	Hip OA subjects walked with approximately 4.5 degrees higher peak hip flexion (p=0.006) 3 degrees lower peak hip extension (p=0.048) and 3.5 degrees lower hip extension at toe off (p=0.032) compared to control. Higher KL grade was associated with greater peak hip	"In conclusion, we observed lower hip extension in people with mild-moderate radiographic hip OA compared to controls. Subjects with hip OA had worse cartilage lesions in femoral and acetabular surfaces but the difference in labral tear scores were not significant. Finally, KL grade, and	Data suggest decreased hip extension and increased hip flexion during walking are associated with cartilage lesions in those with mild-moderate hip OA.

								flexion, lower peak hip extension, and lower hip extension at toe-off ($p<0.05$).	lesions in the inferior and posterior femur region had weak but significant associations with greater peak hip flexion and lower peak hip extension during walking."	
Schwaiger 2016 (score=6.0)	MRI/hip osteoarthritis	Diagnostic	No mention of sponsorship or COI.	N = 54 patients without history of hip surgery, knee or anle OA, severe hip OA, femoroacetabular impingement, inflammatory arthritis, hematochromatosis, sickle cell disease, hemoglobinopathy, presence of any condition other than OA which limits lower extremity function and mobility.	Mean age: 47.2 ± 13.2 years; 31 males, 23 females.	Hip osteoarthritis	OA subjects with a KL score of 2 or 3 (n=18) vs control subjects with a KL score of 0 or 1 (n=36).	Over 1.5 years, the progression rate of subchondral cysts for OA subjects was 16.7% vs 0.0% for control ($p=0.033$). BMEP was associated with worsening pain (HOOS subscale; $p=0.018$) and hip-related quality of life (HOOS subscale; $p=0.044$)	"In this relatively young study population without or with mild to moderate radiographic hip OA, only minimal differences were found between groups regarding the progression of hip abnormalities as assessed by SHOMRI over 1.5 years. However, BMEP predicted clinical worsening and	Data suggest BMEP was better than SHOMRI in predicting clinical worsening of hip abnormalities.

									subchondral cyst progression was associated with worsening symptoms. Although longer follow-up periods are required, this suggests that SHOMRI is a useful tool to monitor hip abnormalities and their progression longitudinally. ”	
Taljanovic 2008 (Score=5.5)	Hip osteoarthritis/ MRI/ bone marrow edema	Diagnostic	No mention of sponsorship or COI.	N=19 patients underwent hip replacement surgery.	Mean age: 66 years; 11 males, 8 females.	Advanced hip osteoarthritis	Symptomatic hips in study group (n=16) vs. contralateral hips in control group (n=16).	Microfractures were significantly correlated to focal W/W+F, r=-0.48 ($p<0.05$). No significant correlation was found between MRI and bone marrow edema.	“The amount of BME in the OA hip, as measured by MRI, correlates with the severity of pain, Radiographic findings, and number of microfractures.”	Data suggest there is substantial correlation between amounts of BME in an OA hip measured by MRI with pain severity, radiographic results and numbers of microfractures.
Horii 2000 (Score=5.0)	Hip osteoarthritis/ radial MRI	Diagnostic	No mention of sponsorship and COI.	N=24 patients with moderate osteoarthritis.	Mean age: 45 years; 2 males,	Moderate hip osteoarthritis	Hips with moderate osteoarthritis with	Comparing with healthy hips, More abnormalities	“[R]adial MRI may be a useful non-invasive	Data suggest that radial MRI may be a non-

					22 females.		radiographs marked narrowing (n=30) vs. healthy and unilateral non-traumatic osteonecrosis in control groups (n=10).	showed in images of moderate hip osteoarthritis. "Attenuation" and "disappearance" abonormalities showed higher rate in anterosuperior images, rather than in posterosuperior or mid-superior images.	diagnostic method for demonstrating pathology in moderate osteoarthritis of the hip."	invasive diagnostic tool to determine moderate hip OA pathology.
Zilkens 2013 (Score=4.5)	Hip joint cartilage/ MRI/ 3D dGEMRIC	Diagnostic	Sponsored by the German Osteoarthritis Aid. No mention of COI.	N=21 patients with symptomatic hip osteoarthritis underwent hip replacement.	Mean age: 60.9±9.6 years; 7 males, 14 females.	Hip joint cartilage degeneration	MRI with 3D dGEMRIC and 3D VIBE for T1Gd mapping vs. histological section analysis with Mankin score system.	Significant moderate correlation (r=0.411 to 0.525) was found between histological cartilage assessment and morphological MRI ($p<0.001$). histological cartilage assessment and biochemically sensitive MRI indicated strong	"Gradient-echo dGEMRIC is reliable while offering the unique features of high image resolution and 3D biochemically sensitive MRI for the assessment of early cartilage degeneration. "	Data suggest gradient-echo 3D delayed gradolinium-enhanced MRI of hip joint cartilage may be useful for detecting early cartilage degeneration .

								correlation:r=-0.658 to -0.802 (p<0.001).		
Maksymowych 2016 (Score=4.0)	Hip osteoarthritis/ MRI/	Diagnostic	Sponsored by the Alberta Osteoarthritis. No mention of COI.	N=23 patients with osteoarthritis diagnosis.	Mean age: 59.6±13.8 years; 12 males, 11 females.	Hip osteoarthritis	Exercise 1 group with 3 naïve readers to HIMRISS method with excellent score for BML (n=16) vs. exercise 2 group with 3 naïve readers to HIMRISS method after Web-based DICOM viewer design (n=23).	Femoral BML change in 8 weeks was very good assessed with interobserver reliability: ICC=0.82 (95%CI=0.7 to 0.9); in acetabular BML was moderate: ICC=0.57 (95%CI=0.37 to 0.74); in synovitis-effusion was poor: ICC=0.45 (95%CI=0.23 to 0.65).	"Development and validation of a systematic method for KT may enhance external validation of certain imaging instruments."	Data suggest the development of a tool for knowledge transfer may improve imaging instruments.

Evidence for use of radiographs to diagnosis hip osteoarthritis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Roentgenogram, X-ray, radiography; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; Sensitivity and Specificity, Predictive Value of Tests, Gold-standard, accurate, accuracy, precision, precise, test. We found and reviewed 1 article in PubMed, 368 in Scopus, 6 in CINAHL, 191 in Cochrane Library, 101 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 7 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 6 diagnostic studies and 2 systematic studies met the inclusion criteria.

Evidence for the Use of Radiographs (X-rays)

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Xu, 2013 (score=8.0)	Roentgenograms	Diagnostic	Sponsored by grant of "Private Practice for Musculoskeletal MRI", Ulmer Landstr. COI: Third author is President of Boston Imaging Core Lab (BICL), LLC and is a consultant to Genzyme, Stryker, Merck Serono, Novartis and Astra Zeneca. Fourth author is supported by Australia Research Council (ARC) Future Fellowship and receives research or institutional support from ARC, NIH, and NHMR. Senior author is CMO of BICL and is a consultant to	N =44 patients with chronic hip pain	Mean age: 63.3±9.5 years; 20 males, 24 females.	Hip Osteoarthritis	Diagnostic comparison of radiography compared with MRI and area under curve	MRI was used as reference standard. Radiography had low sensitivity for diffuse cartilage damage detection for superior (0.57) and medial (0.57) lesions. Radiography showed higher specificity (0.9 vs 0.76) and positive predictive value (0.87 vs 0.72) for diffuse cartilage damage. Area under the curve of radiography was 0.76 for overall diffuse cartilage damage.	"Diagnostic performance of radiography is good for bone attrition, fair for marginal osteophytes and cartilage damage, but poor for subchondral cysts."	Data suggest radiography is good for detection of femoral head bone attrition, marginal for diffuse cartilage damage and osteophytes and poor for detecting acetabular subchondral cysts compared with MRI. Less radiographic diagnostic sensitivity compared to MRI.

			MerckSerono and National Institute of Health. Seventh author is part of Management Team of BICL (European operation).					Radiography showed high specificity for detection of femoral osteophytes (0.89 for superior and 0.83 for inferior lesions) and positive predictive value (0.88 superior, 0.92 inferior), but sensitivity and accuracy were lower. Radiography sensitivity was 0.91 for superior acetabular osteophytes and 0.42 specificity. Area under curve radiography was 0.78 for overall marginal osteophytes. Sensitivity and specificity of radiography was 0.44 and 0.89 for detection of		

								acetabular subchondral cysts; 0.78 and 0.86 for bone attrition of femoral head. Area under curve of radiography was 0.67 for acetabular subchondral cysts and 0.82 for bone attrition of femoral head.		
Birrell, 2001 (score=6.0)	Radiography	Diagnostic	Sponsored by Arthritis Research Campaign (ARC) core funding. COI: FB was an ARC Clinical Epidemiology Training Fellow.	N=195 patients with hip pain	Mean age: 63 years; 65 males, 130 females.	Hip Osteoarthritis	Comparing range of movement for each plane to identify those with radiographic OA	Internal rotation was best at discriminating moderate and severe hip OA with a 3rd quintile threshold (28º). Restriction in any single plane had sensitivity of 86% for moderate hip OA and 100% for severe hip OA. Specificity was 54% for any single plane in	"Restriction in range of movement was predictive of the presence of OA in these new presenters to primary care with hip pain, and the results of this examination could be used to inform decisions regarding radiography."	Data suggest decreased range of movement was predictive of OA.

								moderate OA and 42% for severe. Restriction in all 3 planes showed sensitivity of 33% for mild to moderate OA and 54% for severe OA; specificity was 93% for moderate and 88% for severe.		
Kim, 2015 (score=5.5)	Radiography	Diagnostic	Sponsored by National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Merck Research Laboratories, Novartis Pharmaceuticals, GlaxoSmithKline, and Pfizer. No COI.	N=5312 patients pelvic radiographs	Mean age:61.4 years; 2252 males, 3060 females	Hip Osteoarthritis	Compared pelvic radiographs from Framingham Osteoarthritis Study and radiographs from Osteoarthritis Initiative	Radiographs in Framingham study showed sensitivity of 15.6% and specificity of 9039% for radiographic hip OA. Positive predictive value was 20.7% and negative predictive value was 87.6%. Radiographs from Osteoarthritis Initiative showed	"Hip pain is discordant with radiographic hip osteoarthritis. We showed that pain was not present in many hips with evidence of osteoarthritis on radiography, and many painful hips did not show radiographic evidence of hip osteoathritis."	Data suggest hip OA as identified radiographically exists without concomitant hip pain and many hips with hip pain did not show hip OA on radiography. Therefore, a diagnosis of hip OA cannot be based solely on radiographs.

								sensitivity of frequent hip pain in hip OA of 9.1% and specificity of 94.3%. Positive predictive value was 23.8% and negative predictive value was 84.1%.		
Ratzlaff 2014 (score=4.5)	Radiography	Diagnostic	Sponsored by NIH, NIAMS, and the Canadian Institute of Health Research. No COI.	N=212 participants from the osteoarthritis Initiative (OAI) data collection.	88 males, 124 females; mean age of 63.1±8.8.	Hip osteoarthritis	Group 1: Participants who had Total Hip replacement after a 48 month visit (N=27) vs. Group 2: Healthy case matched (w/ Group 1) control patients (N=27) vs Group 3: participants that had total Hip replacement any time after baseline with good	Minimum joint space width (mJSW) at 48 month follow up, group 1 vs group 2: 1.89±1.01 vs 3.52±0.85 (p<0.00). mJSW, 4 month follow-up, group 3 vs 4: 3.12±0.92 vs 3.46±0.85 (p<0.01). mean change in mJSW, baseline to 4 years, Group 1 vs 2: -1.18±1.18 vs 0.06±0.71 (p=0.000). mean change	"A new computer-assisted location-specific method of hip JSW is feasible and may provide a superior method to mJSW for radiographic OA progression. Evidence from this study suggests that the superior-medial hip may be the best location for measuring longitudinal	Data suggest the new location-specific hip joint space tool may be appropriate for OA progression.

							contralateral hip radiographs (N=79) vs Group 4: healthy case matched (w/ Group 3) control patients (n=79)	in mJSW, baseline to 4 years, Group 3 vs 4: -0.29±0.81 vs -0.02±0.59 (p=0.01).	JSW change in the hip joint, outperforming mJSW for responsiveness in all analyses."	
Rapan, 2013 (score=4.0)	Radiography	Diagnostic	Sponsored by grant from Croatian Ministry of Science, Education and Sport. No mention of COI.	N=89 hip joint x-rays	Mean age: 62.3 years; 41 males, 58 females.	Hip osteoarthritis	Comparing digitalized conventional x-ray images of femoral heads in osteoarthritic and healthy hip joints	Arithmetic means and medians of variance coefficients for columns were higher in osteoarthritic hips (MWU-Test, p=0.00456, and p=0.00117, respectively). For horizontal rows, healthy hips compared to osteoarthritic hips showed mean and median of variance coefficient of p=0.136525 and p=0.44760,	"Results suggest that in the analyzed set of digitalized x-ray femoral head images, information regarding osteoarthritic changes in the central part of the femoral head is detectable mainly through mathematic post-processing of vertically oriented patterns."	Data suggest the degenerative changes in the central portion of the femoral head replace the fine bone structure with a changed trabecular pattern which is visualized on digitalized X-ray femoral head images. This information seems limited mostly to vertically oriented patterns.

								respectively. Distribution of variance coefficients for vertical columns of coxarthrotic femoral heads compared to controls showed lower median and mean values ($p<0.001$) and wider standard deviation ($p=0.0274$). Horizontal rows were similar in coxarthrotic femur heads and controls ($p=0.5258$ and $p=0.8502$) while standard deviation was lower in coxarthrotic heads ($p<0.001$).		
Sipola, 2011 (score=4.0)	Radiograph	Diagnostic	Sponsored by EVO grant from Kuopio University	N=31 radiographs of hips (healthy and hip OA)	Mean age: 62.4 years; 11	Hip osteoarthritis	Compared radiographs of healthy hip and	Lateral segments were assessable for subjections	"The number of study subjects required to detect a	Small sample. Data suggest the sample size to determine

			Hospital. No COI.		males, 20 females		osteoarthrotic hips	with OA, but only 1 for laterocranial, 2 for cranial, and 3 mediocranial segments were nonassessable. Reason for this is that cases had insufficient delineation of subchondral bone to permit quantitative measurement.	significant joint space narrowing in follow-up studies is influenced by the baseline hip joint OA severity. The JSW measurements with computerized image analysis did not improve the reproducibility and thus performing JSW measurement with a digital caliper is acceptable."	joint space narrowing in follow-up studies is related to hip OA severity.
Xue, 2017 (score=3.5)										Data suggest a deep convolutional neural network (CNN) model may assist medical imaging in the diagnosis of hip OA.

Evidence for use of ultrasound to diagnose hip OA

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Ultrasound, Ultrasonography, Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency.

We found and reviewed 35 articles in PubMed, 375 in Scopus, 20 in CINAHL, 7 in Cochrane Library, 2495 in Google Scholar, and 3 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 0 systematic studies met the inclusion criteria.

Evidence for the Use of Ultrasound

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Qvistgaard 2006 (score=5.5)	Ultrasound	Diagnostic	Sponsered by the Oak Foundation and the Erna Hamilton foundation. No COI.	N=100 patients with hip OA	Mean age: 66 years; 36 mlaes,64 females.	Radiographically verified hip osteoarthritis. .	Observation performed by a specialist in ultrasonography. Vs. Observation performed by a rheumatologist trained in musculoskeletal ultrasound examination.	Good correlation is represented by the intraclass correlation coefficients (ICC): osteophyte score 0.8, femoral head score 0.78, fluid score 0.71, synovial profile score 0.69.	"This study suggests that ultrasound is a reproducible method for the assessment of changes in the osseous surface and synovium-related inflammation. The semiquantitative scoring system presented seemed to match the global assessment of a trained ultrasound investigator and might be used by less trained investigators."	Data suggest US may be a useful tool to assess changes which occur in hip OA.
Young 2011 (score = 4.0)	Ultrasound	Diagnostic	No sponsorship. COI, Mrs. Verna Hamilton and Mrs. Joan Bryant for data collection and maintaining the hip	N=138 patients with Hip OA.	Mean age: 68 years; 44 males, 94 females.	Patients who underwent ultrasound guided hip injection between 2006 and 2009.	Patient with complete relief after diagnostic injection. (n=71) Vs. Patients with partial pain relief after diagnostic injection (n=18)	Total of 54/58 patients (93%, 95% CI: 84–97%) with good post-operative result after hip replacement following a relief of pain after diagnostic injection. Five of eight (63%, 95% CI: 31–86%) had a good post-operative outcome. Forty-four	"Diagnostic ultrasound-guided local anaesthetic injection of the hip joint is a useful test in confirming hip pathology. Complete relief of hip pain following intracapsular injection of local anaesthetic is associated with	Data suggest guided anesthesia, may be beneficial for confirming hip OA.

			arthroplasty database.				Vs. Patients with no pain relief after diagnostic injection (n=49)	of 49 (90%, 95% CI: 78–96%) patients who had no response to diagnostic injection did not undergo arthroplasty surgery.	good surgical outcome following joint replacement."	

Evidence for use of measures to prevent falls

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: fall prevention, fall protection; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 46 in Scopus, 0 in CINAHL, 13 in Cochrane Library, 2470 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 6 from Google Scholar, and 0 from other sources. Of the 9 articles considered for inclusion, 2 randomized trials and 4 systematic studies met the inclusion criteria.

Evidence for the Use of Fall Protection

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Arnold 2010 (score= 5.5)	Fall Protection	RCT	Sponsored by Saskatchewan-Canadian Institutes of Health Research regional Partnerships Program (Sask-CIHR RPP) provided a 2 year fellowship grant for the primary author, and the Physiotherapy foundation of Canada. No COI mentioned.	N = 79 Patients with hip OA	Mean age: 74.4; 23 males, 56 females.	Aquatics and education (n=28) (aquatic exercise twice a week with once a week group education for 11 weeks) Vs aquatics only (n=26) (2 times a week aquatic exercise for 11 weeks.) Vs control (n=25) (usual activity no added on exercise program.)	No follow up mentioned.	No significant difference in physical activity level among the three groups (one-way ANOVA; p=0.73) MANCOVA for change in fall risk factors for the intention-to-treat analysis was significant, F(5, 68) = 2.8, p=.038.	"The combination of aquatic exercise and education was effective in improving fall risk factors in older adults with arthritis."	Data suggest combining aquatic exercise with education is beneficial in fall prevention for older adults with hip OA.
Yamashita 2012										Data suggest chair rising exercise is better than the standing exercise for increasing

(score= 3.5)										dynamics body balance at 1-month post intervention.

Evidence for use of aerobic exercise for treatment of hip osteoarthrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: stair climbing, elliptical training, indoor rower, stair master, stationary bicycle, treadmill, jogging, walking, cycling, running, cross country skiing, cross country running, Nordic walking, inline skating, rowing, kickboxing, skipping rope, jump rope, circuit training, jumping jacks, 5BX, XBX, aerobic exercise, aerobics, aerobic exercises, exercise, cardio exercise, cardio exercises, aerobic programs, aerobics programs, aerobic exercise therapy; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthritis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 467 articles in PubMed, 767 in Scopus, 95 in CINAHL, 7 in Cochrane Library, 752 in Google Scholar, and 22 from other sources. We considered for inclusion 17 from PubMed, 6 from Scopus, 7 from CINAHL, 1 from Cochrane Library, 5 from Google Scholar, and 22 from other sources. Of the 58 articles considered for inclusion, 29 randomized trials and 22 systematic studies met the inclusion criteria.

Evidence for the Use of Aerobic Exercises

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Ettinger 1997 (Score=8.0)	Aerobic exercises	RCT	Sponsored by the Claude D. Pepper Older Americans Independence Center of Wake Forest University grant from National Institutes of Health, and General Clinical Research Center. No mention of COI.	N = 439 Knee OA	Mean age: 68.7 years; 131 males, 308 females.	Aerobic exercise program (3-month facility-based, 15 month home walking, 1 hour with 40 minutes walking a session, 3 sessions a week) (n=144) vs. resistance exercise program (2 sets of 12 reps, 1 hour class with 40-minute resistance exercise, 3 days a week for 18 months; leg extension, curl,	Follow-up at baseline, 3, 9, and 18 months.	6-minute walk test: aerobic 1507 vs. resistance 1406 vs. education 1349 feet, p <0.02 compared with education. Stair climb: 12.7 vs. 13.2 vs. 13.9s (p = 0.05 aerobic c/w education; 0.21 resistance c/w education). Lift and carry task: 9.1 vs. 9.3 vs. 10.0 s, p <0.002. Disease activity intensity score 2.14 vs. 2.21 vs. 2.40 (p = 0.001, p = 0.02). Peak VO2 18.3 vs. 17.9 vs. 17.5 mL/kg/minute. Knee extension	"Older disabled persons with osteoarthritis of the knee had modest improvements in measures of disability, physical performance, and pain from participating in either an aerobic or a resistance exercise program. These data suggest that exercise should be prescribed as part of the treatment for knee osteoarthritis."	Exercise superior to education. Data also suggest weight bearing/walking may be modestly preferable to resistance training for knee OA. Compliance was approximately 69% and results were better with more compliance, especially with the aerobic training.

						step up, heel raise, chest fly, upright row, military press, biceps curl, pelvic tilt) (n=146) vs. health education program (monthly 1.5 hour education session for 3 months, included exercise topics) (n=149).		strength 89.0 vs. 90.2 vs. 87.0 Nm at 30º. Overall self-reported disability scores: 1.72 vs. 1.74 vs. 1.90 (p <0.001 and p = 0.003). Pain intensity scores 2.14 vs. 2.21 vs. 2.46. Self-reported disability by compliance with aerobic exercise (0-39%/40-79%/80-100%): 2.08/1.88/1.70 vs. resistance: 1.96/1.95/1.87.		
Van Baar 1998 (Score=7.5)	Aerobic exercises	RCT	Sponsored by the Dutch Fund of Investigative Medicine of the Dutch Health Insurance Council. No mention of COI.	N = 200 Hip or knee OA	Mean age: 68 years; 157 females, 44 males.	Individual exercise therapy with PT (strength, ROM, ADLs) 1 to 3 times a week (n=100) vs. no exercise for 12 weeks treatment and 24 weeks follow-up. Both groups treated with education and medication (n=100).	Follow-up at baseline 12 weeks.	Most patients reported adherence. Baseline paracetamol use higher in exercise group (52% vs. 38%). Pain in past week reduced after treatment: exercise -22.8 vs. controls -5.7 (p <0.01). NSAID medication use 42% vs. 36%, p = 0.38. Paracetamol use 35% vs. 51%, p = 0.02. Observed disability -0.21 vs. -0.02, p = 0.04. No significant effectiveness differences between hip and knee.	"[E]xercise therapy reduces pain and disability in patients with OA of the hip or knee. The size of the effects is medium to small, respectively."	Physical therapy, exercise groups not structured, precluding assessment of value of specific treatments. Physical therapy program as described had modest effect over home exercise education when used in conjunction with regular care. Pain and disability assessments improved although no difference in amount of NSAIDS consumed.

Nguyen 1997 (Score=6.5)	Aerobic exercises	RCT	Sponsored partially by the spa resort of Vichy. No mention of COI.	N = 180 Lumbar spine, knee and hip OA	Mean age: 63.5 years; 153 females, 35 males.	Spa therapy (n=91) vs. "usual therapy" for 3 weeks (n=97). Spa included "journey, rest, blaneotherapy, spring water and medical attention."	Follow up at baseline 6 months.	NSAID tablets consumed over 24-week follow-up period: spa 144±192 vs. 216±240, p = 0.01. Graphic data suggest reduction in benefits over time. VAS pain scores (9 baseline/4 weeks/24 weeks): spa (50±20/-15±29/-9±28) vs. controls (47±22/1±22/3±24), p <0.0001.	"This study suggests that spa therapy of 3 weeks duration has a prolonged, beneficial, symptomatic effect in osteoarthritis."	Treatments likely heterogeneous with multiple co-interventions, precluding strong conclusions. No long-term follow-up beyond 6 months; results not significantly different by months 4-6 by tablet count.
Villadsen, 2014 (Score=6.5)	Aerobic exercises	RCT	Sponsored by Region of Southern Denmark, the Danish Rheumatism Association, and TrygFonden. No mention of COI.	N = 165 patients with severe osteoarthritis for knee or hip arthroplasty.	Mean age: 67±8 years; 92 females, 73 males.	Intervention group with 8 weeks of exercise program and educational package (n=84) vs. Control group with only educational package (n=81).	No mention of follow-up period.	Greater ADL and pain improvement showed in intervention group (p=0.0488, p=0.0472), compared to control group ADL: 5.6(95%CI: 0.03-10.3) and pain: 5.4 (95%CI: 0.1-10.8). Self-reported general health by EQ5D-VAS (7.6) was also greatly improved in intervention group (95%CI: 2.1-13.0).	"Eight weeks of supervised neuromuscular exercise prior to total joint arthroplasty (TJA) of the hip or knee did not confer additional benefits 3 months postoperatively compared with TJA alone. However, the intervention group experienced a statistically significant short-term benefit in ADL and pain, suggesting an earlier onset of postoperative recovery."	Lack of efficacy. Data suggest no benefit to 8 weeks of preoperative exercise.

Austin 2017 (Score=6.5)	Aerobic exercises	RCT	No sponsorship mentioned. COI: One or more of the authors have received benefits for personal or professional use.	N=120 unilateral hip arthroplasty patients.	Mean age: 61.7 years; 61 males, 54 females.	Experimental group with unsupervised home exercise (n=54) vs. Control group with formal home standard physical therapy with physical therapist visits. (n=54).	Follow-up from baseline for 1 month, 6-12 months.	Primary outcome was improved in the HHS by 21.5 points from baseline to first visit at 1 month for formal outpatient therapy cohort (95%CI: 16.2-26.9); 23.3 points for unsupervised home exercise group (95%CI: 18.3-28.4). WOMAC improved both in formal outpatients therapy group (36.9 points, 95%CI: 32.2-41.8) and unsupervised home exercise group (36.4 points, 95%CI: 31.8-41.1).	"[U]nsupervised home exercise is both safe and efficacious for a majority of patients undergoing total hip arthroplasty, and formal physical therapy may not be required."	Standard case bias. 28% of patients crossed over. Data suggest comparable efficacy between groups
Ravaud 2004 (Score=6.0)	Aerobic exercises	RCT	Sponsored by Merk Sharp & Dohme at Chibret, France. No mention of COI.	N = 867 rheuma-tologists N = 2,957 (2216 knee OA; 741 hip OA)	Mean age: 66 years; 449 males, 418 females.	Standardized tools (adjusted medications) (n=220) vs. booklet with exercises and videotape (ROM and strength) for HEP 4 times a week/6 months (n=213) vs. standardized tools and exercise (n=213) vs. usual medical care by rheumatologists (n=221). All patients given rofecoxib 12.5mg	Follow-up at baseline, 4 and 12 weeks.	VAS pain ST (-17.6±27.2) vs. exercise (-19.7±28.7) vs. ST+EX (-14.5±26.5) vs. usual care (-19.1±28.8). WOMAC function and global assessments also not different as improved in all 4 arms (p <0.001). Diaries completed by <50%. Patients in EX and ST+EX groups more likely to agree that rheumatologists provided advice about muscular strengthening (p 0.001) and that he	"Although patients' assessments favoured the exercise programme, results from this study failed to demonstrate a short term symptomatic effect of the two non-pharmacological treatments (weekly recording of condition and exercise) in patients with OA concurrently receiving nonsteroidal anti-inflammatory drugs."	Cluster randomized controlled study with randomization at physician level may result in relative lack of homogeneity of interventions. Study data do not clearly support exercise program, but implementation of rofecoxib as a co-intervention may have confounded results.

						QD first month and 25mg QD after if needed.		"has done his best to preserve their muscular function and their physical activities" (p <0.001).		
Lyngberg 1994 (Score=6.0)	Aerobic exercises	RCT	Sponsored by Danish Rheumatism Association, Grosserer A. V. Lykfeldt Foundation, and P. Carl Petersen Foundation. Authors declared no COI.	N = 24 RA with low dose steroids for 2 years	Mean age: 67 years; 22 females, 2 males.	Progressive interval training – aerobic with ergometer – bicycling and strengthening exercises, stretching trained muscles twice a week, 45 minutes for 3 months (n=12) vs. no program control group (n=12).	No mention of follow-up.	Tended towards lower tender joints with exercise. Changes in medication use NS. Borderline reduction in number of swollen joints (p = 0.06). ESR (baseline/post): training (33/22) vs. control (17/23) favored treatment p = 0.13.	"Individually adapted exercise programs can therefore be recommended for elderly rheumatoid arthritis patients on steroid treatment."	Data suggest physical training in elderly, fragile patients does not increase RA disease activity measured by blinded assessor. ESR reduced with exercise compared with controls.
Lyngberg 1988 (Score=6.0)	Aerobic exercises	Crossover Trial	Sponsored by Danish Rheumatoid Arthritis Foundation. No mention of COI.	N = 20 RA, moderately active disease	Age range: 30 to >50 years; 14 females, 4 males.	Training program of aerobic capacity training and dynamic strength exercises 45 minutes twice a week for 8 weeks (n=9) vs. no program (n=9).	No mention of follow-up.	No significant change in ESR, C3. Number of swollen joints decreased after training (77 to 56, p <0.02). No comparable reduction in swollen joints during control period (42 to 49). Hemoglobin level increased approximately 8% (p<0.01) with training.	"RA-patients with some activity are trainable without aggravating the disease, even in the chronically swollen joints. The rheumatoid arthritis activity decreased with fewer swollen joints and higher hemoglobin level after training."	Main outcomes of serological markers of inflammation negative. However, disease activity reduced with exercise as measured with blinded assessor.

Tak 2005 (Score=5.5)	Aerobic exercises	RCT	Sponsored by the Netherlands Health Research and Development Council. No mention of COI.	N = 109 Hip OA (n=15 dropouts)	Mean age: 68.2 years; 30 males, 64 females.	Hop with the Hip exercise program (strengthening, treadmill, weight control, assistive devices) weekly 1-hour appointments for 8 weeks (n=55) vs. no intervention (n=54).	Follow-up at baseline 3 months.	VAS pain (baseline/post/ follow-up): Exercise (3.8±2.1/3.6±2.5/3.5± 2.1) vs. control (4.2±2.2/4.1± 2.1/5.1±2.3) (p = 0.38 and p = 0.02 at follow-up). Harris Hip Score: exercise (71.1± 12.9/77.0±11.6/75.4± 14.6) vs. control (71.0±13.3/ 71.2±13.2/71.1±15.1) (p = 0.031 and p = 0.081). Lower level of restrictions in exercise group but NS. Physical subscale of SIP improved in exercise group at follow-up (p <0.05).	"The exercise program had positive effects on pain and hip function, which are important mediators of disability. This study fulfilled a need for older adults with hip OA and provides evidence of the benefit of exercise in the management of hip OA."	Non-interventional control group may bias in favor of intervention. Dropouts had worse disease measures. Data suggest exercise benefits hip OA patients.
Teirlinck 2016 (Score=5.5)	Aerobic exercises	RCT	Sponsored by the Netherland Organization for Health Research and Development, and Dutch Arthritis Foundation. COI: One or more of the authors have received benefits for personal or professional use.	N=203 hip OA patients with new hip complaints.	Mean age: 64±8.5; 117 females, 86 males.	Intervention group with general practitioner care with exercise therapy (n=101) vs. Control group with only general practitioner care (n=102).	Follow-up from baseline for 12 months.	Adjusted overall HOOS pain in 12 months follow-up period were -1.7 (95%CI:-4.8 to 1.4) and HOOS function were -3.3 (95%CI:-6.7 to 0.2). The difference of HOOS pain (-3.7; 95%CI: -7.3 to -0.2) and HOOS function (-5.3; 95%CI:-8.9 to -1.6) was statistically different during follow-up period.	"No differences were found during 12-months follow-up on pain and function. At 3-months follow-up, pain and function scores differed in favor of patients allocated to the additional exercise therapy compared with GP care alone."	Control group participants were discouraged from but not restricted from seeing a physical therapist. Data suggest at 12 months between groups for pain or functional improvement. However, the short term follow-up at 3 months showed a tread for improvement in the exercise group.

Hopman-Rock 2000 (Score=5.0)	Aerobic exercises	RCT	Sponsored by the Netherlands Health Research and Development Council. No mention of COI.	N = 120 Hip or knee OA	Mean age: 65.3 years; 83 females, 22 males.	Two hour weekly exercise sessions (1.25 hour education, 45-minute exercises with HEP at least 3 times a week for 6 weeks (n=56) vs. non-interventional controls (n=49).	Follow-up at baseline 6 months.	IRGL pain scale (baseline/post/follow up): exercise (14.0±4.0/13.6±3.6/14.2±4.0) vs. controls (13.7±3.5/14.9±3.8/14.3±4.0), p = 0.045. Pain intolerance also favored exercise (p = 0.011) as did quality of life (p = 0.039).	"[T]his self-management program was reasonably effective in terms of the educational and exercise components."	Non-interventional control group may bias in favor of intervention. Exercises appear unstructured and not well described. Data support exercises, although results did not persist at follow-up.
Mangione 1999 (Score=5.0)	Aerobic exercises	RCT	Sponsored by New Investigator Grant from the Arthritis Foundation. No mention of COI.	N = 39 Knee OA	Mean age: 71.1±6.9 years; 26 females, 13 males.	High (70% heart rate max from graded exercise test) (n=19) vs. low (40% HR max) intensity stationary cycling for 1 hour session, 3 times a week for 10 weeks (n=20).	No mention of follow-up.	Chair rise time (baseline/ post): HI 23.54±10.15/ 19.26±8.18 vs. LO 23.09 ±8.21/18.96±4.83 (NS). 6-minute walk test: HI 488.06±117.72/540.62±98.72 vs. LO 491.12± 103.74/526.94± 113.74 (NS).	"Cycling may be considered as an alternative exercise modality for patients with knee OA. Low-intensity cycling was as effective as high-intensity cycling in improving function and gait, decreasing pain, and increasing aerobic capacity."	Data suggest no meaningful differences between low vs. high bicycle exercise program.
Baslund 1993 (Score=4.5)	Aerobic exercises	RCT	Sponsored by Danish National Association against Rheumatic Disease. No mention of COI.	N = 18 RA	Mean age: 48 years; 16 females, 2 males.	Progressive bicycle training (ergometric bicycle 4-5 times a week with 3 short exercise periods of 5 minutes to target HR) (n=9) vs.	No mention of follow-up.	VO2max training (27.2±1.7/ 33.3±1.9) vs. controls (20.9 ±2.9/22.2±2.6) mL/kg/min (p = 0.04). HR decreased, RPE reduced, work load increased in exercise group. No difference in leukocytes,	"8 wk of bicycle training does not influence the immune system of patients with rheumatoid arthritis."	Small sample size. Baseline higher VO2max in training group (27.2 ±1.7 vs. 20.9±2.9 mL/kg/min). No immunological effects found (were trial's primary outcome

						controls for 8 weeks (n=9).		lymphocytes, neutrophils, C-reactive protein or erythrocyte sedimentation rate. Concentrations of IL-1α, IL-1β, and IL-6 not changed in training group. NK cell activity and lymphocyte proliferative responses did not differ.		measures). Training group's VO2max improved despite use of short bursts of exercise.
van den Ende 1996 (Score=4.5)	Aerobic exercises	RCT	Sponsored by the Nationale Commissie Chronisch Zieken Foundation, and Health Assurance Company-Zorgen Zekerheid. No mention of COI.	N = 100 RA	Mean age: 52 years; 63 females, 37 males.	High intensity group exercises (12 exercises, 20 minute cycling to 70-85% HR Max, 1 hour sessions, 3 times a week) (n=25) vs. low intensity group exercise program (ROM, isometric strengthening, 1 hour sessions, twice a week) (n=25) vs. low intensity individual exercise program (same exercises, durations unclear) (n=25) vs. home exercise program (ROM and isometric exercises at least 2 times a week	Follow-up at baseline 24 weeks.	Mean aerobic capacity ($V0_2max$) increases: high intensity (27.6 to 32.3) +4.7mL/kg/min (17%) vs. low group +0.9 vs. low individual -1.2 vs. home +0.3 ($p < 0.001$ for high intensity group). Joint mobility (EPM-ROM) improved from 10.9 to 9.2 (15.6%) in high intensity group ($p < 0.001$) compared with other groups. Muscle strength in high intensity group superior to HEP ($p = 0.02$), but not to low intensity groups; HAQ and Dutch AIMS NS. Medications unchanged.	"Intensive dynamic training is more effective in increasing aerobic capacity, joint mobility, and muscle strength than ROM exercises and isometric training in rheumatoid arthritis patients with well controlled disease."	High intensity group tended towards longer disease duration and more active disease at baseline, potentially biasing against that group. Unequal treatment contact times among groups. Pain and/or physical fitness impaired ability of some to complete ergometer test. Data suggest best improvements in aerobic capacity and joint mobility with high intensity exercises. Data also suggest results did not persist to 24 weeks.

						for 15 minutes (n=25); all 12 weeks.				
Ekdahl 1990 (Score=4.5)	Aerobic exercises	RCT	Sponsored by Swedish Association Against Rheumatism, Signe and Reinhold Sund Foundation, Malmohus County Council, and Greta and Johan Kock Foundation. No mention of COI.	N = 67 RA	Mean age: 53 ±10.2 years; 43 females, 24 males.	Dynamic program, strengthening and aerobic capacity 12 visits (2 a week/6 weeks) (n=16) vs. dynamic program, ROM and strengthening exercises 4 visits (2 at 1 week, 1 at 3 weeks, 1 at 6 weeks) (n=16) vs. static program 12 visits (n=16) vs. 4 visits. HEP daily (n=16). Three were excluded from analysis.	Follow-up at baseline, 3 months.	VO2Max (baseline-6 weeks difference/baseline-18 weeks): dynamic (5.6/2.6) vs. static (0.9/-0.1). VAS pain muscle tests (-0.5/0.0) vs. (-0.2/0.4). Walking 60m (-3.7/-1.9s) vs. -0.5/0.1). All changes for dynamic group on 25 subtests were positive vs. 12 subtests negative among static group. During 18 weeks, significant difference on 17 of 25 subtests.	"[D]ynamic training gives a greater increase in physical capacity than does static training."	No differences between 4 and 12 visits, so data collapsed. Data suggest dynamic exercise superior to static.
Ekblom 1975 (Score=4.5)	Aerobic exercises	RCT	No mention of sponsorship or COI.	N = 34 RA, hospitalized but "non-acute stage"	No mention of age or sex.	"Ordinary" physical rehab program – QAM, 5 a day 1 week (control) (n=4) vs. ordinary program plus training group (bicycle ergometer and quadriceps table strengthening) 20-40 minutes BID for 5 weeks (n=26). Four	No mention of follow-up.	850m walk test (baseline/post): training group (9.36/8.02, p <0.05) vs. control group (9.17/8.97). Stair test up: TG (6.92/5.25s) vs. control (5.53/4.54).	"[T]he intensive physical training program resulted in a considerable improvement in physical performance capacity, cardio-respiratory fitness and leg muscle strengths in the (training group), indicating that lack of physical activity could be a major reason for the low physical	Practicality of a 6-week hospital stay limits the utility of the results. Group sizes unequal and possible 2:1 randomization process, but not described. Data suggest training program successful.

						were excluded from analysis.			fitness in the RA patient."	
Daltroy 1995 (Score=4.5)	Aerobic exercises	RCT	Sponsored by NIH grant AR36308 and NIDRR G008635121. No mention of COI.	N = 71 RA or systemic lupus erythe-matosus	Mean age: 37 years; 66 females, 5 males.	12-week home cardio-pulmonary conditioning program with stationary bicycles provided. Prescription 60-80% HR max, 3 times a week for 30 minute sessions (n=35) vs. controls to maintain current activity level for 12 weeks (n=36).	No mention of follow-up time length.	Measures favored exercise (mostly NS). ETT minutes at 12 weeks: exercise 9.6 vs. 9.2 minutes controls (p = 0.33). CES-D depression scores 11.3 vs. 15.0 (p = 0.07). POMS fatigue 7.6 vs. 10.3, p = 0.03. Exercise group averaged 2.7 sessions a week. Patients reporting greater physical activity had greater baseline exercise tolerance, p = 0.0003 and at 3 months, p = 0.002.	"[A]lthough safe, un-supervised home exercise programmes may benefit few patients."	Data suggest exercise program may be relatively unsuccessful, although fatigue measures positive. Mixed rheumatological disorders. RA controls exercised somewhat longer at baseline, providing some potential bias against exercise.
Hansen 1993 (Score=4.5)	Aerobic exercises	RCT	Sponsored by Danish Arthritis Foundation, Danish Research Council, Danish Physiotherapists' Research Fund, and Fund for Medical Research, South Jutland. No mention of COI.	N = 75 RA	Mean age: 53 years; 49 females, 26 males.	Five groups: 1 non-exercise controls (E) (n=15) vs. All exercise groups self training with 15 minute overall training and 30 minute aerobic (swim, cycle, run, jog) 3 times a week, up to 90 minutes a day: A) self	Follow-up at 24 months.	ESR (baseline/24 months): A (35/22) vs. B (28/19) vs. C (20/17) vs. D 22/16) vs. E (23/28). Numbers of swollen joints not different. Pain scores: A (1.6/1.4) vs. B (1.8/1.9) vs. C (1.9/2.1) vs. D (1.9/1.4) vs. E (1.9/1.9). Average aerobic fitness declined in all 5	"[A]lthough most patients are in favour of training, the present study does not support that training lessons per se affect the disease activity or the progression of the disease."	Subgroups are small at 15 subjects each arm. No aggregate analyses reported although some groups may have been comparable. Only no-exercise controls had rise in ESR. Lack of increases in aerobic capacity suggest lack of compliance

						training only (n=15) vs. B) weekly PT (15 minute standard program, 15 minute biking, 15 minute relaxation (n=15) vs. C) weekly in-hospital training as per B (n=15) vs. D) same as C but hot pool instead of bikes; all 2 years (n=15).		groups. Attendance rate for training sessions >50% for groups B, C, and D. "There were no statistically significant effect of the training on any of the measured variables. 66% of all patients experienced a general improvement of disease activity or activity of daily living. [T]here were no statistically significant differences between the groups."		with HEP. Lack of data from end of training impair ability to conclude short to intermediate term efficacy (or lack) of the program.
Halbert 2001 (Score=4.5)	Aerobic exercises	RCT	Sponsored by JH & JC Gunn Medical Research Foundation (Australia) and National Health and Medical Research Council, Department of Health, Local Government and Community Services. No mention of COI.	N = 69 Hip or knee OA	Mean age: 68.9 years; 28 males, 41 females.	Individualized physical activity advice (at 0, 3, 6 months; emphasis on aerobic 3 sessions a week for ≥20minutes) (n=37) vs. nutritional pamphlet (n=32).	Follow-up at baseline, 3, 6, and 12 months.	More intervention moved up category or 2 to intend to exercise (p = 0.013). Somewhat more exercise in the intervention group. OA symptoms unchanged and not different between groups. Well being did not change between groups.	"An offer of primary care-based physical activity advice, with an emphasis on the benefits for general health (rather than "treatment" for OA), will attract individuals with OA symptoms. Although the present study was unable to demonstrate intervention-control group differences for the majority of outcomes, intention to exercise did appear to be positively influenced."	Differences in exercising between groups minimal, suggesting advice had minimal influence.

Krauß,2014 (Score=4.5)	Aerobic exercises	RCT	Sponsored by the companies Theraband and Ludwig Artzt. COI: authors declared no conflict of interest.	N=225 patients with unilateral or bilateral hip osteoarthritis.	Age range: 51 to 70 years; 88 females, 130 males.	Patients in Tübingen exercise therapy (n=71) vs. Patients in control group (n=69) vs. Patients in placebo ultrasound group (n=70) vs. Patients in ultrasound group (n=8).	Follow-up from baseline for 1 year.	Intervention group reported statistical difference of greater pain reduction (7.4 points) comparing with control group on the WOMAC Index (p=0.001, 95% CI: 3.0-11.8); same statistical difference was found between intervention and placebo groups with 5.1 points (p=0.024, 95%CI: 0.7-9.4)	"Twelve weeks of exercise therapy in hip osteoarthritis patients of normal vitality reduced pain and improved physical function. No significant improvement was found in these patients' general health-related quality of life."	Standard case bias. Data suggest 12 weeks of hip OA exercise therapy did reduce pain with improved physical function.
Bieler,2016 (Score=4.5)	Aerobic exercises	RCT	Sponsored by the TrygFonden, Nordea Foundation, Health Foundation, Danish Rheumatism Association, and Lundbeck Foundation. COI: no mention of conflict of interest.	N=152 patients with hip osteoarthritis.	Mean age: 69.6 years; 49 males, 103 females.	Patients in Nordic walking group (n=50) vs. Patients in strength training group (n=50) vs. Patients in home-based exercise group (n=52).	Follow-up from baseline for 12 months.	30 seconds chair stand test was improved to patients of better physical function: 2.0-2.6 chair stands among hip osteoarthritis patients. Timed test to ascend or descend stair without using handrail by 10 steps with 16.3cm step height and 35.8cm step depth.	"[N]W is the recommended exercise modality compared with ST and HBE."	High dropout rate before 12 month follow-up. Data suggest NW is superior for improved function.

Harkcom 1985 (Score=4.0)	Aerobic exercises	RCT	Sponsored by USPHS training grant (AM 07080). No mention of COI.	N = 20 women RA, functional class II	Mean age: 52±12 years, 20 females.	Bicycle ergometer 3 times a week for 12 weeks (n=4) vs. 3 different exercise time progressions (n=13).	No mention of follow-up.	Aerobic capacity Group A (lowest) vs. B vs. C (baseline/post): A (14.6± 4.9/21.5±6.5) vs. B (20.3± 15.8/22.9±17.9) vs. C (21.9 ±9.0/29.1±17.4). Joint count: A (38.0±21.7/24.0 ±10.9) vs. B (26.0±15.1/ 10.3±7.0) vs. C (32.5± 19.4/23.0± 10.7).	"Exercise duration up to 35 minutes of exercise 3 times/ week is sufficient to improve aerobic capacity in rheumatoid arthritis patients with severe limitations."	Pseudorandom-ization (patient chose a time block to show up for assignment). Suggests increased benefits with increased exercise time.
Häkkinen 2001 (Score=4.0)	Aerobic exercises	RCT	Sponsored by Central Finland Health Care District and Yrjo Jahnsson Foundation, Finland. No mention of COI.	N = 70 RA	Mean age: 49 years; 24 males, 38 females.	Strength training (50-70% repetition max) (n=31) vs. control group (n=31).	Follow-up at baseline, 2 years.	ESRs (baseline/6 months/12 months/24 months): strengthening (24.4±17.8/ 9.7±9.5/9.5±7.5/10.9± 9.8) vs. controls (24.8±15.7/16.7 ±12.7/17.3±16.1/15.4 ±11.5). VAS: strengthening (41.7± 19.5/20.0±16.4/21.1± 20.6/ 13.7±16.2) vs. controls (41.3 ±27.1/28.6±23.1/24.2 ± 22.7/24.9±22.8) (p <0.05 Months 18-24). Compliance average 1.5 times a week first 12 months; 1.4 times a week Months 13-24 both groups. Muscle strength increased with strength training except trunk flexion, p	"Regular dynamic strength training combined with endurance-type physical activities improves muscle strength and physical function, but not (bone mineral density), in patients with early RA, without detrimental effects on disease activity."	Data suggest superiority of strength training likely combined with aerobic exercise to range of motion exercises. As aerobic activities handled differently in the two groups, impacts of either strengthening or aerobic exercise alone are unclear. Strength training reduced ESR and pain ratings more.

								= 0.002-0.025. Joint damage not significant. Walking speed increased 16±17% in strength training, p <0.001, vs. 9±12% controls, p = 0.025.		
Minor 1989 (Score=4.0)	Aerobic exercises	RCT	Sponsored by NIH grant (AM-20658) and Department of Education award (H133_b80075). No mention of COI.	N = 120 OA (hip, knee, or tarsal) or RA	Mean age: 60.6 years; 98 females, 22 males.	Aerobic walking (n=28) vs. aerobic pool (n=38) vs. range of motion exercise classes, 1 hour sessions, 3 sessions a week for 12 weeks. Both aerobic groups targeted 60-80% of HR Maximum for 30 minutes (n=28).	Follow-up at baseline, 3 and 9 months.	Aerobic capacity (baseline/ 12 weeks): walk (18.9±4.8 /22.4±4.8mL/kg/minutes) vs. pool (19.3±6.7/23.2± 7.2) vs. ROM (17.4±5.9/ 17.3±3.6) (p = 0.009 comparing walk plus pool vs. ROM). AIMS pain scores (baseline/12 weeks): walk (5.1±1.9/3.9±1.9) vs. pool (5.0±1.6/4.4±1.7) vs. ROM (5.5±1.6/4.8±1.9) (p = 0.22). Active joints (n): aerobic OA -2.0±5.2 vs. ROM (-1.8±5.9). Active RA joints aerobic (-6.8± 11.8) vs. ROM (3.3±10.9).	"Our findings document the feasibility and efficacy of conditioning exercise for people who have rheumatoid arthritis or osteoarthritis."	Data suggest efficacy of walking or pool exercise for arthritis patients. Targeted 60-80% HR maximum in walking/pool groups. Improve greater OA vs. RA for exercise endurance but better for total active RA joints. Both appear to benefit. Suggests aerobic exercise reduces active RA joints.
Veenhof 2006 (Score=4.0)	Aerobic exercises	RCT	Sponsored by the Health Care Insurance Board. No mention of COI.	N = 200 Hip or knee OA	Mean age: 64.8 years;154 females, 46 males.	Behavioral graded activity program (n=97) vs. usual care for 12 weeks and a maximum 18 sessions, then up	Follow- up at baseline, 13, 39 and 65 weeks.	VAS pain (baseline/change at 13 weeks/65 weeks): BGA 4.3±2.8/-0.61/-1.01 vs. UC 3.7±2.5/-0.47/-0.58. WOMAC pain scores and	"Because both interventions resulted in beneficial long-term effects, the superiority of (behavioral graded activity program) over	Cluster randomization by physical therapist. Baseline data somewhat worse disease in usual care group. Many

						to 5 booster sessions (n=103).		WOMAC physical function subscales not different between groups. Patient global assessments % improved (13 weeks/65 weeks): BGA 41/56 vs. UC 36/49 (NS).	(usual care) has not been demonstrated. Therefore, BGA seems to be an acceptable method to treat patients with hip and/or knee OA, with equivalent results compared with UC."	protocol deviations. Data suggest behavioral graded exercise program ineffective compared with usual care.
Alkatan, 2016 (Score=4.0)	Aerobic exercises	RCT	No mention of sponsorship or COI.	N=48 middle aged or older individuals lived in sedentary life.	Mean age: 60 years; 4 males, 44 females	Patients assigned to cycling group (n=24) vs. Patients assigned to swimming group (n=24).	No mention of follow-up period.	Visceral adiposity, body mass, waist and hip circumference in exercise intervention groups were decreased after 12 weeks ($p<0.01$). The difference of magnitude of reductions in the training groups ($p=0.13$). Joint pain, functional limit and stiffness reduced in two groups measured by WOMAC index ($p<0.001$).	"Regular swimming exercise reduced joint pain and stiffness associated with OA and improved muscle strength and functional capacity in middle-aged and older adults with OA. Additionally, the benefits of swimming exercise were similar to the more frequently prescribed land-based cycling training."	Data suggest significant improvements in muscle strength with reduction in joint stiffness and pain with regular swimming or cycling.
Bossen, 2013 (Score=3.5)	Aerobic exercises	RCT								Data suggest at 12 months the intervention group showed higher objective and subjective outcomes involving physical activity.
Wang, 2006 (Score=3.5)	Aerobic exercises	RCT								Sparse methodological details. Data suggest short term improved knee and hip flexibility

										strength & aerobic fitness but did not provide pain relief.
Allen, 2017 (Score=3.0)	Aerobic exercises	RCT								Usual care bias. Data show no difference between groups.

Evidence for use of ergonomic interventions to prevent/facilitate recovery from hip or groin disorders

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Ergonomic interventions; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 36 in Scopus, 0 in CINAHL, 11 in Cochrane Library, 373 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic studies met the inclusion criteria.

Evidence for use of stretching exercises for Hip OA

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: stretching, muscle stretching, stretching exercises, stretching exercise, muscle stretching exercises, stretch, flexibility, flexibility, exercise, exercises, flexible, stretching, passive, static, static passive, relaxed, relax, isometric, active, static active, ballistic, dynamic, proprioceptive neuromuscular facilitation, PNF, specific stretching; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 21 articles in PubMed, 311 in Scopus, 30 in CINAHL, 92 in Cochrane Library, 40 in Google Scholar, and 3 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 8 articles considered for inclusion, 3 randomized trials and 1 systematic studies met the inclusion criteria.

Evidence for the Use of Stretching Exercises

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:

Hoeksma 2004 (Score=8.0)	Exercise for Osteoarthrosis	RCT	No mention of sponsorship or COI.	N = 109 Hip OA	Mean age: 71.5 years; 76 females, 33 males.	Manual therapy (stretching, manipulation and mobilization of hip joint) (n=56) vs. exercise program (tailored to patients' needs). Both 2 times a week for 9 treatments (n=53).	Follow-up at baseline, 5 to 29 weeks.	Percent improved after 5 weeks 81% manual therapy vs. 50% exercise, p <0.05. SF-36 (baseline/week 29): manual therapy (41.1±18/ 51.4±22) vs. exercise (37.9±18/49.9±24), NS. Harris hip scores manual (54.0±15/70.2±20) vs. exercise (53.1±14/59.7± 18), p <0.05. Pain scores at rest not significant. Pain scores walking favored manual therapy (p <0.05).	"The effect of the manual therapy program on hip function is superior to the exercise therapy program in patients with OA of the hip."	Exercise program unstructured. Manual therapy group also included advice to exercise, potentially confounding results and impairing an ability to draw a firm conclusion.
Svege 2016 (Score=6.5)	Stretching Exercises	RCT	No mention of COI. Sponsored by EXTRA funds from the Norwegian Foundation for Health and Rehabilitation, through the Norwegian Rheumatism Association, and by Oslo University Hospital.	N = 109 with hip pain for 3 months, radiographically verified minimum joint space via Danielsson's criterion, and a Harris Hip Score between 60 and 95 points	Mean age: 57.81 years; 50 males, 59 females.	All attended a patient education program (3 group sessions over 3 weeks, led by physical therapists). Then randomized into either exercise group, 2 to 3 times per week for 12 weeks, with being	Follow-up at 4, 10, and 29 months.	No significant group differences in range of motion, muscle strength, predicted maximal oxygen consumption, or distance in the six-minute walking test (6MWT) during follow-up period. Less pain during 6MWT in exercise group compared to control at 10 months (mean difference = -8.5	"The previously described effect of exercise on self-reported function was not reflected by beneficial results for ROM, muscle strength, physical fitness, and walking capacity, but exercise in addition to	Secondary analysis. Data suggest at 29 months no significant difference between groups for self-reported function but combined exercise and PE appears to decrease pain from walking. High drop out and non-

						supervised by physical therapist once a week (n=55) vs control group (n=54)		mm; 95% confidence interval = -16.1, 0.9) and 29 months (-9.3 mm; 95% CI = -18.1, -0.6)	patient education resulted in less pain during walking in the long term."	compliance to exercise rates.
Lyngberg 1994 (Score=6.0)	Exercise for Rheumatoid Arthritis	RCT	Sponsored by Danish Rheumatism Association, Grosserer A. V. Lykfeldt Foundation, and P. Carl Petersen Foundation. Authors declared no COI.	N = 24 RA with low dose steroids for 2 years	Mean age: 67 years; 22 females, 2 males.	Progressive interval training – aerobic with ergometer – bicycling and strengthening exercises, stretching trained muscles twice a week, 45 minutes for 3 months (n=12) vs. no program (n=12).	No mention of follow-up.	Tended towards lower tender joints with exercise. Changes in medication use NS. Borderline reduction in number of swollen joints (p = 0.06). ESR (baseline/post): training (33/22) vs. control (17/23) favored treatment p = 0.13.	"Individually adapted exercise programs can therefore be recommended for elderly rheumatoid arthritis patients on steroid treatment."	Data suggest physical training in elderly, fragile patients does not increase RA disease activity measured by blinded assessor. ESR reduced with exercise compared with controls.

Evidence for strengthening exercises for the treatment of hip OA

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: endurance training, tolerance training, exercise tolerance, strengthening exercise, weight lifting, weight bearing, weight, lifting, bearing; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthritis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 59 articles in PubMed, 101 in Scopus, 44 in CINAHL, 0 in Cochrane Library, 70 in Google Scholar, and 8 from other sources. We considered for inclusion 2 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 8 from Google Scholar, and 8 from other sources. Of the 20 articles considered for inclusion, 10 randomized trials and 10 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Graded exercise; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 15 articles in PubMed, 1 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 10400 in Google Scholar, and 1 from other sources. We considered for inclusion 4 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 5 articles considered for inclusion, 3 randomized trials and 1 systematic studies met the inclusion criteria.

Evidence for the Use of Strengthening Exercises

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Svege 2015 (Score= 5.5)	Strengthening Exercise	RCT	No COI. Sponsored by the former science council at Ullevaal University Hospital, Oslo, and the EXTRA funds from the Norwegian Foundation for Health and Rehabilitation through the Norwegian Rheumatism Association.	N = 109 with hip pain for 3 months, radiographically verified minimum joint space via Danielsson's criterion, and a Harris Hip Score between 60 and 95 points	Mean age: 57.81 years; 50 males, 59 females.	Exercise therapy, two to three times each week for 12 weeks, with training diareies completed weekly (N=55) vs Non-intervention group (N=54)	Follow-up at 4, 10, 16, and 29 months.	22 patients from exercise group and 31 from control group underwent total hip replacement (THR) between 3.6 to 6.1 years during follow-up period (median time to THR for exercise group – 5.4 years and for control group – 3.5 years). Cumulative 6-year survival of native hip to THR via Kaplan–Maier curve: 0.41 in exercise group, 0.25 In control group (p=0.034).	"Our findings in this explanatory study suggest that exercise therapy in addition to patient education can reduce the need for THR by 44% in patients with hip OA."	Data suggest education bomined with exercise may reduce subsequent THA. Group differences at baseline, specifically the exercise group, had better hip function.
PIster 2010 score = (5.0)	Strengthening Exercise	RCT	No mention of sponsorship. No COI.	N = 200 with hip and or Knee osteoarthritis.	Mean age: (65 years). 45 males, 154 females.	Experimental group; received behavioral exercise program including individually-tailored exercise to	Follow up at week 18, 25, 34, 42, and 55.	Adherence higher in the experimental group vs control group at 13 weeks (OR 4.3, 95% CI 2.1 to 9.0), at 65 weeks (OR 3.0, 95% CI 1.5 to 6.0). More experimental vs control group met recommendations for physical activity at 13 weeks (OR 5.3, 95% CI 1.9 to 14.8) and at 65 weeks (OR 2.9, 95% CI 1.2 to 6.7).	"Behavioral graded activity results in better exercise adherence and more physical activity than usual care in people with osteoarthritis of	Usual care bias. Data suggest better exercise compliance both short and long term in intervention groups compared to usual care.

						reduce impairment limiting performance (n = 97) vs. Control group received standard care (n = 103)			the hip or knee, both in the short- and long-term."	
Juhakoski,2011 (Score= 4.5)	Strengthening Exercise	RCT	Sponsored by EVO-grant from Mikkeli Central Hospital. COI: authors declared no conflict of interest.	N=120 patients with hip osteoarthritis diagnosis.	Mean age: 66 years; 83 females, 35 males.	Patients had combined exercise and general practitioner care (n=60) vs. Patients had general practitioner care (n=58).	Follow-up from baseline for 2 years.	The combined exercise and GP care intervention reduced 20% in primary outcome WOMAC pain with standard deviation of 16.5mm. Statistical difference was found in exercise intervention on WOMAC pain (p=0.04).	"The mostly home-based exercise training programme provided in this study did not result in reduced hip pain during the 2-year follow-up period."	Data suggest home based exercise training in this study did not decrease hip pain during the 2-year follow-up period.
van Baar 2001 Score = (4.5)	Strengthening Exercise	RCT	Sponsorship by grant form Dutch Fund of Investigative Medicine of the Dutch Health Insurance Council. No mention of COI	N = 216 patients with hip of knee OA	Mean age: 67.9 years; 43 males, 157 females.	Exercise treatment; exercises for muscle functions, mobility, and coordination, elementary movement abilities locomotion abilities. (N = 98) vs control received general care (N = 102)	Follow-up at 12, 24, and 36 weeks.	At 24 difference in change between the two groups −11.5 (95% CI −19.7 to −3.3). At 36 weeks no differences between groups.	Beneficial effects of exercise decline over time and finally disappear.	Data suggest at 24 weeks the benefits of the treatment (exercise) group were diminishing in term of decreased pain and NASAID use and improved function.
Pisters 2010	Graded exercise	RCT	No mention of sponsorship. No COI.	N = 200 with hip and or	Mean age: (65 years). 45 males,	Experimental group; received	Follow up at 3, 9, 15,	Both treatments showed beneficial within-groups effects in	"No differences between treatment groups	Usual care bias. Study population of both hip and knee

score = (4.0)	(behavior al)			knee osteoarthritis	154 females.	behavioral exercise program including individually-tailored exercise to reduce impairment limiting performance (n = 97) VS Control group received standard care (n = 103)	months, and 5 years.	the long-term. In patients with knee OA no differences between treatments were found on the short-, mid-long and long-term. In patients with hip OA significant differences in favor of BGA were found at 3 months' (pain and physical performance) and 9 months' follow-up (pain, physical function, patients' global assessment and patient-oriented physical function). Furthermore, UC resulted in patients with hip OA in more joint replacement No significant differences between treatment groups in pain (-0.18 [-1.7;1.]), physical functions (-1.92 [-6.5;2.6]), and PGA (OR=.67 [0.3;1.4])	were found in the long-term on the primary outcome measures. Although more research is needed to confirm the study findings, the results indicate that BGA reduces the risk for joint replacement surgeries compared to UC in patients with hip OA, which probably can be explained by better outcome in favor of BGA in the short- and mid-long-term."	OA data suggest at 60 no difference between groups in long term efficacy.
Murphy, 2016 (3.5)	Graded exercise (behavior al)	RCT								Standard care bias. High dropout rate. Data suggest at 6 months, time based activity pacing was not sustained and outcome were not improved
Husby 2010 (Score= 3.5)	Strengthening Exercise									Standard care bias. Data suggest an approximate 30% increase in work efficiency 6 months and 12 months post early postoperative maximal strength

										training in those <60 years of age.
Okoro, 2016 (Score= 3.5)	Strengthening Exercise									High dropout rate.
Bossen 2013 (Score= 3.5)	Strengthening Exercise									Waitlist control bias. Data suggest at 12 months the intervention group showed higher objective and subjective outcomes involving physical activity.
Williams 2011 (Score= 3.5)	Strengthening Exercise									Data suggest minimal improvement in exercise, physical activity, fear avoidance beliefs and overall illness.
Steinhilber 2012 Score = (3.0)	Strengthening Exercise									Small sample. Half of PHSEP group dropped out.
Allen 2017 (Score= 3.0)	Strengthening Exercise									Cluster randomized RCT. Usual care bias. Data show no difference between groups.
Allen 2016 (Score= 2.5)	Strengthening Exercise									Cluster randomization. Usual care bias. Data from self reported questionnaire patients with either hip or knee OA.

										Data suggest that there may be modest improved outcome in a combination patient and provider management approach for hip or knee OA.

Evidence for aquatic therapy for patients with hip osteoarthrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: aquatic therapy, pool therapy, swimming, aqua therapy, hydrotherapy, Ai Chi, Aqua running, Bad Ragaz Ring Method, Watsu, deep water exercise, deep water exercises, shallow water exercise, shallow water exercises; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 36 articles in PubMed, 613 in Scopus, 9 in CINAHL, 73 in Cochrane Library, 590 in Google Scholar, and 0 from other sources. We considered for inclusion 7 from PubMed, 1 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 10 from other sources. Of the 20 articles considered for inclusion, 12 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for the Use of Aquatic Therapy

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Hinman 2007 (score= 8.0)	Hydrotherapy	RCT	No conflict of interest stated. Sponsored by a National Arthritis and Musculoskeletal Conditions Improvement grant from the Australian Government Department of Health and Aging.	N = 71 Hip or knee OA	Mean age: 62.4 years; 23 males, 48 females	Aquatic physical therapy: (n=36) received (45-60 minute sessions, twice weekly) of aquatic physical therapy vs. Control Group: (n=35) received no aquatic physical therapy for 6 weeks.	6, 12 weeks	WOMAC pain scores (baseline/6 weeks): aquatic (202±79/ 143±79) vs. controls (199±85/ 198±108), p <0.001. VAS pain with movement (p = 0.003), WOMAC stiffness (p = 0.007), WOMAC function (p <0.001) all favored aquatic therapy.	"[A] 6-week program of aquatic physical therapy results in small improvements in pain, stiffness, hip strength, and quality of life in people with hip OA or knee OA compared with no intervention."	Data suggest aquatic therapy program superior to no aquatic therapy program, although study design is biased towards intervention as controls had no intervention.
Foley 2003 (score= 6.5)	Hydrotherapy	RCT	No mention of sponsorship of COI.	N = 105 Hip and/or knee OA	Mean age: 70.9±8.8 years; 53 males, 52 females	Hyrdotherapy: (n=35) received exercise in water including walking and strengthening exercises vs. Gym: (n=35) received in gym exercise including cycling and other strengthening exercise vs. Control: (n=35) received no-exercise and a phone call to record changes in condition, drug use, or injuries.Exercise sessions 3 a week for 6 weeks.	6 weeks	WOMAC function (baseline/ follow-up): hydro (34.0/ 33.0) vs. gym (28.0/27.0) vs. control (37.0/37.0). No differences in pain and most other measures. Walking speed and distance improved significantly from baseline in both exercise groups, p <0.001. Increases in some strength measures in both exercise groups. Stated decline in WOMAC from baseline in hydrotherapy, but data do not support a change (both 10.0).	"[B]oth the gym and hydrotherapy interventions produce positive functional outcomes for patients with OA."	Some baseline differences with less distance walked in hydrotherapy (257m) vs. gym (336m) vs. control (388m). WOMAC function also different. Graphic data support increases in distance walked and walking speed.

Wang 2002 (score= 5.0)	Hydrotherapy	RCT	No conflict of interest is stated. Sponsored by the Biobehavioral Nursing Research Training grant, the Women's Health Nursing Research Training grant, the Hester McLaw Nursing Scholarship, and the deTornyay Center for Health Aging Scholarship from the University of Washington.	N = 28 Patients scheduled to undergo hip arthro-plasty	Mean age: 67.1 years; 6 males, 32 females	Exercise Group: (n=15) received hydrotherapy, stationary bike riding, resistive exercises, 2 home sessions, week of strengthening and flexibility (2 1-hour sessions a week for 8 pre-op weeks vs. Control Group: (n=13) received usual peri-op care. All given post-op exercises during Weeks 3-12, with some to Week 24.	Follow up was conducted after the 12 week program and tested knee extension, flexion, hip extension, flexion, abduction, and adduction	Mean walk distances (Week 12/Week 24): exercise (503.7/549.7m) vs. controls (450.2/485.1m), p = 0.061. Numbers of steps per minute, stride length, gait velocity all comparable at baseline, but favored exercise group at Weeks 3, 12, 24.	"[P]erioperative customized exercise program(s) are well tolerated in the elderly patient with endstage hip arthritis and are effective in improving the rate of recovery in ambulatory function in the first 6 mo after total hip arthroplasty."	Data suggest short term benefits for aquatic exercise for hip or knee OA improving flexibility, strength and aerobic fitness but does not appear to decrease pain. Sparse methodological details. Data suggest short term improved knee and hip flexibility strength and aerobic fitness, but did not provide pain relief.
Stener-Victorin 2004 (score= 5.0)	Hydrotherapy	RCT	Sponsored by Research and Development Unit, Västra Götaland, Sweden. No mention of COI.	N = 45 Hip OA	Mean age: 67.2 years; 18 males, 27 females	Electro-acupuncture (most painful hip area, 4 of BL54, 36, GB29, 30, 31 and ST31; and distal points GB34, BL60) plus education (2x2-hour meetings) (n=15) vs. hydrotherapy (warm-up, mobility, strengthening) plus education (n=15) vs. education alone for 30 minute	1, 3, 6 months	Pain related to motion and on load (baseline/after 10 treatments/3 months/6 months): EA (37/22/ 24/17) vs. hydrotherapy (55/35/ 25.5/28) vs. control (56/--/48.5/ 59), p <0.05 comparing EA and hydro at 3 months to baseline and EA vs. baseline at 6 months. Disability rating index: EA (36/28/ 33.5) vs. hydro (45/23.5/26.5) vs. control (43/--/45). Daytime	"EA and hydrotherapy, both in combination with patient education, induce long-lasting effects, shown by reduced pain and ache and by increased functional activity and quality of life, as demonstrated	Small sample sizes and high dropouts by 6 months. Trial had multiple interventions, thus attribution of benefits to any one intervention difficult. Use of educational intervention as control might bias in favor of intervention.

						appointments, 10 times over 5 weeks (n=15).		ache improved in EA and hydrotherapy for 3 months. Night-time ache reduced 3 months with hydrotherapy vs. 6 months EA. Quality of life improved in EA and hydrotherapy groups up to 3 months after last treatment. No changes in education group alone.	by differences in the pre- and post-treatment assessments."	
Sylvester 1990 (score= 4.5)	Hydrotherapy	RCT	No mention of sponsorship or COI.	N = 14 Hip OA	Mean age: 66 years; 5 males, 9 females	Group A: (n=7) received a 6 week course of hydrotherapy (2-1/2 hour sessions a week) vs. Group B: (n=7) received a 6 week course of diathermy and supervised exercises (same exercises as in pool) for (2-1/2 hour sessions a week)	6 weeks	VAS pain (median pre/post treatment): hydrotherapy 78/41 vs. 83/51. Oswestry questionnaires: hydrotherapy 49/27 vs. 67/58.	"Functional ability had improved in the group treated by hydrotherapy ($p<0.05$, who also reported a higher score on the life satisfaction scale…It would be of interest to expand this study to include a greater number of subjects in order to attempt to validate the use of hydrotherapy in this patient population."	Small sample size. Pilot study. Both groups improved markedly on VAS but hydrotherapy improved more.
Schenck ing 2012 (score= 4.5)	Hydrotherapy	RCT	Sponsored by grants from the Otto-Schönfisch Foundation, Bad Wörishofen, Germany. No COI.	N=30 hip or knee OA	Mean age: 73.37±10 years; 10 males, 20 females	Hydrotherapy Group 1 (n=10) received hydrotherapy daily and some soft massage techniques 3 times/week vs Physiotherapy Group 2: (n=10) received 30 min of joint-related stretching elements, muscle strengthening,	2, 10 weeks	Results for SF-36 physical score is group 1 +8.0%, group 2 13.5%, group 3 +7.2%, and for mental score; group 1 -6.3%, group 2 +9.1%, and group 3 +12.2%. For lequense test	"The results of this pilot study demonstrate beneficial effects of hydrotherapy. The study design is feasible. For statistically significant evidence and a robust conclusion	Pilot RCT. Small sample (n=30). Data suggest benefit of hydrotherapy for OA.

						and resistance exercises 3 times/week vs Combined hydro-physiotherapy Group 3: (n=10) received joint-related alternate thigh affusions daily and joint-specific physiotherapy 3 times/week			of efficacy of Kneipp's hydrotherapy, a larger sample size is necessary."	
Liebs 2012 Hip Study (score= 4.0) Knee Study (score= 4.0)	Hydrotherapy	2 RCTs	Sponsored by the Society for Support of Research in and Fighting of Rheumatic Diseases Bad Bramstedt, the Society for Support of Rehabilitation Research in Schleswig-Holstein, the State Insurance Agency of the Free and Hanseatic City of Hamburg, and the German Arthrosis Society. No COI.	N=465 undergoing primary THA (n=280) or TKA (n=185)	Mean age: 68.7 years; 156 males, 309 females	Hip Arthroplasty: Early Aquatic Therapy: (n=138) received aquatic therapy after 6th postoperative day for 30 min sessions 3 times/week vs Late Aquatic Therapy: (n=142) received aquatic therapy on the 14th postoperative day for 30 min sessions 3 times/week Knee Arthroplasty: Early Aquatic Therapy: (n=87) received aquatic therapy after 6th postoperative day for 30 min sessions 3 times/week vs Late Aquatic Therapy: (n=98) received aquatic therapy on the 14th postoperative day for 30 min sessions 3 times/week	3, 6, 12, 24 months	Post hip arthroplasty showed effect size for primary outcome ranged from .01 (3 months, p=0.8) to 0.19 (6 months, p=0.52). Post knee arthroplasty showed better mean outcomes for early aquatic therapy group at 3, 6, 12, and 24 months. WOMAC stiffness score for late aquatic therapy group at 12 months was better (effect size=.03). Effect sizes for primary outcome WOMAC physical function ranged from .22 at 6 months (p=0.45) to .39 at 24 months (p=.12).	"Early start of aquatic therapy had contrary effects after TKA when compared with THA and it influenced clinical outcomes after TKA. Although the treatment differences did not achieve statistically significance, the effect size for early aquatic therapy after TKA had the same magnitude as the effect size of nonsteroidal anti-inflammatory drugs in the treatment of osteoarthritis of the knee. However, the results of this study do not support the use of early aquatic therapy after THA. The timing of	Data do not support early aquatic therapy post THA but there was a trend for improved outcomes for TKA.

									physiotherapeutic interventions has to be clearly defined when conducting studies to evaluate the effect of physiotherapeutic interventions after TKA and THA."	
Minor 1989 (Score= 4.0)	Hydrotherapy	RCT	Sponsored by NIH grant (AM-20658) and Department of Education award (H133_b80075). No mention of COI.	N = 120 OA (hip, knee, or tarsal) or RA	Mean age: 60.6 years; 98 females, 22 males.	Pool Group: (n=38) received aerobic aquatic exercise for 1 hour, 3 times/week, for 12 weeks vs Walk Group: received aerobic walking exercise for 1 hour, 3 times/week, for 12 weeks (n=28) vs ROM Group: (n=28) received range of motion exercise classes, 1 hour sessions, 3 sessions a week for 12 weeks. Both aerobic groups targeted 60-80% of HR Maximum for 30 minutes.	Follow-up at baseline, 3 and 9 months.	Aerobic capacity (baseline/ 12 weeks): walk (18.9±4.8 /22.4±4.8mL/kg/minutes) vs. pool (19.3±6.7/23.2± 7.2) vs. ROM (17.4±5.9/ 17.3±3.6) (p = 0.009 comparing walk plus pool vs. ROM). AIMS pain scores (baseline/12 weeks): walk (5.1±1.9/3.9±1.9) vs. pool (5.0±1.6/4.4±1.7) vs. ROM (5.5±1.6/4.8±1.9) (p = 0.22). Active joints (n): aerobic OA -2.0±5.2 vs. ROM (-1.8±5.9). Active RA joints aerobic (-6.8± 11.8) vs. ROM (3.3±10.9).	"Our findings document the feasibility and efficacy of conditioning exercise for people who have rheumatoid arthritis or osteoarthritis."	Data suggest efficacy of walking or pool exercise for arthritis patients. Targeted 60-80% HR maximum in walking/pool groups. Improve greater OA vs. RA for exercise endurance but better for total active RA joints. Both appear to benefit. Suggests aerobic exercise reduces active RA joints.
Alkatan M. 2015 (score= 4.0)	Hydrotherapy	RCT	No mention of sponsorship or COI.	N=48 with hip OA	Mean age: 60 years; 4 males, 44 females	Cycling group: (n=24) received active cycling training for a few weeks, 20-30 min/day, 3 days/week at 40-50% HRR for duration of 12	12 weeks	There is an improvement in all categories for both cycling and swimming groups. Before and after results for swimming are: Pain (0-20) 6.9 ± 0.7 vs 4.2 ± 0.5, stiffness (0-	"Regular swimming exercise reduced joint pain and stiffness associated with OA and improved	Data suggest significant improvement in muscle strength with reductions in joint stiffness and pain with

						weeks vs Swimming Group: (n=24) received active swimming training for a few weeks, 20-30 min/day, 3 days/week at 40-50% HRR for duration of 12 weeks		8) 3.8 ± 0.3 vs 2.6 ± 0.3, and Functional limitation (0–68) 20.9 ± 2.1 vs 11.7 ± 1.9.	muscle strength and functional capacity in middle –aged and older adults with OA. Additionally, the benefits of swimming exercise were similar to the more frequently prescribed land-based cycling training."	regular swimming or cycling.
Hale 2012 (Score= 3.5)										Likely underpowered (n=39) data suggest lack of efficacy.
Fagnani 1998 (score= 3.0)										Non-blinded, no control for co-interventions as to allow standard practice and evaluate standard therapies. Mixture of therapies questionable. If control group received more of same that previously failed, then study likely biased in favor of intervention.
Cochrane 2005 (1.5)										Abstract only. Compliance low, and dropped in subsequent 6 month period to 18%.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Hartman 2000 (score=4.0)	Tai Chi	RCT	No sponsorship mention. COI, Julia Chevan, MPH,OCS, and Lind J. Tsoumas, MS, PT, of Springfield College for their insight during each phase of study, Dr. David Pier angelo facilitation participant recruitment, and the 33 participant for dedication to study.	N= 33 Participants with lower extremity osteoarthritis.	Mean age: 68 years; 5 males, 28 females.	T'ai Chi Group (n=18): consisted of two 1 hour T'ai Chi classes per week. Vs. Control Group (n=15): participants instructed to continue their usual physical activities and routine care procedure.	No mentioned of follow up	Self-efficacy for arthritis symptoms showed a significant (P = .012) group by time interaction, with the T'ai Chi group having a significant (P = .000) improvement and the control group experiencing no significant (P = .623) change. Significant improvement (P< 0.05) in T'ai Chi participants in self-efficacy for arthritis symptoms, total arthritis self-efficacy, satisfaction with general health and level of tension.	"A moderate T'ai Chi intervention can enhance arthritis self-efficacy, quality of life, and functional mobility among older adults with osteoarthritis. T'ai Chi training is a safe and effective complementary therapy in the medical management of lower extremity osteoarthritis."	Data suggest Tai Chi improved quality of life and self-efficacy.
Fransen 2007 (score= 4.0)	Tai Chi	RCT	No sponsorship mentioned: COI, hydrotherapy physiotherapists (Guni Hinchey, Kim Walker, Cathy Brand, and Khim Kwan) and the Tai Chi trainers (Joan Peters, Pat Weber, Fiona Black, and Jenny Alfonso). Lai-Hoong Wong kindly allowed	N=152 Patients with symptomatic OA of the hips or knees.	Mean age: 70.1; 42 males, 112 females.	Hydrotherapy classes (n=55) for 1 hour, twice a week for 12 weeks Vs. Tai Chi classes (n=56) for 1 hour, twice a week for 12 weeks Vs.	Follow up at baseline, 12 weeks, and 24 weeks.	Treatment effect for physical function was moderate for both hydrotherapy and Tai Chi classes (SRM 0.62; 95% CI 0.49, 0.75 and SRM 0.63; 95% CI 0.50, 0.76, respectively) compared with the control Group hydrotherapy classes resulted in significant improvement in pain scores, with a small treatment	"Access to either hydrotherapy or Tai Chi classes can provide large and sustained improvements in physical function for many older, sedentary individuals with chronic hip or knee OA."	Data suggest both hydrotherapy and Tai Chi may improve OA pain and function in sedentary OA patients with hydrotherapy being better than Tai Chi for joint pain improvement.

			the use of the physiotherapy department facilities at St George Hospital.			Waiting list Control Group (n=41): Same schedule after completion of the 12-week waiting list period.		effect (SRM 0.43; 95% CI 0.30, 0.56) compared with the control group (25)		
Zeng 2014 (score= 3.5)										Data suggest no significance difference between groups for improved pain or side hip motion although the TCST group had improved balance and aerobic capacity
Song 2010 (score=3 .5)										Data suggest at 6 months, T'ai Chi groups had improved muscle strength.
Song 2002 (score=2 .0)										High dropout rate.

Evidence for the Use of Gait Training

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Mejjad 2000	Gait Training	Randomized Crossove	No mention of sponsorship or COI.	N = 16 Unilateral hip OA	Mean age: 61±11 years; 8	Etodolac 300mg (n=8) vs. placebo one dose.	7 days	Walking speed increased significantly between t0 and t180 under etodolac	"[W]alking speed increased under etodolac, but not	Small sample size. Suggests drug had

(score= 7.5)		r Experim ental Trial			males, 8 females	Assessed effects on gait (n=8).		but not placebo (p <0.0004). Cadence expressed in cycles/min, did not differ. VAS scores decreased between t0 and t180 for etodolac and placebo groups (p <0.0009 and p <0.03, respectively).	placebo…conclude that gait improvement was closely associated with the administration of a single, oral 300mg dose of etodolac. Three hours after taking a single tablet, gait was improved.	positive effect on gait in 3-hour experiment.
Bennell, 2014 (score= 6.0)	Gait Training	RCT	Sponsored by National Health and Medical Research Council, Australian Research Council Future Fellowship, and Australian National Health and Medical Research Council Practitioner Fellowship. COI: One or more of the authors have received benefits for personal or professional use.	N = 102 patients with hip osteoarthri tis related pain.	Mean age: 62.3 years; no mention of sex.	The active group with baseline mean visual analog scale score of 58.8mm (13.3) (n=49) vs. The sham group with baseline mean visual analog scale score of 58.0mm (11.6) (n=53).	Follow-up from 2010 May to 2013 Feb, 24 weeks.	Two primary outcomes improved in both groups. Average pain score in active group was improved for 17.7mm, and 22.9mm in sham treatment group. Physical function was improved in active group for 5.2 units, and 5.5 units in the sham treatment group.	"Among adults with painful hip osteoarthritis, physical therapy did not result in greater improvement in pain or function compared with sham treatment, raising questions about its value for these patients."	Data suggest lack of efficacy.
Sherrin gton 2003 (score= 5.5)	Gait Training	RCT	Sponsored by Health Research Foundation Sydney South West and the Arthritis	N = 80 All had hip fracture from a fall and in inpatient	Mean age: 81±8 years; 26 males, 54 females	Two week programs of daily weight-bearing exercise program (n=41) vs. non-weight-bearing (exercises same as Sherrington 2004 above) (n=39). All received	2 weeks	Physical performance and mobility examination scores (pre/post): weight bearing (5.4/7.5) vs. non-weight bearing (4.5/6.8) NS. Gait (m/s): weight bearing (0.12/0.25) vs. non-	"Weight-bearing and non-weight-bearing exercise programs produce similar effects on strength, balance, gait and functional performance among	Trial length of only 2 weeks and co-interventions of exercises with both weight-bearing appear likely to have reduced possible differences.

			Foundation. No mention of COI.	rehabilitation		practice with walking and advancement with walking aids.		weight-bearing (0.09/0.19), NS. Strength measures not different between groups. Ability to walk with either 1 stick or no aid 20% vs. 5%, p <0.05.	inpatients soon after hip fracture."	Walking ability favored weight bearing exercise group.
Weber, 2016 (score= 5.0)	Gait Training	RCT	Sponsored by DePuy International, Leeds, UK, and Technologie und Wissenschaftsnetzwerk Ostbayern. No mention of COI.	N=120 patients with no previous hip trauma nor prior THR; N=64 for intervention group.	Mean age: 61years; 31 females, 29 males.	Computer assisted femur first THR group (n=28) vs. Conventional THR group (n=32)	2 follow-ups: one for 6 months, and another one for 12 months.	No significant differences were find between comparison groups. Parameters increased during follow-up for comparison groups, but with no differences between groups.	"Patients undergoing CAS FF showed a trend to improved hip flexion angle indicating a possible long-term benefit."	Data suggest a trend towards the improvement of hip flexion angle at 6 months and 12 months post intervention.
Wang 2002 (score= 5.0)	Gait Training	RCT	No mention of sponsorship or COI.	N = 28 Patients scheduled to undergo hip arthro-plasty	Mean age: 67.1 years; 10 males, 18 females	Exercises (2 1-hour sessions a week for 8 pre-op weeks of hydrotherapy, stationary bike riding, resistive exercises, 2 home sessions, week of strengthening and flexibility) (n=15) vs. controls with usual peri-op care. All given post-op exercises during Weeks 3-12, with some to Week 24 (n=13).	24 weeks	Mean walk distances (Week 12/Week 24): exercise (503.7/549.7m) vs. controls (450.2/485.1m), p = 0.061. Numbers of steps per minute, stride length, gait velocity all comparable at baseline, but favored exercise group at Weeks 3, 12, 24.	"[P]erioperative customized exercise program(s) are well tolerated in the elderly patient with endstage hip arthritis and are effective in improving the rate of recovery in ambulatory function in the first 6 mo after total hip arthroplasty."	Small sample sizes. Suggests perioperative exercise has short term benefits with differences lasting to 6 month duration of observations.
Tinetti 1999 (score= 4.5)	Gait Training	RCT	Sponsored by the Claude D. Pepper Older Americans Independence Center grant from the	N = 304 27 home care agencies All had had surgical repair of hip fracture	Mean age:79.9 years; 55 males, 249 females	Home-based multicomponent rehabilitation program (n=148) vs. usual care; multi-component program included identification of deficits and tailoring PT program	12 months	Regaining prefracture level of self-care ADLs at 6 months: multicomponent rehabilitation 71% vs. usual care 75%, p = 0.40. Complete independence 67% vs. 71% (p = 0.49). Complete ADL	"The systematic multicomponent rehabilitation program was no more effective in promoting recovery than usual home-based rehabilitation."	Large size and multiple agencies may improve generalizability of results, however dropouts high. Suggests multi-component

			National Institute on Aging. COI: Dr. Marottoli was supported as a Career Development Awardee from the Veterans Administration. Dr. Gill was supported as a Pfizer Scholar, a Paul Beeson Scholar, and a Robert Wood Johnson Generalist Physician Scholar.			plus functional therapy; usual care included home PT (n=156).		independence at 6 months 9% vs. 16%, p = 0.07 and 12 months 19% vs. 25%, p = 0.23. No differences in mobility, balance of lower extremity strength. Gait performance at 6 months favored rehabilitation program (p = 0.08).		rehabilitation program not superior to usual care.
Sherrington 1997 (score= 4.0)	Gait Training	RCT	No mention of sponsorship. No COI.	N = 42 All hip fracture mean 7 months earlier	Mean age: 78.6 years; no mention of sex.	Home exercise program (step exercises) (n=20) vs. no exercise controls (n=20); 1 follow-up visit at 1 week	1 month	Quadriceps strength improved (baseline/post-test): exercise (7.7±4.6kg/10.4±4.9, p <0.01) vs. no exercise (6.6±2.7kg/7.3±3.7, NS). Gait velocity: exercise (0.46±0.28/0.51±0.34 m/s, p <0.05) vs. no exercise (0.52±0.33/0.50±0.35, NS).	"This exercise program improved strength and mobility following hip fracture. Further research is needed to ascertain whether the extent of this improvement in these fall risk factors is sufficient to prevent falls."	Baseline differences of uncertain effect. Suggests home exercise program of step exercises is effective.
Unlu 2007 (score= 4.0)	Gait Training	RCT	No mention of sponsorship or COI.	N = 26 1-2 years after hip arthroplasty	Mean age: 51.7 years; 8 males, 18 females	Group 1 (home exercise program) (n=9) vs. group 2 (PT supervised hospital based program) (n=8) vs. group 3 (control) (n=9).	12-24 months	Improvements in gait speed (pre/post): group 1 (67.8±23/74.4±24) vs group 2 (48.5±4/56.7±5) vs. group 3 (58.0±12/59.8±14). Maximum isometric	"[B]oth home and supervised exercise programmes are effective one year after total hip arthroplasty. Home exercise	Small sample sizes. Suggests improvements in either home exercise or supervised training groups. No clear

								abduction torque group 1 (30±12/38±11 ft-lbs.) vs. group 2 (18±10/30±9.8) vs group 3 (18±10/19±8).	programmes with close follow-up could be recommended."	functional advantage of supervised program.
Eitzen, 2015 (score= 3.5)	Gait Training	Secondary analysis of RCT								Data suggest lack of efficacy.
Husby, 2010 (score= 3.5)	Gait Training	RCT								Standard care bias. Data suggest an approximately 30% increase in work efficiency 6 months and 12 months post early postoperative maximal strength training in those <60 years of age.
Sonne-Holm 1982 (score= 3.5)	Gait Training									Author suggests patients and observers were blinded. Lack of methodology details.
Baker 1991 (score= 0.5)	Gait Training									Methods sparse; unclear if RCT; quasi-randomization. Intervention not described in detail. Analyses of strength included 12 of 18 subjects. Unclear if other analyses partial or complete. If an RCT, suggests treadmill superior to conventional training.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Bodoky 1993 (score=10 .0)	Antibiotics (Systemic and/or within Cement)	RCT	Sponsored by Ciba-Geigy, Basel, Switzerland; the authors declared no conflict of interest.	N = 239 Internal fixation with dynamic hip screw for hip fractures	Mean age: 76 years old; 55 males, 184 females.	Cefotiam 2gm at anesthesia induction and 12 hours later (n=124) vs. placebo (n=115)	Follow-up at least 6 weeks.	Major wound infections: 5% placebo (n = 6) vs. 1% (n = 1) antibiotics (p <0.05). No differences in pulmonary infection (9% vs. 6%). Urinary infections: 31/115 (18%) vs. 15/124 (12%). Pre-op albumin and operation duration most predictive of minor wound infections.	"The most powerful predictors of major wound infection were the duration of the operation, the interval between the accident and admission to the hospital, and the duration of postoperative urinary catheterization. The preoperative level of serum albumin and the absolute lymphocyte count were significant predictors (p<0.05) of minor wound infection and systemic infection, respectively."	Data suggest peri-operative antibiotics effective for reducing risk of major wound infections in hip fracture patients.
Gatell 1984 (score=8. 0)	Antibiotics (Systemic and/or within Cement)	RCT	No mention of sponsorship or COI.	N = 284 Any metal device inserted to be eligible (plates, screws, wires). No open fracture; no hip surgery; no joint replaceme nts	Mean age: 55.4 years; 116 males, 168 females.	Cefamandole 2gm IV 30 minutes before, 2gm 2 hours after start of operation, 1gm IV or IM 8, 14, and 20 hours later (n=134) vs. placebo (n=150).	Follow-up at 60, 115, and 132 weeks after roller traction, cerclage wiring and interlocking nail insertion, respectively.	Superficial wound infections in 0/ 134 (0%) patients given cefamandole vs. 7/150 (4.7%), p <0.05. Two deep-wound infections developed in cefamandole group vs. four controls (p >0.05).	"Cefamandole (five doses) reduced the rate of wound infection in patients undergoing clean orthopaedic surgery that required an internal fixation device."	Varied diagnoses. Does not apply to hip. Cefamandole appears prevent superficial wounds, but not deep infections. Mortality was higher in Cefamandole group unrelated to infection, although did not reach statistical significance.

Wahlig 1984 (score=7.0)	Antibiotics (Systemic and/or within Cement)	RCT	No mention of sponsorship or COI.	N = 30 67% OA, 10% fracture	Mean age: 60.4 years; 8 males, 22 females.	Hip replacement using antibiotic-loaded acrylic cement containing 0.5g (n=15) vs. 1.0g gentamicin base/ 40g polymer powder. No systemic antibiotics (n=15).	No mention of follow-up.	Gentamicin concentrations in drainage fluid higher than minimal inhibitory concentrations or minimal bactericidal concentration values necessary for usual pathogens. Serum levels acceptably low.	"[A]pproximately twice as much gentamicin is detectable in the urine and from suction drainage when one gram is added to 40g of powdered polymer… compared with the half gram used…While these pharmacokinetic results are conclusive, they do not prove whether or not one gram of half a gram of gentamicin added to the cement is more efficacious clinically."	Pharmacokinetic study without any clinical outcomes to indicate reduced infections.
McQueen 1987 (score=4.5)	Antibiotics (Systemic and/or within Cement)	RCT	No mention of sponsorship or COI.	N = 295 Hip or knee arthro-plasties	Mean age: 68 years old; 89 males, 185 females.	Cefuroxime in bone cement (1.5g mixed in 40gm CMW cement powder) (n=146) vs. cefuroxime 1.5gm IV at induction and 750mg Q6 hour x 2 (n=149)	No mention of follow-up.	21 infections in 3-month period (6.8%), 11 (7.5%) in cement vs. 6.7% parenteral (NS). Three deep infections, 1 in cement (0.7%) vs. 2 in parenteral (1.3%), (NS).	"Both methods of administering Cefuroxime appear to be satisfactory in the prevention of early infection after total joint replacement."	Data suggest equivalent efficacy for IV vs. antibiotic in the cement for prevention of infections.
Josefsson 1993 (score=4.0)	Antibiotics (Systemic and/or within Cement)	Ten-Year Survey RCT	No mention of sponsorship or COI.	N = 1688 85% OA, 6.8% fracture, 4.1% RA	Mean age: 70 years; 783 males, 905 females.	Prophylaxis with systematic antibiotics (not standardized) (n=835) vs. gentamicin bone cement (n=853).	Follow-up at 8.4 to 12.6 years, average 10.3 years.	During 10-year period, 585 hips developed signs of aseptic loosening of 1 or both components: 301 hips (55%) SA; 284 (50%) GBC. Christiansen prosthesis showed high (80%) loosening rate in both groups.	"[T]he differences between the SA and GBC groups found at both the two- and five-year reviews are no longer significant at ten years after surgery."	Methodology details sparse. Systemic antibiotics not standardized at start. Higher rates of aseptic loosening among systemic antibiotic group.

Josefsson 1990 (score=4.0)	Antibiotics (Systemic and/or within Cement)	Five-Year Survey RCT	No mention of sponsorship or COI.	N = 1,688 85% OA, 6.8% fracture, 4.1% RA	Mean age: 70 years; 783 males, 905 females.	Prophylaxis with systematic antibiotics (not standardized) (n=835) vs. gentamicin bone cement (n=853).	Follow-up at 5 years.	After 1-2 years follow-up, infection rates favored gentamicin cement. After 5 years, difference unaltered. Total 16 deep infections SA group (1.9%), 7 (0.8%) in gentamicin ($p < 0.05$). Roentgenographically, aseptic loosening 29% vs. 24% respectively, suggesting admixture of antibiotic did not weaken cement.	"The results of this five-year review clearly showed the prophylactic value of gentamicin cement against deep infection after THA but did not support the hypothesis that this effect was prolonged over one year."	2nd of 3 publications of this population. Participants increased from original. Methodology details sparse. Study demonstrated poor results of Christensen prothesis, which was "obsolete:" at time of this follow-up.
Josefsson 1981 (score=4.0)	Antibiotics (Systemic and/or within Cement)	RCT	No mention of sponsorship or COI.	N = 1,544 with hip OA, fracture, or RA	Mean age: 70 years; 783 males, 905 females.	Prophylaxis with systematic antibiotics (not standardized) (n=772) vs. gentamicin bone cement (n=772)	Follow-up at 5 years.	Systemic antibiotic: 49 (5.9%) vs. 71(8.3%) gentamicin cement with superficial infections. Difference statistically significant ($p < 0.05$). Deep infections favored gentamicin cement (0.4% vs. 1.6%, $p < 0.01$).	"The difference in deep infection frequency between the antibiotic and gentamicin group was statistically significant."	First of 3 publications on same group. Sparse methodological description weakens score. Systemic antibiotics not standardized. More superficial infections in cement group, but fewer deep infections.

Evidence for the Use of NSAIDs

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Zacher 2003 (score=11.0)	NSAIDs	RCT	Sponsored by a grant from Merck & Co Inc, Whitehouse Station, New Jersey, USA. No mention of COI.	N = 516 Knee or hip OA	Mean age: 63.0 years; 101 males, 415 females.	Etoricoxib 60mg QD (n=256) vs. diclofenac 50mg TID (n=260) for 6 weeks.	Follow up at baseline, 2, 4, 6 and 8 weeks	WOMAC pain subscale changes over 6 weeks: etoricoxib -31.3 (95% CI -33.6, -29.0) vs. diclofenac -30.9 (-33.2, -28.6) (NS). Other WOMAC scales NS. Percent patients good or excellent 65.6% vs. 66.5% (NS). Etoricoxib demonstrated greater benefit (good/excellent responses) first 4 hours after 1st dose (p = 0.007). GI adverse effects in E 12.9% vs. D 14.2%.	"Etoricoxib is clinically effective in the therapy of osteoarthritis providing an effect similar to the maximum dose of diclofenac."	Equivalency demonstrated with no significant difference in adverse effects.
Wagenitz 2007 (Score=10.0)	NSAIDs	RCT	Sponsored by Mepha Ltd in Aesch, Switzerland. COI: two authors have or will receive benefits for personal or professional use.	N = 210 Hip and/or knee OA	Mean age: 62.3 years; 71 males, 138 females.	Diclofenac 100mg in a SR-cap (n=104) vs. SR-tab QAM (n=105) for 14 days.	No mention of follow-up.	VAS pain scores (ITT) (baseline/Day 14): Cap 64.8±11.2/21.2±19.7 vs. Tab 63.8±11.0/27.7± 23.0. Total adverse events higher Tab group (39.0%) than Cap group (30.8%).	"Diclofenac was found to be clinically non-inferior to the reference formulation for reducing pain in patients with painful OA of the knee and/or hip."	Diclofenac in both formulations are effective for pain relief, but SR-capsule had modestly lower reported adverse effects.

Puopolo 2007 (score=10.0)	NSAIDs	RCT	Sponsored by Merck Research Laboratories. COI, Authors Boice,Ko, Cichanowitz, and Reicin are employees of Merck & Co., Inc., and own stock and/or hold stock options.	N = 548 Hip or knee OA	Median age: 63 years; 133 males, 415 females.	Etoricoxib 30mg QD (n=224) vs. Ibuprofen 800mg TID (n=213) vs. placebo (n=111) for 12 weeks. Double dummy.	Follow-up at 12 weeks after initial treatment.	WOMAC pain scores (baseline/12 weeks): etoricoxib 66.46/-28.14 vs. ibuprofen 64.74/-24.10 vs. placebo 64.66/-16.47. Both active treatments superior to placebo for multiple endpoints. Etoricoxib superior to ibuprofen at some time intervals after randomization. Post-hoc analysis for minimally clinically important improvement among 80.0% etoricoxib vs. 70.1% ibuprofen vs. 55.1% placebo.	"Treatment with etoricoxib 30 mg q.d. for the treatment of OA is well tolerated and provides therapeutic effectiveness that is superior to placebo and comparable to ibuprofen 2400 mg (800 mg t.i.d)."	High dropout rate in this 2-week study for adverse effects. Results suggest comparable efficacy.
Saag 2000 (score=9.5)	NSAIDs	RCT (2 trials)	Sponsored by Merck & Co. Inc. No mention of COI.	N = 736 Knee or hip OA	Mean age: 61.1 years; 188 males, 548 females.	Two trials: 1) Rofecoxib 12.5 QD (n=219) vs. 25mg QD (n=227) vs. ibuprofen 800 TID (n=221) vs. placebo (n=69) 6 weeks; 2) rofecoxib 12.5mg QD (n=231) vs. 25mg QD (n=232) vs. diclofenac 50mg TID (n=230) for 1 year.	Follow-up at 6 weeks and 1 year.	Study 1: rofecoxib superior to placebo (p <0.001) and comparable with ibuprofen for WOMAC pain, physical function, and stiffness subscales. Adverse effects placebo 5.8% vs. rofecoxib 12.5mg (5.5%), 25mg (6.6%), ibuprofen (4.1%). Discontinuation higher in placebo (27.5%, p <0.05). Rofecoxib 25mg produced marked improvement and comparable efficacy with diclofenac on WOMAC physical function, stiffness, pain subscales over 1-year treatment period. Rofecoxib 12.5mg was significantly different from diclofenac. Greater adverse effects with diclofenac (17.8%) vs. rofecoxib (8.7%, 10.3%). Discontinuance rates not different.	"Rofecoxib is effective in treating OA with once-daily dosing for 6 weeks and 1 year. Rofecoxib was generally safe and well-tolerated in OA patients for 6 weeks and 1 year."	Rofecoxib comparable with ibuprofen 800mg. Diclofenac similar to rofecoxib at 1 year

Bellamy 1992 (score=9.5)	NSAIDs	RCT	Sponsored by a grant from the Upjohn Company. No mention of COI.	N = 85 Hip or knee OA	Mean age: 58.0 years; 33 male, 52 female.	Flurbiprofen-SR 200mg (n=42) vs. diclofenac sodium-SR 100mg QHS (n=43) for 6 weeks	Follow up at enrollment, baseline, 3 and 6 weeks.	Joint pain on active movement at final assessment: flurbiprofen SR -0.83 (SE 0.13) vs. diclofenac-SR -0.91 (SE 0.13), p = 0.64. Other outcomes (e.g., pain on passive motion, joint swelling) NS. More drug-related adverse reactions in diclofenac sodium-SR (n = 15) than flurbiprofen-SR (n = 9), NS.	"Flurbiprofen-SR 200 mg is similar in efficacy, tolerability and safety to Diclofenac Sodium-SR."	Dosages were low, considered to be frequent starting doses for general population. Data suggest comparable efficacy.
Agrawal 1999 (Score=9.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 1,398 Hip or knee OA	Mean age: 62.2 years; 449 males, 949 females.	Upper GI safety of arthrotec 75 (diclofenac sodium 75mg misoprostol 200µg) BID (n=393) vs. nabumetone 1,500mg QD (n=426) vs. placebo (n=380) for 6 weeks.	No mention of follow-up.	Overall adverse events in 67% arthrotec vs. 61% nabumetone vs. 57% placebo. Final endoscopy showed lower combined incidence of gastric and duodenal ulcers Arthrotec 4% vs. nabumetone 11% (p <0.001). No significant differences in combined gastric and duodenal ulcers based on H pylori status among groups (p = 0.560).	"There appeared to be no consistent correlation between the presence or absence of H pylori infection and an increase or decrease in the overall incidence of ulcers associated with NSAID use."	Naproxen arm discontinued due to high incidence of ulceration rate (37%). Data suggest diclofenac/misoprostol effective at reducing gastric ulcers compared with nabumetone and naproxen.
Chan 2002 (Score=9.5)	NSAIDs	RCT	Sponsored by Chinese University of Hong Kong and Health Services Research Committee of Hong Kong. No mention of COI.	N = 290 RA, OA, and other forms of arthritis with ulcer bleeding	Mean age: 67.6 years; 126 males, 161 females.	Omeprazole 20mg plus amoxicillin 1g plus clarithromycin 500mg (n=143) vs. celecoxib 20mg and placebo	Follow-up at baseline, 6 months.	H pylori eradicated in 90% vs. 6% controls.6-month probability of ulcers 12.1% (95% CI 3.1-21.1) in eradication group vs. 34.4% (21.1-47.7) in controls (p = 0.0085); 6-month probabilities of complicated ulcers 4.2% (1.3-9.7) vs. 27.1% (14.7-39.5), p = 0.0026.	"Screening and treatment for H pylori infection significantly reduces the risk of ulcers for patients starting long-term NSAID treatment."	One week treatment 6 months diclofenac SR. Data suggest antibiotics plus omeprazole effective.

						antibiotics each BID (n=144) for 1 week.				
Kruger 2007 (score=9.5)	NSAIDs	RCT	Sponsored by Chephassar GmbH. No mention of COI	N = 167 Knee or hip OA	Mean age (59.9 years); 84 male, 166 female.	Oxaceprol 400mg TID (n=77 for SA dataset, n=56 for FA dataset) vs. placebo (n=76 for SA dataset, n=41 for FA data set) for 3 weeks	1, 2, and 3 weeks.	Pain following exercise (baseline/3 weeks): Oxaceprol 61.8±14.9/ 45.2±22.2 vs. placebo 63.0±13.9/58.5±21.6 (p = 0.002). Adverse effects in 50/77 (64.9%) oxaceprol vs. 65/76 (85.5%) placebo.	"A statistically significant and clinically relevant efficacy of oxaceprol was shown. The good safety and tolerability of oxaceprol was confirmed."	Forty-six (46) of 159 subjects excluded after randomization due to inclusion/exclusion or protocol violations, which were not included in modified intent to treat.
Raskin 1995 (Score=9.0)	NSAIDs	RCT	Sponsored by G.D. Searle & Co. No mention of COI.	N = 1,623 Patients with upper gastro-intestinal symptoms during NSAID therapy and no endo-scopic evidence of gastric or duo-denal ulcers	Median age: 58 years; 948 females, 670 males.	Placebo QID (n=454) vs. misoprostol 200µg BID and placebo BID (n=462) vs. misoprostol 200µg TID and placebo QD (n=474) vs. misoprostol 200µg QID (n=228).	Follow-up at baseline, 4, 8, and 12 weeks.	Gastric ulcers in 51/325 (15.7%) on placebo vs. 29/358 (8.1%) on misoprostol BID vs. 13/336 (3.9%) on misoprostol TID vs. 6/152 (4.0%) on QID. The incidence of gastric ulcers lower compared with placebo with misoprostol BID (difference, 7.6% [95% CI, 2.7% to 12.5%]; p = 0.002), TID (difference, 11.8% [CI, 7.4% to 16.3%]; p < 0.001), and QID (difference, 11.7% [CI, 6.7% to 16.8%]; p < 0.001).	"In patients receiving long-term NSAID therapy who are being considered for misoprostol therapy, dosages of 200 µg twice or three times daily are effective and better tolerated alternatives to the 200 µg four times daily regimen. Protection against NSAID-induced gastric ulcers increases with the dose of misoprostol, but maximum protection appears to be achieved with doses of 400 to 600 µg daily. Maximum protection against NSAID-induced duodenal ulcers can be achieved with doses as low as 400 µg daily. Physicians	Twelve week trial. Data support BID or TID dosing as well as QID.

									prescribing misoprostol should choose a dosage that best balances the drug's mucosal protective effects with its side effects."	
Labenz 2002 (Score=9.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 660 H pylori positive	Mean age: 54.8 years; 396 females, 264 males.	Clarithromycin 500mg BID for 1 week (OAC), plus 4 weeks of placebo QD (OAC-P) (n=161) vs. OAC for 1 week plus 4 weeks omeprazole 20mg QD (OAC-O) (n=173) vs. omeprazole 20mg QD for 1 plus 4 weeks (O-O)(n=155) vs. placebo for 5 weeks (P-P) (n=171).	No mention of follow-up.	Relative risk reduction (%) (95% CI) and absolute risk reduction (%) (95% CI) for the treatment groups was as follows: OAC-P: 79 (4.5-95), 4.6 (0.7-8.5); OAC-O: 80 (11.1-96), 4.7 (0.8-8.6); O-O: 100, 5.8 (2.1-9.5).	"In H pylori infected patients, all three active therapies reduced the occurrence of NSAID associated peptic ulcer and dyspeptic symptoms requiring therapy."	All diclofenac 50mg twice a day for 5 weeks. Other arms treatment for 1 week. Three treatment arms all reduced risk comparably. Results may not be generalized beyond H pylori infected patients.

Geba 2002 (score=9.0)	NSAIDs	RCT	Sponsored by Merck & Co, Inc. COI, Dr. Schnitzer has served as a consultant to AstraZeneca, GlaxoSmithLkine, Merck & Co, Novartis, Ortho-McNeil, McNeil Pharmaceuticals, and Wyeth-Ayerst.	N = 382 Knee OA	Mean age: 62.6 years; 121 male, 261 female.	Rofecoxib 12.5mg a day (n=96) vs. rofecoxib 25mg a day (n=95) vs. celecoxib 200mg a day (n=97) vs. acetaminophen 1gm QID (n=94) for 6 weeks	Follow up at baseline, 2, 3 and 6 weeks.	Changes in night pain first 6 days: acetaminophen (-18.8) vs. celecoxib (-18.7) vs. rofecoxib 12.5mg (-22.0) vs. rofecoxib 25mg (-25.2), p <0.05 comparing rofecoxib 25mg to acetaminophen or celecoxib. Rest pain results: -12.5, -15.5, -18.6, -21.8. Walking pain after 6 weeks: -30.3, -36.2, -35.1, -42.0 (p <0.01 comparing rofecoxib 25mg to acetaminophen).	"Rofecoxib, 25 mg/d, provided efficacy advantages over acetaminophen, 4000 mg/d, celecoxib, 200 mg/d, and rofecoxib, 12.5 mg, for symptomatic knee OA."	More discontinued acetaminophen than other treatments. Rofecoxib appeared superior to other treatment arms.
Scheiman 2006 (Score=9.0)	NSAIDs	RCT	Sponsored by AstraZeneca R&D in Molndal, Sweden. No mention of COI.	N=1429 At-risk patients (≥60 years and/or ulcer history)	Mean age: 65.1 years; 982 females, 399 males.	Esomeprazole 20mg (n=476) vs. esomeprazole 40mg (n=480) vs. placebo QD (n=473) for 6 months.	Follow-up at baseline, 1, 3, and 6 months.	16.5% (95% CI: 9.7–23.4) on COX-2s or placebo developed ulcers over 6 months vs. 0.9% (95% CI: 0–2.6) esomeprazole 20mg and 4.1% (95% CI: 0.6–7.6) esomeprazole 40mg (p < 0.001, p = 0.002) vs. placebo, respectively.	"For at-risk patients, esomeprazole was effective in preventing ulcers in long-term users of NSAIDs, including COX-2 inhibitors."	Two RCTs with large sample size. Study suggests efficacy.
Regula 2006 (Score=9.0)	NSAIDs	RCT	Sponsored by ALTANA Pharma AG in Konstanz, Germany. One or more of authors have received or will receive benefits for personal or professional use.	N = 595 Rheumatic patients on continual NSAIDs with at least 1 more re-cognized risk factor	Mean age: 65.7 years; 172 males, 423 females.	Pantoprazole 20mg (n=196) vs. pantoprazole 40mg (n=199) vs. omeprazole 20mg QD (n=200) for 6 months.	Follow-up at baseline, 3 and 6 months.	At 6 months, probability of therapeutic remission 90% pantoprazole 20mg QD, 93% pantoprazole 40 mg QD, and 89% omeprazole 20mg QD. Probabilities of endoscopic failure 9% vs. 5% vs. 7% respectively (NS).	"For patients taking NSAIDs continually, pantoprazole 20 mg o.d., pantoprazole 40 mg o.d., or omeprazole 20 mg o.d. provide equivalent, effective, and well-tolerated prophylaxis against GI lesions, including peptic ulcers."	Large population of rheumatoid arthritis, osteoarthritis, multiple conditions and spine for 6 months of treatment. Suggests equal efficacy.

				that contributes to GI injury						
Yeomans 2008 (Score=9.0)	NSAIDs	RCT	Sponsored by AstraZeneca. One or more of authors have received or will receive benefits for personal or professional use.	N = 991 Patients ≥60 years without baseline gastro-duodenal ulcer receiving aspirin 75-325mg daily	Mean age: 69.3 years; 566 males, 425 females.	Esomeprazole 20mg QD (n=493) vs. placebo (n=498) for 26 weeks.	No mention of follow-up.	Twenty-seven (5.4%) in placebo group with gastric or duodenal ulcer during 26-week treatment vs. 8 (1.6%) inesomeprazole group (life-table estimates: 6.2%vs 1.8%; p = 0.0007). At 26 weeks, cumulative proportion with erosive esophagitis lower for esomeprazole vs. placebo (4.4% vs. 18.3%, respectively; p <0.0001).	"Esomeprazole 20 mg once daily reduces the risk of developing gastric and/or duodenal ulcers and symptoms associated with the continuous use of low-dose aspirin in patients aged > or =60 yr without preexisting gastroduodenal ulcers."	Large population. Suggests efficacy.
Hawel 2003 (score=9.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 148 Hip OA	Mean age: 54.2 years; 75 males, 73 females.	Dexibuprofen 400mg BID (n=74) vs. celecoxib 100mg BID for 15 days (n=74). Double dummy.	Follow up at baseline, 8 and 15 days.	Improvements in WOMAC OA indices: dexibuprofen -5.97±3.72 vs. celecoxib -5.82±2.84 (NS). Patient global judgment of efficacy (excellent/very good): dexibuprofen 61.3% vs. celecoxib 50.0%. Gastrointestinal complaints: 8.1% vs. 9.5% (NS).	"[D]exibuprofen has at least equal efficacy and a comparable safety/tolerability profile as celecoxib in adult patients suffering from osteoarthritis of the hip."	Data suggest equivalent efficacy.
Fleischman n 2008 (score=9.0)	NSAIDs	RCT	Sponsored by Novartis Pharma AG. No mention of COI.	N = 3,036 Hip, knee or spine OA	Mean age: 62.91 years; 883 males, 2153 females.	Lumiracoxib 100mg QD (n=755) vs. lumiracoxib 100mg BID (n=1519) vs. celecoxib 200mg QD (n=758).	Follow-up at week 4, 13, 20, 26, 39, and 52.	Improvements in target joint pain did not differ (improvement in 50.6% vs. 52.3% vs. 53.6%). Global assessment of disease activity and physician assessments did not differ. Adverse events nearly identical (12.7% vs. 12.3% vs. 11.7%, NS). One-year retention rates not different (46.9% vs. 47.5% vs. 45.3%, NS).	"Long-term treatment with lumiracoxib 100 mg o.d., the recommended dose for OA, was as effective and well tolerated as celecoxib 200 mg o.d. in patients with OA."	No significant differences in efficacy. Only 50% retention rate at 1-year for all treatment arms, with 70% of participants reporting adverse events.

						Double dummy.				
Fogarty 1995 (score=8.5)	Treatment of Adverse Anesthesia Effects	RCT	No mention of sponsorship. COI: Dr. K.R. Milligan and Dr. D.J. Fogarty were in receipt of DHSS research grants.	N = 60	Mean age: 66.8 years; 26 males, 34 females	Ketorolac: (n=30) vs. Saline: (n=30) received injections (30mg IM at beginning of surgery and Q6 hours for 4 doses)	12 hours	VAS pain scores also favored ketorolac at 10 hours and at 0800 the next day (3.7±8.2 vs. 11.5±16.7, p <0.05).	"Non-steroidal anti-inflammatory analgesics drugs such as ketorolac, when used in conjunction with intrathecal opioids, improve analgesia and reduce post-operative analgesic requirements. Patients suitable for NSAID medication might benefit from combination of a small dose of IT morphine and a NSAID, i.e. Ketorolac."	Study supports ketorolac IM injections.
Golden 2004 (score=8.5)	NSAIDs	2 RCTs	Sponsored by F. Hoffmann-La Roche AG. No mention of COI	N = 465 Knee OA	Mean age 60.6 years; 284 male, 646 female.	Naproxen sodium 440/660 mg (n=162) vs acetaminophen 4000 mg (n=148) vs placebo (n=155)	1, 2, 3, 4, 5, 6 and 7 days.	Nearly all measures improved for naproxen (rest pain, pain on passive motion, pain on weight bearing, stiffness, day pain, night pain), but only day pain relief improved for acetaminophen compared with placebo. Adverse effects in 17.4% of placebo vs. 20.9% acetaminophen vs. 24.2% naproxen.	"Nonprescription doses of naproxen sodium (440/660 mg) effectively relieve pain and other symptoms of osteoarthritis. Naproxen sodium is an alternative initial treatment of osteoarthritis and may be preferred to acetaminophen as first-line therapy in patients with moderate or severe pain."	Two very short term studies of 7 days each reported in pooled analyses. Submaximal naproxen dose vs. full acetaminophen dose. Acetaminophen appears inferior to naproxen, and not clearly superior to placebo.

Dorta 2000 (Score=8.5)	NSAIDs	RCT	Sponsored by Swiss Cancer League / Cancer Research Switzerland and Astra Hassle AB Molndal Sweden. No mention of COI.	N = 12 Healthy volunteers	Median age: 29 years; 5 females, 7 males.	Two-week course of omeprazole (40mg) plus "separate 2-week course of an identical looking placebo."(n=6) vs. Water-soluble diclofenac (50mg) taken 2nd week (n=6).	Follow-up at baseline, 1 week.	No differences in healing scores after administration of placebo/diclofenac (median = 6; range 0-6) and omeprazole/ diclofenac (median = 9; range 0-6; p = 0.17) were found.	"In healthy subjects, omeprazole does not accelerate the healing of pre-existing mucosal lesions or prevent the development of small diclofenac-induced mucosal lesions."	Crossover study with small sample size. Short-term treatments of unclear clinical significance.
Bianchi Porro 2000 (Score=8.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 104 RA or OA	Mean age: 59.5 years; 86 females, 18 males.	40mg pantoprazole (n=70) vs. placebo QD (n=34) for 12 weeks.	No mention of follow-up.	Difference in probability of remaining free of peptic ulcer 5% (95% CL-13%, = 23%) at 4 weeks and 13% (-9%, = 33%) at 12 weeks.	"Pantoprazole 40mg once daily was well tolerated and is more effective than placebo in the prevention of peptic ulcers in patients with rheumatic diseases who require continuous, long-term, treatment with NSAIDs."	RA or OA 12 week treatment. Suggests efficacy.

Pope 2004 (score=8.5)	NSAIDs	RCT	Sponsored by Physicians Services Incorporated Foundation. No mention of COI	N = 51 Hip, knee or hand OA	Mean age 56.6 years. Sex not mentioned.	Multiple crossover trials of diclofenac 50mg plus misoprostol 200µg (n=27) vs. placebo (n=24) for 2 week durations for 6 months.	1, 2, 3, and 6 months.	In one group, 11 patients preferred diclofenac, none preferred placebo, and 11 had no preference. NSAID appeared to be effective in 81% of patients.	"N of 1 trials were time-consuming in these patients and are more expensive, but with slightly better outcomes. In addition, NSAID seem to be effective in a majority of subjects with OA who have been uncertain of their benefit."	Subjects at enrollment were "uncertain the nonsteroidal anti-inflammatory drugs were helpful." Results suggest NSAIDs are efficacious for majority of patients who were uncertain if they were effective.
Day 2000 (score=8.5)	NSAIDs	RCT	Sponsored by grants from Merck & Co Inc., West Point, Pa. No mention of COI.	N = 809 Knee or hip OA	Mean age: 63.9 years; 162 male, 647 female.	Rofecoxib 12.5mg QD (n=244) vs. 25mg QD (n=242) vs. ibuprofen 800mg TID (n=249) vs placebo (n=74) for 6 weeks	Follow up at baseline, 2, 4 and 6 weeks.	Rofecoxib 25mg superior to ibuprofen for 2 of 3 primary end points (graphic presentations, $p < 0.05$). All active treatments superior to placebo ($p < 0.001$). Significant discontinuation rate due to adverse effects from ibuprofen ($p < 0.05$), but not rofecoxib.	"Rofecoxib was well tolerated and provided clinical efficacy comparable with a high dose of the NSAID ibuprofen."	Data suggest superiority of rofecoxib vs. ibuprofen. Suggests rofecoxib better tolerated than ibuprofen.
Bellamy 1986; 1988 (score=8.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 57 Hip and/or knee OA	Mean age: 66.5 years; 26 male, 31 female.	Isoxicam 200mg QD (n=28) vs. piroxicam 20mg QD (n=29) for 6 weeks	Follow up at baseline, 2, 4, and 6 weeks.	Night pain (baseline/6 weeks): isoxicam (1.68± 0.72/0.63) vs. piroxicam (1.83±1.0/0.77). No differences in outcome measures between groups ($p > 0.05$). Total adverse reactions: isoxicam 12/28 (42.9%) vs. piroxicam 24/29 (82.8%). Totals with severe adverse drug reaction higher in piroxicam (0 vs. 5, $p = 0.03$); 93% isoxicam vs. 69% piroxicam improved.	"[I]soxicam is an efficacious and well-tolerated once-daily NSAID for elderly patients with osteoarthritis."	Comparable efficacy in elderly population, although trends favored isoxicam over piroxicam.

Temple 2006 (score=8.0)	NSAIDs	RCT	Sponsored by McNeil Consumer and Specialty Pharmaceuticals. COI, Dr. Benson served as consultant for McNeil Consumer and Specialty Pharmaceutica	N = 581 Mild to moderate hip or knee OA	Mean age 59.3 years, 176 male, 395 female.	Acetaminophen 1g Q4-6 hours (n=287) vs. naproxen 375mg BID (n=284) for up to 12 months. Single dummy.	1, 3, 6, 9, 12 months.	Few data on efficacy. WOMAC scores at 6 months improved in both groups; not significantly different. Adverse effects in 38.3% acetaminophen vs. 43.4% naproxen (NS). More constipation with naproxen (9.9% vs. 3.1%, p <0.002) and more peripheral edema (3.9% vs. 1.0%, p <0.033).	"With physician supervision, acetaminophen was found to be generally well tolerated in these patients for the treatment of osteoarthritis pain of the hip or knee for periods up to 12 months."	Maximal dose acetaminophen vs. submaximal dose naproxen likely biases in favor of acetaminophen. No significant differences in primary outcomes. Both groups had high dropouts.

Fioravanti 2002 (score=8.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 287 Moderate or severe hip and/or knee OA	Mean age: 66.0 years; 71 male, 216 female.	Nimesulide-beta-cyclodextrin 400mg BID (n=146) vs. naproxen 500mg BID (n=141) for 2 weeks scheduled treatment and 5.5 months on-demand dosing	Follow up at baseline, 1 and 2 weeks and 6 months.	VAS scores (baseline/2 weeks): NBC 67.9/39.7 vs. naproxen 66.9/39.8 (NS). Other outcomes (e.g., pain on movement, morning stiffness) not different between treatments; 37 discontinued nimesulide-beta-cyclodextrin vs. 38 naproxen; 19 nimesulide-beta-cyclodextrin group, 8 naproxen took other NSAIDs as additional treatment for OA.	"[N]imesulide-beta-cyclodextrin is comparable to naproxen in terms of therapeutic efficacy in the short-term treatment of OA. Medium-term treatment on demand was also similar with the 2 drugs."	Lack of compliance data, high dropout rate weaken conclusions. Data suggest comparable efficacy.
Le Loët 1997 (score=8.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 290 Knee or hip OA	Mean age: 63.3 years; No mention of gender.	Diclofenac SR 75mg BID (n=113) vs. diclofenac 50mg TID (n=123) for 7 days. Double dummy.	Follow up at baseline, 30 minutes, 1, 2, 4, and 12 hours, 1, 2, 3, 4, 5, 6, and 7 days.	Mean spontaneous pain intensity decreased in both groups within first 36 hours and from Day 1 to Day 7 ($p = 0.0001$). 24.5% and 31.3% adverse effects (NS). Good compliance greater with diclofenac 75mg (81.6%) vs. 50mg (53.1%), ($p < 0.001$).	"The results…show the equivalence of efficacy of diclofenac SR 75 mg one tablet 2x daily and diclofenac enteric coated 50 mg one tablet 3x daily given for 7 days for the symptomatic treatment of painful osteoarthritis."	Despite difference in "good compliance (>90%)," treatment groups had similar efficacy. Very short term trial of 7 days.
Hawkey 2005 (Score=7.5)	NSAIDs	RCT	Sponsored by research grant from AstraZeneca R&D in Molndal Sweden. COI: All authors except Joseph Sung have received or will receive benefits	2 RCTs: N = 608 and N = 556 (NASAI, SPACE 1) Con-tinuous NSAID users	NASA1 mean age: 56.1 years; 438 females, 157 males. SPACE1 mean	Esomeprazole 20mg (n=382) vs. esomeprazole 40mg (n=386) vs. placebo QD (n=396) for 4 weeks.	No mention of specific follow-up time length.	Time to relief superior with active treatments with esomeprazole 20mg and 40mg vs. placebo (NASA1: $p = 0.0137$, $p = 0.0053$; SPACE1: $p < 0.0001$, $p = 0.0002$). Symptom relief shorter for esomeprazole 20mg and 40mg vs. placebo in each study (11 and 10 days vs. 17 days NASA1	"Esomeprazole 20 mg and 40 mg improve upper GI symptoms associated with continuous, daily NSAID therapy, including selective COX-2 inhibitors."	2 large studies. NASA I-E40 group had higher percentage >75 years old.

			for personal or professional use.	free of gastro-duodenal ulcers, erosive esophag-itis, and H pylori	age: 53.8 years; 419 females, 135 males.			and 10 and 11 days vs. 21 days in SPACE 1). Symptom-free days over 4 weeks higher for esomeprazole in both studies (31% esomeprazole 20mg, 29% esomeprazole 40mg vs. 21% on placebo in NASA1, p = 0.0025 and p = 0.0103, respectively, 29%, 27% and 14% respectively, in SPACE1, p <0.0001 vs. placebo both esomeprazole doses).		
Bocanegra 1998 (Score=7.5)	NSAIDs	RCT	Sponsored by G.D. Searle & Co. in Skokie, Illinois. No mention of COI.	N = 572 Knee or hip OA	Mean age: 62.5 years; 392 females, 180 males.	Diclofenac (D50/M200) 50mg plus misoprostol 200µg TID (n=152) vs. diclofenac 75mg plus misoprostol 200µg BID (D75/M200) (n=175) vs. diclofenac 75mg bid (D) (n=154) vs. placebo (n=91) for 6 weeks.	No mention of follow-up.	Patient global assessments Week 6: D (-1.46±1.21) vs. D50/M200 (-1.38±1.03) vs. D75/M200 (-1.50±1.12) vs. placebo (-0.85±1.27). Improvements on all active treatments (p <0.002); no differences among active treatments. Dyspepsia most common adverse event in all treatment groups. Endoscopic stomach and/or duodenal ulcers: diclofenac 17% vs. 8% D50/M200 vs. 7% D75/M200 vs. 4% placebo (p <0.04 between diclofenac and other active treatments). Overall withdrawals from adverse events not different.	"Diclofenac 50 mg/misoprostol 200 µg tid and diclofenac 75 mg misoprostol 200 µg bid are as efficacious as diclofenac 75 mg bid in the treatment of OA, but are associated with significantly lower incidence of gastric and/or duodenal ulcers."	Lack of details on blinding, randomization. 6 week study with pre and post endoscopy demonstrated GI protective effect of misoprostol.

Reginster 2007 (score=7.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 997 Hip or knee OA	Mean age: 62.8 years; 279 male, 718 female.	Etoricoxib 60mg QD (n=446) vs. naproxen 500mg BID (n=439) vs. placebo (n=112) 12 weeks. Then placebo randomized to active treatment for 40 weeks, 86-week follow-up.	Follow up at 2, 4, 8, 12, 19, 26, 33, 39, 45, and 52 weeks during the base studies, 69, 86, 104, 121, and 138 weeks during the extension studies.	Active treatments with comparable efficacy over 12-week trial; 52 week results for WOMAC pain scale: etoricoxib -31.03 vs. naproxen -30.60 (NS). Over 12 weeks, discontinuation due to adverse effects: placebo 17.0% vs. etoricoxib 21.5% vs. naproxen 29.2%.	"Both etoricoxib and naproxen demonstrated long-term clinical efficacy for the treatment of OA. Etoricoxib and naproxen were generally well tolerated."	Low power to detect differences in adverse effects between active treatment groups. Both drugs had comparable efficacy over placebo. Data suggest higher adverse effects for naproxen.
Kidd 1996 (score=7.5)	NSAIDs	RCT	Sponsored by a grant of the Forschungsforderungsfond der gewerblichen Wirtschaft Osterreichs. No mention of COI.	N = 135 Hip or knee OA	Mean age: 63 ± 10 years; 62 male, 73 female.	Lornoxicam 4mg TID (n=46) vs 8mg BID (n=44) vs diclofenac 50mg TID (n=45) for 12 weeks with 40 week continuation phase. Double dummy.	Follow up at baseline, 4, 8 and 12 weeks.	37% failed to complete RCT phase; 28/85 (32.9%) failed to complete continuation phase due to inefficacy. Functional indices of severity (baseline/difference): lornoxicam 4mg TID (11.1±4.4/-2.4±4.2) vs. lornoxicam 8mg BID (10.6±2.2/-1.7±5.9) vs. diclofenac (10.1±1.8/-2.7 ±2.2) (p = 0.013 comparing lornoxicam doses, p <0.01 comparing either lornoxicam doses with diclofenac. Other measures of disease activity, pain relief not different.	"[L]ornoxicam is an effective treatment for OA when administered in a 3 times daily (4 mg) or twice daily (8 mg) regimen. Furthermore, it has an efficacy and tolerability profile comparable to that of the well established drug diclofenac."	No placebo control. High dropout rate in both phases of study. No clear superiority of any arm.

Bradley 1991 (score=7.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 184 Knee OA	Mean age: 59.6 years; 47 male, 137 female.	Ibuprofen 600mg QID (n=61) vs. ibuprofen 300mg QID (n=62) vs. acetamino phen 1gm QID (n=61) for 4 weeks	Follow up at baseline , 3 to 7 days, and 4 weeks.	Walking pain score changes: acetaminophen (0.13) vs. ibuprofen 1200mg (0.31) vs. ibuprofen 2,400mg (0.45), p = 0.10. Rest pain scores were: 0.06 vs. 0.33 vs. 0.40, p = 0.05.	"[S]ymptomatic treatment of osteoarthritis of the knee, the efficacy of acetaminophen was similar to that of ibuprofen, whether the latter was administered in an analgesic or an anti-inflammatory dose."	At baseline, trend towards more advanced disease in high-dose ibuprofen group. Walking pain score, rest pain both favored ibuprofen (some measures showed no difference).
Leung 2002 (score=7.5)	NSAIDs	RCT	Sponsored by a grant from Merck & Co., Inc. No mention of COI.	N = 501 Knee or hip OA	Mean age: 63.2 years; 109 male, 392 female.	Etoricoxib 60mg QD (n=224) vs. naproxen 500mg BID (n=221) vs. placebo (n=56) for 12 weeks. Double dummy.	Follow up at baselein e, 2, 4, 8, and 12 weeks.	WOMAC pain scale responses over 12 weeks: placebo -15.33 (95% CI -20.7, -9.96) vs. etoricoxib -25.76 (-28.58, -22.94) vs. naproxen -25.32 (-28.13, -22.50). Etoricoxib equivalent to naproxen, and both superior to placebo. Adverse effects higher for naproxen (n = 69, 31.2%) vs. etoricoxib (n = 57, 25.4%) vs. placebo (n = 14, 25.0%). More etoricoxib patients completed trial (91.1%) than naproxen (83.3%) and placebo (78.6%).	"Etoricoxib showed rapid and durable treatment effects in patients with OA of the knee or hip."	No significant differences between naproxen and etoricoxib. Power may have been limited to detect adverse effect differences, but trends in favor or etoricoxib present.

Beaulieu 2008 (score=7.5)	NSAIDs	RCT	Sponsored by Purdue, Pharma, Canada. No mention of COI.	N = 129 Hip and/or knee OA	Mean age: 62.24 years; 42 males, 86 females.	Tramadol CR 200mg (n=45) vs. diclofenac SR 75mg (n=52). Doses titrated (up to 400mg a day vs. up to 150mg).	Follow up: six weeks after initial treatment.	Significant improvement both groups for physical functioning: CR tramadol mean change of 257.0±354.4, p = 0.0005, SR diclofenac mean change 247.4±379.5, p = 0.0001, and stiffness: CR tramadol mean change of 34.3±61.4 p = 0.0005, SR diclofenac mean change 36.8±57.4, p = 0.0001. Adverse events or withdrawals related to study drug similar for both treatments (tramadol 16.1%/27.4% vs. diclofenac 15.2%/21.2%) (NS).	"CR tramadol, a once-daily formulation marketed as Zytram XL, is as effective as SR diclofenac in the treatment of pain due to knee or hip OA."	Baseline comparability not presented. Study results suggest equal efficacy.
Boureau 2004 (score=7.5)	NSAIDs	RCT	Sponsored by Boots Healcare, France. COI, some authors are affiliated with Boots healthcare (H Schneid & N Zeghari).	N = 222 Knee or hip OA	Mean age 66.5; 60 males, 162 females.	Ibuprofen 400mg TID (n=111) vs. paracetamol 1,000mg TID (n=111) for 14 days. Double dummy.	Baseline, and every day for 2 weeks.	Pain intensity over hours or days reduced to greater extent with ibuprofen (p <0.05). Stiffness scores (baseline/final): ibuprofen 56.2±17.5/ 32.5±18.7 vs. paracetamol 56.2±17.5/ 43.7±20.0 (p = 0.002). Pain scores: ibuprofen 50.0±13.5/27.0±17.0 vs. 50.0±12.5/35.5±18.0 (p <0.001). Physical function scores: -19.8 vs. -12.8 (p = 0.002). Global efficacy higher for ibuprofen (67.5%) than paracetamol (37.8%), p = 0.001. Adverse effects did not differ (23.4% vs. 22.5%) (NS).	"[S]hows that a significant and a more marked reduction in pain was experienced by patients with OA of the hip or knee with ibuprofen 400 mg than with the paracetamol 1000mg."	Study used sub-maximal doses and demonstrated Ibuprofen 400 mg TID was more effective than paracetamol for OA of hip and knee at every time interval from hours to days 1 to 14.
Mejjad 2000 (score=7.5)	NSAIDs	Randomized Crossover Experimental Trial	No mention of sponsorship or COI.	N = 16 Unilateral hip OA	Mean age 61 years; 8 male, 8 female.	Etodolac 300mg vs. placebo one dose. Assessed effects on	60, 120, and 180 minutes.	Walking speed increased significantly between t0 and t180 under etodolac but not placebo (p <0.0004). Cadence expressed in cycles/min, did not differ. VAS scores	"[W]alking speed increased under etodolac, but not placebo…conclude that gait improvement was closely associated with	Small sample size. Suggests drug had positive effect on gait in 3-

						gait. All patients received both treatments in random order.		decreased between t0 and t180 for etodolac and placebo groups (p <0.0009 and p <0.03, respectively).	the administration of a single, oral 300mg dose of etodolac. Three hours after taking a single tablet, gait was improved.	hour experiment.
Pincus 2001 (score=7.5)	NSAIDs	Randomized Crossover Trial	Sponsored by Pharmacia. No mention of COI.	N = 227 Hip or knee OA	Mean age 61.4 years; 67 male 160 female	Diclofenac 150mg plus misoprostol 400µg (n=112) vs. 4,000 mg acetaminophen (n=115) for 6 weeks	6 weeks.	WOMAC scores for most-involved joint (baseline/6 weeks): diclofenac + misoprostol (42.5±2.1/ 30.3±2.0) vs. acetaminophen (37.4± 2.5/35.3±1.9) (p = 0.011). Acetaminophen first, results (baseline/6 weeks): 44.8±2.1/38.2 ±1.7) vs. diclofenac+ misoprostol (40.5±2.6/ 27.6±2.1) (p <0.01). Multidimensional Health Assessment Questionnaire VAS and SF-36 also favored diclofenac. Results comparing treatments by OA severity index [WOMAC total score estimate (p-values) for quartiles lowest to highest): 0.78 (0.86), -1.45 (0.70), -6.72 (0.63), -14.70 (p <0.001). Non-serious adverse GI events more common for diclofenac + misoprostol (p = 0.006). Diclofenac + misoprostol reported "better" or "much better" by 57%.	"Patients with osteoarthritis of the hip or knee had significantly greater improvements in pain scores over 6 weeks with diclofenac + misoprostol than with acetaminophen, although patients with mild osteoarthritis had similar improvements with both drugs. Acetaminophen was associated with fewer adverse effects."	No placebo arm. Data demonstrate diclofenac superior for pain relief and measures of function to acetaminophen, particularly for moderate to severe disease.
Bianchi Porro 1997 (Score=7.5)	NSAIDs	RCT	Sponsored by Searle Italy. No mention of COI.	N = 70 RA or OA with endoscopically	Mean age: 54 years; 62 females, 8 males.	Misoprostol TID: misoprostol 200µg and ranitidine	No mention of follow-up.	70% of MISO TID group vs. 48% in MISO BID group vs. 21% in RAN group with normal gastroduodenal mucosa (score = 0) (p <0.01 between MISO TID and RAN). Incidence of	The study confirms that "[M]isoprostol is as effective as ranitidine in the short-term prevention naproxen-induced duodenal lesions, but	RA or OA. Data suggest misoprostol is superior to ranitidine.

				normal mucosa		placebo after every meal 3 times daily (n=23) vs. misoprostol BID: Misoprostol 200µg after breakfast and dinner, misoprostol placebo after lunch; ranitidine placebo after every meal (n=23) vs. ranitidine 150mg after breakfast and dinner, ranitidine placebo after lunch, and misoprostol placebo after each meal for 14 days (n=24).		gastrointestinal symptoms did not differ between 3 treatment groups. 56% with gastroduodenal ulcer had no gastrointestinal symptoms.	significantly better as far as the gastric mucosa is concerned. Because the dosages used in this specific study proved to be effective and well tolerated, misoprostol b.i.d. might, in our opinion, be proposed as an alternative in patients who need prophylaxis against NSAID damage."	
Bakshi 1993 (Score=7.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 129 Knee and/ or hip OA	Mean age: 62.1 years; 35 males,	Diclofenac dispersible (n=62) vs. enteric-coated	No mention of specific follow-	No differences in treatment efficacy (graphic data, approximately 60% reductions in VAS joint pain with activity). No differences in adverse	"Overall assessments of efficacy by the patients and the investigator indicated a positive response rate for both	Data suggest comparability with no benefits of enteric

					93 females.	50mg TID (n=68) for 12 weeks.	up time length.	events (40.3% vs. 37.3%, p <0.73). Total GI adverse events (++ and +++): dispersible 21/62 (33.9%) vs. EC 16/67 (23.9%).	diclofenac formulations ranging between 71% and 82%. The proportion of patients reporting adverse effects, predominantly gastro-intestinal, was slightly higher in the dispersible group, 40.3%, compared to 37.3% with enteric-coated diclofenac sodium."	coating of diclofenac.

Levi 1985 (Score=7.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 68 Hip or knee OA	Mean age: 61.2±9.7 years; 27 males, 39 females.	Indomethacin SR 75mg. Medication taken at 8am (n=20) vs. noon (n=28) vs. 8pm (n=20) for 1 week intervals.	No mention of follow-up.	Circadian pain rhythms confirmed 23/57 (40%) of subjects and suspected in 9 (15.8%). More adverse effects for morning dosing (p <0.001); 96% of 25 subjects with undesirable adverse effects found changed dosing time changed tolerance.	"Evening dosing was most effective in subjects with predominantly nocturnal or morning pain; conversely, morning or noon dosing was most effective in subjects with greater afternoon or evening pain."	Study suggests relationship of optimal dosing to circadian pain rhythms, suggesting optimal dosing of SR indomethacin should be individualized (taken anticipating when maximal pain occurs).
Lisse 2003 (Score=7.0)	NSAIDs	RCT	Sponsored by Merk & Co., Inc. COI: one or more of the authors have received or will receive benefits for personal or professional use.	N = 5,557 Knee, hip hand or spine OA	Mean age: 63 years; 1609 males, 3948 females.	Rofecoxib 25mg day (n=2785) vs. naproxen 500mg twice daily (n=2772) for 3 months. Double dummy.	No mention of follow-up.	Discontinuation due to adverse GI events lower in rofecoxib (5.9% vs. 8.1%), RR = 0.74 (95% CI 0.60-0.92, p = 0.005). Similar findings in low-dose ASA takers. Less GI medication use in rofecoxib group (9.1% vs. 11.2%, p = 0.014). Two perforations, ulcers, or bleeding episodes in rofecoxib vs. 9 naproxen (RR = 0.22, p = 0.038).	"[R]ofecoxib, 25 mg once daily, was as efficacious as naproxen, 500 mg twice daily, in controlling symptoms over a 3-month period and was associated with significantly better GI tolerability."	Very large sample size. No placebo. Participants allowed H-2 blockers. Results suggest equivalent efficacy for pain, but higher adverse GI symptoms and bleeds for naproxen vs. rofecoxib.

Edworthy 1999 (Score=7.0)	NSAIDs	RCT	Sponsored partially by Searle Canada by the Arthritis Society and partially by the Medical Research Council of Canada. COI: two authors have received or will receive benefits for professional use.	N = 252 Hip or knee OA	Mean age: 63.2 years; 173 females, 79 males.	Diclofenac with misoprostol treatment with in depth computer program about disease, treatment, patient involvement (n=126) vs. medication with generic information about OA (n=126).	Follow-up at 8 weeks.	Significant effect of education on appropriate utilization (p = 0.029). Changes in medication knowledge (p = 0.02), self-efficacy (p = 0.005), ease of adherence (p = 0.002), realistic expectations (p = 0.01) greater intervention group. No difference between groups for illness intrusiveness, pain, or disability; greater improvement in stiffness in experimental group (p = 0.04).	"Patient education emphasizing the distinction between appropriate and inappropriate utilization of medication is a promising new adjunct to the management of OA. Patient involvement is essential in proper treatment of disease."	Blinding methods are not clear. The study demonstrated positive benefits of educational material in improving compliance and setting realistic expectations.
Vinje 1993 (Score=7.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 163 Hip or knee OA	Mean age: 64.3 years; 108 females, 55 males.	Ketoprofen 200mg QAM in the morning (n=73) vs. QPM in the evening (n=90) for 4 weeks each.	No mention of follow-up.	Both schedules effective (p <0.01); most results NS between treatment. Mean unused ketoprofen tablets: 1.2am vs. 0.6pm dosings (p = 0.05). Rescue use higher with evening dosing (p = 0.10); 64 preferred morning dosing vs. 52 evening. Total frequency of GI symptoms not different.	"No significant differences were detected in degree of GI-symptoms between the two treatment periods."	Although statistical significance needed for differences on VAS pain scale, patient preference was only 53% for morning dose over evening dose. Data suggest no meaningful differences.

Smugar 2006 (score=7.0)	NSAIDs	2 RCTs	Sponsored by Merck and Company, Inc. COI, Drs. Smugar and Tershakovec and Mr. Polis are employees of Merck & Co., Inc.	N = 2,603 Knee or hip OA	Median age: 62.0 years; 366 males, 716 females.	1) rofecoxib 12.5mg (n=456) vs. rofecoxib 25mg (n=459) vs. celecoxib 200mg (n=456) vs. placebo QD (n=150) for 6 weeks; 2) rofecoxib 25mg (n=471) vs. celecoxib 200mg (n=460) vs. placebo QD (n=151)	Follow up at baseline, 2, 4, and 6 weeks.	Rofecoxib 25mg provided faster relief than celecoxib 200mg in both studies (Study 1 median 3 vs. 5 days, p = 0.004; Study 2 median 4 vs. 5 days, p <0.001). Study 1, pain at night not significantly different between active treatments. Study 2, rofecoxib 25mg significantly reduced pain at night over 6 weeks compared to celecoxib (p <0.05, graphic data). Higher dropouts in placebo vs. other treatment arms in both studies (approx. 62% vs. 82-88% completions).	"Rofecoxib 25 mg was significantly better than celecoxib 200 mg in relieving night pain at 6 weeks in one study; this was not confirmed in the accompanying study."	Results between two studies conflict somewhat with no clear superiority of one NSAID over another for pain relief during 6 week trial, although rofecoxib 25mg provided faster pain relief in both studies and trends in night pain also favored rofecoxib over celecoxib.
Perpignano 1994 (score=7.0)	NSAIDs	RCT	No mention of sponsorship of COI.	N = 120 Knee and/or hip OA	Mean age: 70.7 years; 14 males, 106 females.	Etodolac SR 600mg QD (n=48) vs. tenoxicam 20mg QD (n=58) for 8 weeks. Double dummy.	Follow up at baseline, 2, 4, and 8 weeks.	Significant improvements from baseline in all efficacy assessments at Weeks 2, 4, and last visit in each group. No differences between groups. VAS scores (ITT): etodolac 69.2±11.8 vs. tenoxicam 72.0±13.0 (NS). No difference in erosive GI lesions after 8 weeks. Adverse reactions in 14/60 (23.3%) patients treated with tenoxicam vs. 5/60 (8.3%) etodolac (p <0.05).	"[E]todolac SR 600 mg once daily is as effective as tenoxicam 20 mg once daily in relieving symptoms of OA of the knee and of the hip. Both the overall and the G-I specific safety profiles were found to be more favorable in patients treated with etodolac SR."	Randomization, allocation details missing. Although author reports safety .3 for total adverse events, the study data do not reflect all conclusions. Data suggest equal efficacy.

Lindén 1996 (score=7.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 256 Hip OA	Mean age: 67.2 years; 95 males, 161 females.	Meloxicam 15mg (n=129) vs. piroxicam 20mg QD (n=127) for 6 weeks	Follow up at baseline, 7, 21, and 42 days.	Pain on movement (VAS) (baseline/Day 42): meloxicam (59.7±15.2/31.7±24.3) vs. piroxicam (60.2±14.7/34.9±24.4). No differences in worst rest pain or reductions in total index severity. Global tolerance borderline better for meloxicam.	"The frequency of adverse events (GI or otherwise) and global tolerance were similar in the meloxicam-treated and piroxicam-treated groups. The global tolerance of the drugs assessed by the patient at the end of the study suggested a slightly better tolerance of meloxicam over piroxicam although this difference was not statistically significant."	Blinding, randomization details sparse. No placebo control. Comparable efficacy shown.
Wegman 2003 (score=7.0)	NSAIDs	N of 1 trials	Sponsored by Leo Pharma, the Netherlands. No mention of COI.	N = 13 Hip or knee OA	Median age: 77 years; 2 males, 11 females.	Each patient received 5 treatment pairs with 2 weeks NSAID (ibuprofen 400mg TID, diclofenac 50mg BID, diclofenac 25mg TID, naproxen 375mg BID) and 2 weeks paracetamol 1gm TID	Follow up every two weeks.	Largely no difference in preference of either paracetamol or NSAIDs found.	"The results of n 1 trials varied across patients. n of 1 trials can be used to investigate which treatment is best for any specific person, thus avoiding unnecessary prolonged treatment with NSAIDs. However, practical reasons may cause patients to switch from NSAIDs to paracetamol or not."	Small sample size. Many did not complete the trial (6/13). Submaximal NSAID doses preclude conclusions on relative merit of paracetamol vs. NSAID.

Lisse 2003 (score=7.0)	NSAIDs	RCT	Sponsored by a grant from Merck & Co. Inc. COI, Employment: C.S. Skalky (Merck and Co., Inc.), M.E. Dixon (Merck and Co., Inc.), A.B. Polis (Merck and Co., Inc.), G.P. Geba (Merck and Co., Inc.); Consultancies: J.R. Lisse (Merck and Co., Inc.); Honoraria: J.R. Lisse (Merck and Co., Inc.); Stock ownership (other than mutual funds): C.S. Skalky (Merck and Co., Inc.), M.E. Dixon (Merck and Co., Inc.), A.B. Polis (Merck and Co., Inc.), G.P. Geba (Merck and Co., Inc.).	N = 5,557 Knee, hip hand or spine OA	Mean age: 63.0 years; 1609 males, 3948 females.	Rofecoxib 25mg a day (n=2785) vs. Naproxen 500mg twice daily for 3 months (n=2772). Double dummy.	Follow up at 3, 6, 9 and 12 weeks.	Discontinuation due to adverse GI events lower in rofecoxib group (5.9% vs. 8.1%), RR = 0.74 (95% CI 0.60-0.92, p = 0.005). Similar findings in low-dose ASA takers. Less GI medications in rofecoxib group (9.1% vs. 11.2%, p = 0.014). Two perforations, ulcers or bleeding episodes rofecoxib vs. 9 naproxen (RR = 0.22, p = 0.038).	"[R]ofecoxib, 25 mg once daily, was as efficacious as naproxen, 500 mg twice daily, in controlling symptoms over a 3-month period and was associated with significantly better GI tolerability."	Very large sample size. No placebo. Participants allowed to take H-2 blockers. Results suggest equivalent efficacy for pain, but higher adverse GI symptoms and bleeds for naproxen vs. rofecoxib.

Pavelka 1998 (score=7.0)	NSAIDs	Crossover trial	Sponsored by Grünenthal GmbH, Aachen, Germany. No mention of COI.	N = 60 Hip or knee OA without clinical joint inflammation	No mention of mean age. Age range 44 to 85 years; 8 males, 52 females.	Tramadol 50-100mg up to TID vs. diclofenac 25-50mg up to TID for 4 weeks. Doses titrated. All patients received both treatments in a random order.	Follow up: 4 weeks after initial treatment.	Mean tramadol dose 164.8 ±54.1mg, mean diclofenac dose 86.9±21.4mg. Three in each group terminated (reasons not noted). Adverse events greater during tramadol treatment (20.0% vs. 3.3%, p = 0.0056). No patient preference (46.7% tramadol vs. 45.0% diclofenac, p = 0.85). Functionality scores improved in tramadol group: 39.6±16.0 to 32.0± 17.4 vs. diclofenac 40.0± 17.2 to 30.1±17.0; no significant difference between groups.	"OA patients' response to analgesic treatment was highly individual and the response to one drug was not predictive of that to another drug. As functional scored improved (lower WOMAC scores) on analgesic vs. NSAID, pain rather than inflammation may be the most important aspect of treatment. A significant proportion of patients were not treated satisfactorily with diclofenac or tramadol alone."	The results suggest and support other studies (Bradley 1991) that OA pain is not necessarily caused by inflammation, as both paracetamol and in this study tramadol had similar analgesic efficacy with improvement in functional scores to that of NSAIDs.
Raskin 1996 (Score=7.0)	NSAIDs	RCT	Sponsored by G.D. Searle & Co. No mention of COI.	N = 538 Patients on chronic NSAID therapy with NSAID-related upper GI pain without gastric or duodenal ulcers	Median age: 60.5 years; 296 females, 242 males.	Misoprostol 200µg QID (n=269) vs. ranitidine 150mg BID (n=269) for 8 weeks.	Follow-up at 4 and 8 weeks after treatment.	More gastric ulcers (p = 0.009) in ranitidine group (11 ulcers with a rate of 5.64%) vs. misoprostol (1 ulcer with a rate of 0.55%). Total gastrointestinal AEs more (p <0.05) more often in misoprostol group.	"[M]isoprostol and ranitidine are equally effective for the prevention of duodenal ulcers. NSAID-induced ulcers can occur in either the stomach or duodenum. Since only misoprostol has been shown effective in the prevention of both NSAID-induced gastric and duodenal ulcers, misoprostol should be the therapy of choice for the prevention of such ulcers in patients at risk."	Eight week trial. Data suggest misoprostol is superior to ranitidine for prevention of GU.

Graham 1993 (Score=7.0)	NSAIDs	RCT	Sponsored by G.D. Searle Company. No mention of COI.	N = 638 Patients with chronic inflamm-atory or nonin-flamator y arthritis taking an NSAID but no gastric or duodenal ulcer	Mean age: 59 years; 300 females, 338 males.	Misoprosto l 200µg (n=320) vs. placebo (n=323) for 12 weeks.	Follow-up at baseline , 4, 8, and 12 weeks.	At 12 weeks, duodenal ulcer in 2/320 (0.6%; 95% CI, 0.2% to 3.9%) misoprostol, vs. 15/323 (4.6%; CI, 2.8% to 8%) placebo (p = 0.002).	"Misoprostol significantly lowers the frequency of both duodenal and gastric ulcer development in patients who require long-term therapy with NSAIDS."	Twelve-week trial. Data support misoprostol efficacious.
Bardhan 1993 (Score=7.0)	NSAIDs	RCT	Sponsored by Searle Medical and Clinical Research Department in UK and Ireland. No mention of COI.	N = 358 Patients requiring chronic NSAID therapy (Group 1 = normal; Group 2 = non-ulcer lesions)	Median age: 59.8 years; 103 males, 198 females.	Misoprosto l 400-800µg daily (n=144) vs. placebo tablets (n=157) for 2 weeks.	Follow up at 2 weeks.	Incidence of severe mucosal damage reduced by misoprostol (odds ratio; 95% CI). Group I: 4.52; 1.94, 10.51 (p = 0.018); Group II: 10.93; 1.09, 109.60 (p = 0.014); Groups I and II combined: 5.95; 3.23, 10.94 (p = 0.0003). Misoprostol protected from progression of minor to severe damage in Group II (p <0.001).	"Significant GD damage occurs early in the course of NSAID treatment and misoprostol significantly reduces the incidence of such damage."	Variable dose NSAID and variable misoprostol. Supports misoprostol and reduces early NSAID damage.

Case 2003 (score=6.5)	NSAIDs	RCT	Sponsored by a Specialized Center of Research osteoarthritis grant from the NIH and an intramural development grant from the Rush Arthritis and Orthopedics Institute. COI, Author Baliunas received a Dean's Summer Research Fellowship from Rush Medical College.	N = 82 Medial knee OA	Mean age: 62.21 years; 41 males, 41 females.	Diclofenac 75mg BID (n=29) vs acetaminophen 1000mg QID (n=29) vs. placebo (n=28) for 12 weeks. Double dummy	Follow up was performed at 0, 2, and 12 weeks.	WOMAC pain scores (baseline/Week 2/Week 12): diclofenac (199.8± 101.5/139.6±105.2/146.0±101.2) vs. acetaminophen (310.8±86.3/206.1± 101.2/186.9±121.5) vs. placebo (198.6±110.9/ 197.1±118.8/183.4±122.9). Only diclofenac significant (p <0.002), while acetaminophen p = 0.13 for Week 0-12 differences and other pain changes negative. Acetaminophen never superior to placebo.	"Diclofenac is effective in the symptomatic treatment of OA of the knee, but acetaminophen is not."	Moderate sample size, lack of study details somewhat weaken results. Placebo arm strengthens conclusions that acetaminophen may be weakly effective or ineffective.
Parr 1989 (score=6.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 846 Mostly hip or knee OA	Mean age: 54.79 years; 355 males, 400 females.	Diclofenac sodium slow release 100mg QD (n=373) vs. dextro-propoxyphene 180mg plus paracetamol 1.95gm QD (n=382)	No mention of follow-up.	Dizziness, lightheadedness less common from diclofenac (14 vs. 30, p <0.05), as was CNS symptoms (48 vs. 93, p <0.01). Abdominal pain higher with diclofenac (40 vs. 18, p <0.01) and diarrhea (14 vs. 2, p <0.01). Overall gastrointestinal effects not different (63 vs. 60). Pain ratings were (change in VAS): diclofenac -27.0 vs. dextropropoxyphene plus paracetamol -22.7, p <0.05. Physical mobility scores were -10.8 vs. -7.4 (p <0.01). Interference of work less common with diclofenac (3 vs. 11, p <0.05), and lost work time (3 vs. 16, p <0.05).	"Pain as measured by a visual analogue scale (VAS) showed 8% greater pain reduction with DSR as compared with D&P (P<0.05). Physical mobility as measured by the (Nottingham Health Profile) improved by 13% more with DSR as compared with D&P (P<0.05)."	Study suggests greater efficacy of diclofenac vs. dextropropoxyphene plus acetaminophen. Benefits suggested for working populations from diclofenac including lower incidence of problems at work and lost work time.

Pincus 2004 (score=6.5)	NSAIDs	RCT	Sponsored by Pfizer Corporation. No mention of COI.	N = 1,080 Knee or hip OA	Mean age: 63.4 years; 385 male, 695 female.	Placebo (n=289) vs. acetaminophen 1000mg QID (n=300) vs. celecoxib 200mg QAM (n=350). 6 weeks each. Double dummy. Patients received 2 of 3 treatments.	Follow up at baseline, 1, 7, 8 and 12 weeks.	Percent improvement in WOMAC scores averaged over treatment: celecoxib 21.6% vs. acetaminophen 13.0% vs. placebo 7.9%. Similar VAS score results. Patient preference strongest for celecoxib, then acetaminophen, then placebo.	"[D]ata indicate a gradient of efficacy from celecoxib to acetaminophen to placebo"	Some variation in results in the two trial periods for acetaminophen vs. placebos. Patients generally reported preference for celecoxib over others.

Lussier 1980 (score=6.5)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 30 Knee or hip OA	Mean age: 60.3 years; 9 male, 21 female.	Floctafenine 300mg QID (n=10) vs. enteric-coated aspirin (ACSA) 625mg QID (n=10) vs. placebo (n=10) for 6 weeks.	Follow up at baseline, 2, 4, and 6 weeks.	Pain score: placebo 1.93 vs. floctafenine 1.80 vs. ASA 2.00 (NS). Walking times did not differ at 6 weeks. Patient assessment of efficacy: placebo 2.78, floctafenine 2.00 and ASA 2.33 (p = 0.05 comparing placebo vs. floctafenine).	"[F]loctafenine was more effective than placebo; (2) floctafenine was found to be approximately equivalent or superior to ACSA; and (3) although the results showing a statistical decrease in (hemoglobin) with floctafenine are not clinically significant."	No washout periods before or during trial crossovers. Adjuvant (rescue medication) was the same as control arm (aspirin), weakening conclusions.
Myllykangas-Luosujärvi 2002 (score=6.5)	NSAIDs	RCT	Sponsored by a grant from Merck & Co., Inc. No mention of COI.	N = 944 Knee or hip OA	Mean age: 61.6 ± 9.3 years; 204 male, 740 female.	Rofecoxib 12.5 QD (Study 1: n=242. Study 2: n=229) vs. naproxen 500mg BID (Study 1: n=240. Study 2: n=233) for 6 weeks.	Follow up at screening, baseline, 2, 3 and 6 weeks.	Treatment outcomes for efficacy did not differ. Fewer rofecoxib patients reported AEs considered to be drug-related than naproxen [19.5% vs. 31.3%; p <0.001]. More GI-related AEs among naproxen treated patients.	"[I]n two separate six-week OA treatment trials, the lowest indicated dose of rofecoxib (12.5 mg) demonstrated comparable onset of action and clinical efficacy to naproxen 1000mg with superior GI tolerability profile."	More than 50% of both groups took escape medication. Results suggest comparable efficacy, but higher adverse effects for naproxen.
Hosie 1996 (score=6.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 336 Hip or knee OA	Mean age: 64.3 years; 137 male, 198 female.	Meloxicam 7.5mg QD (n=169) vs. diclofenac sodium SR 100mg QD (n=166) for 6 months.	Follow up at 2 weeks, 1, 2, 3 and 6 months.	VAS pain ratings (baseline/last visit): meloxicam (65.9±16.9/-28.1±29.4) vs. diclofenac (67.2±14.2/-30.9±29.1), NS. Other measures of pain on movement, global efficacy stiffness and quality of life all were not different. Adverse events in 59.8% of meloxicam vs. 60.5% diclofenac.	"Meloxicam 7.5 mg once daily and diclofenac 100 mg slow release once daily showed comparable efficacy in the treatment of OA, although diclofenac was associated with somewhat higher incidence of severe adverse events, treatment withdrawals and laboratory test abnormalities."	Allocation unclear with at least one baseline variable difference (duration of osteoarthrosis, p<0.05) that may favor meloxicam.

Melo Gomes 1993 (Score=6.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 643 Hip and/ or knee OA	Mean age: 59.6 years; 155 males, 488 females.	Diclofenac sodium 50mg plus misoprostol 200µg BID (n=216) vs. piroxicam 10mg BID (n=217) vs. naproxen 375mg BID (n=210) for 4 weeks.	No mention of follow-up.	Changes in OA severity indices: diclofenac/ misoprostol -4.27 vs. piroxicam -3.19 vs. naproxen -3.79, p = 0.015. Global assessment scores did not differ. On endoscopy, proportion with gastroduodenal ulcers: diclofenac/ misoprostol 3 (1.5%) vs. piroxicam 21 (10.3%) vs. naproxen 17 (8.6%) (p = 0.001).	"[T]he fixed combination of diclofenac and misoprostol is associated with fewer gastroduodenal ulcers than either piroxicam or naproxen."	Regular adult dosages not used. Assessor blinding not clear. Endoscopic results suggest diclofenac/misoprostol reduces risk of adverse GI events compared with 2 other NSAIDs.
Lohmander 2005 (Score=6.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 970 Hip or knee OA	Mean age: 59.3 years; 706 females, 264 males.	AZD3582 750mg BID (n=437) vs. naproxen 500mg BID (n=417) vs. placebo (n=116) for 6 weeks.	Follow-up at baseline, 1 week later or 3 days after the treatment.	Endoscopic evidence of significant GI damage (Lanza scores 3 and 4): AZD3583 (32.2%) vs. naproxen (43.7%) vs. placebo (7.0%). WOMAC: AZD3582 (-15.9) vs. naproxen (-14.7) vs. placebo (-5.8). WOMAC scores tended to decrease more in knee than hip.	"AZD3582 had similar analgesic effects to naproxen…the 30% difference in the incidence of gastroduodenal ulcers after six weeks of treatment…was not (significant)."	Lacks methodology details. Shows no advantage of AZD3582 after 6-week trial for endoscopic GI outcomes or pain outcomes. Trends in data suggest hip OA less treatable with either medication.
Cullen 1998 (Score=6.5)	NSAIDs	RCT	Sponsored by Astra Pharmaceuticals. No mention of COI.	N = 169 Patients taking NSAIDs regularly, chronic-ally, and above defined minimum doses	Mean age: 55.5 years; 112 females, 56 males.	Omeprazole 20mg (n=83) vs. placebo (n=85), given for up to 6 months.	No mention of follow-up.	Fourteen (14) patients treated with placebo (16.5%) developed 15 ulcers compared to 3 patients (3.6%) on omeprazole (p <0.01).	"Omeprazole is an effective agent for gastroduodenal prophylaxis in patients taking NSAIDs. Its main effect is to reduce the rate of development of gastric and duodenal ulcers."	Up to 6 months of treatment.

Stupnicki 2003 (Score=6.5)	NSAIDs	RCT	Sponsored by ALTANA Pharma AG in Konstanz Germany. No mention of COI.	N = 515 Rheum-atic patients likely to take NSAIDs contin-uously for at least 6 months	Median age: 64 years; 139 males, 376 females.	Pantoprazole 20mg plus placebo (n=257) vs. misoprostol 200µg (n=258).	Follow-up at 3 months.	Pantoprazole superior to misoprostol (p = 0.005) for endoscopic failure. Estimated remission rates 3 and 6 months, 98 and 95% (pantoprazole); 95 and 86% (misoprostol). Discontinuations for likely/definitely drug-related adverse effects: 13/257 (5%) pantoprazole vs. 33/258 (13%) misoprostol.	"Pantoprazole 20 mg o.d. is superior to misoprostol 200 microg b.i.d. in the prevention of NSAID-induced gastrointestinal lesions and symptoms in patients on continuous long-term treatment with NSAIDs due to rheumatic diseases and at risk to develop such lesions or symptoms."	Six-month treatment. Study suggests pantoprazole superior to misoprostol.
Desai 2008 (Score=6.5)	NSAIDs	RCT	Sponsored by Pfizer, Inc. and Digestive Disease Research Foundation. No mention of COI.	N = 70 Healthy adults aged 50-75 not taking chronic NSAIDs	Mean age: 58.6 years; 37 females, 33 males.	Naproxen 500mg BID plus omeprazole 20mg QD (n=35) vs. naproxen 500mg BID plus placebo (n=35) for a 6.5-day treatment.	Follow-up at 14th day of last treatment.	Less gastroduodenal ulcers in naproxen plus omeprazole vs. naproxen plus placebo [11.8% (4 ulcers/34 subjects) vs. 46.9% (15/32), RR = 0.25, p = 0.002]. NPX plus OMP associated with decreased risk of ulceration and erosion [5 erosions [38.2% (13/34) vs. 81.3% (26/32), RR = 0.47, P B 0.001].	"[O]MP at the U.S. OTC dosage of 20 mg daily begun on Day 1 of NSAID treatment reduces both GDUs and dyspepsia with OMP. Therefore, in view of the relatively low cost, availability, and good safety profile of OTC OMP, co-prescription of a PPI in relatively healthy older patients requiring short-term non-specific NSAID therapy may be reasonable."	"Pilot Study"; unclear whether endoscopy data translate to clinical outcomes to support conclusion.
Lanza 1988 (Score=6.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 90 Normal volunteers	Age range: 18-47 years; no mention of sex.	Misoprostol 200µg QID (n=29) vs. cimetidine 300mg QID (n=30) vs. placebo (n=30) for 7 days.	No mention of follow-up.	Overall success rates 8/30 (26.7%) for placebo, 19/30 (63.3%) cimetidine, 27/29 (93.1%) misoprostol (p <0.001). Pairwise comparisons: misoprostol vs. placebo (p <0.001), misoprostol vs. cimetidine (p = 0.006), cimetidine vs. placebo (p = 0.004).	"[M]isoprostol is highly effective and significantly better than cimetidine in protecting the gastric mucosa from tolmetin-induced injury; however, both agents were highly protective in the duodenum."	Short-term study. Suggest cimetidine inferior for gastric mucosa but not duodenal.

Agrawal 1991 (Score=6.5)	NSAIDs	RCT	Sponsored by G.D. Searle & Company. No mention of COI.	N = 253 OA patients receiving ibuprofen, piroxicamor napro-xen with abdom-inal pain	Median age: 60 years; 115 females, 85 males.	Misoprostol 200µg (n=179) vs. sucralfate 1g QID a day (n=177) for 12 weeks.	Follow-up at baseline, 4, 8, and 12 weeks.	Gastric ulcer developed in 2/122 (1.6%, 95% CI, 0.3% to 6.4%) on misoprostol vs. 21/131 on sucralfate (16%, CI, 10.4% to 23.7%). Difference in ulcer rates: 14.4% (CI, 10.4% to 19.5%.	"In patients receiving chronic NSAID therapy for osteoarthritis, treatment with misoprostol for 3 months was associated with a significantly lower frequency of gastric ulcer formation, compared with treatment with sucralfate (P less than 0.001)."	OA patients. Study suggests misoprostol is effective compared with sucralfate.
Gordin 1984 (score=6.0)	NSAIDs vs. Other NSAIDs and Trials with Multiple Treatment Arms	Crossover trial	No mention of sponsorship or COI.	N = 44 Hip or knee OA	Mean age: 61.7 years; 14 males, 28 females	Slow-release formulation of indomethacin (50mg) vs. diflunisal (250mg); 2 tablets daily for 6 weeks. All patients received both treatments.	6 weeks	Both treatments reduced pain, 22 preferred slow-release indomethacin; 7 diflunisal; 13 no preference. Patient overall evaluation of efficacy was indomethacin slightly more effective than diflunisal (p <0.01). Total use of rescue analgesics: 540 tablets in indomethacin vs.711 with diflunisal.	"The indomethacin formulation alleviated pain slightly better than diflunisal in patients with arthrosis, and the patients preferred indomethacin to diflunisal in this respect. The tolerability of the drug was about the same."	Suggests indomethacin slightly superior to diflunisal.

Kjaersgaard-Andersen 1990 (score=6.0)	NSAIDs	RCT	No mention of COI or sponsorship.	N = 158 Hip OA	Mean age: 66.0 years; 86 males, 72 females.	Codeine plus paracetamol (60mg/1g TID) (n=83) vs. paracetamol (1g TID) (n=75)	Follow-up at 4 weeks after initial treatment.	First week, more use of rescue medication in paracetamol (21% vs. 5%). Difference disappeared 2nd week (20% vs. 21%). Significantly more adverse reactions with codeine (1st week: nausea 34 vs. 6; dizziness 26 vs. 1; somnolence 14 vs. 5; fatigue 10 vs. 1). Most codeine patients had an adverse reaction in first week (86.7% vs. 37.8% placebo). Six (13.9%) vs. 4 (6.7%) patients reported very good or excellent results.	"When evaluated after 7 days of treatment, the daily addition of codeine 180 mg to paracetamol 3 g significantly reduced the intensity of chronic pain due to osteoarthritis of the hip joint. However, several adverse drug reactions, mainly of the gastrointestinal tract, and the larger number of patients withdrawing from treatment means that the addition of such doses of codeine cannot be recommended for longer-term treatment of chronic pain in elderly patients."	Study prematurely terminated due to high rates of adverse reactions and dropouts. Overall drop-out rate was 51.8% vs. 23.0%.
Quiding 1992 (score=6.0)	NSAIDs	Crossover Trial	No mention of COI or sponsorship.	N = 26 Hip OA	Mean age: 53.0 years; 4 males, 22 females.	Ibuprofen 200mg plus codeine 30mg (n=26) vs. ibuprofen 200mg (n=26) vs placebo (n=25). Used single and repeated dosings; 6 doses in 24-hour period each regimen.	Follow-up at 32 after initial treatment.	Pain intensity ratings after 1st dose (baseline/1-8 hours later): IBU plus codeine (34/25) vs. IBU (37/27) vs. placebo (31/26). Pain intensity ratings after 6th dose: IBU plus codeine (11/10) vs. IBU (19/17) vs. placebo (33/29) ($p < 0.05$ comparisons with placebo or ibuprofen).	"[A]nalgesic efficacy was better differentiated after repeated-doses than after single-dose administration…study design was able to differentiate between 200mg ibuprofen plus 30 mg codeine and 200 mg ibuprofen alone in a relatively small number of patients."	Study purpose is for analgesic effects prior to surgery. Very short-term treatment intervals of 3 days preclude assessments of long-term safety and efficacy.

Bellamy 1995 (score=6.0)	NSAIDs	RCT	Sponsored by a grant from SmithKline Beecham Pharma Inc. No mention of COI.	N = 382 Hip, knee or shoulder OA	Mean age: 62.0 years; 112 male, 268 female.	Nabumetone 1,000mg (n=191) vs. diclofenac SR 200mg QPM (n=189) for 3 months. Dose could be titrated once after 2 weeks of initial dose. Double dummy.	Follow up at 2, 8, 14, 20, and 26 weeks.	More on nabumetone titrated to higher dose (69% vs. 53%, p = 0.002). Physician assessments of disease activity were 63% improved on nabumetone vs. 70% on diclofenac. Pain ratings reduced approximately 40% by either treatment. Adverse effects in 43 diclofenac vs. 27 nabumetone patients (p <0.04).	"Nabumetone is efficacious and well tolerated in patients with OA of the hip, knee or shoulder. In this group of patients it is similar in efficacy and superior in tolerability to diclofenac SR."	Variable doses used. High dropout rate (43%) at 6 months precludes strong conclusions.

Herrmann 2000 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 263 Knee and/or hip OA	Mean age: 61.8 years; 92 male, 127 female.	Oxaceprol 400mg TID (n=132) vs. diclofenac 50mg TID (n=131) for 21 days	Follow up at 1, 5, 10, 15 and 21 days.	Mean total scores (baseline/Day 21): oxaceprol 14.0±3.5/11.5 ±3.8 vs. 14.0±4.1/11.2± 3.9 (NS). Lequesne indices decreased, but not different between treatments (-2.5 points oxaceprol vs. -2.8 points diclofenac, NS); 47% treated with oxaceprol and 56% treated with diclofenac judging efficacy. Adverse effects for 18.9% oxaceprol vs. 25.2% diclofenac.	The results of this phase IV study demonstrate that oxaceprol is as effective as diclofenac in the therapy of osteoarthritis of the knee and/or hip, but is significantly better tolerated.	Blinding unclear. Patients allowed physical therapy. Was phase II trial. Data suggest equal efficacy for total scores, but with lower adverse effects.
Ginsberg 1984 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 24 Knee or hip OA	Mean age: 63.1 years; 9 males, 16 females	Oxaprozin 1,200mg QD (n=12) vs. naproxen 250mg TID (n= 12) for 8 weeks. Double dummy.	4 weeks	Patient opinion of efficacy (baseline/8 weeks): oxaprozin (4.3/-1.9) vs. naproxen (4.4/-2.5). Observer opinion, pain intensity, activity impairments all improved, although all favored naproxen, not statistically significant.	"1200 mg oxaprozin once daily is an effective and relatively well-tolerated form of treatment in osteoarthritis and is at least comparable to 250mg naproxen 3-times daily."	Small sample size and comparison is sub-maximal naproxen, limiting conclusions.
Schnitzer Arth Rheum 2004 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 583 Knee or hip OA	Mean age: 60.3 ± 9.2 years; 188 male, 395 female.	Lumiracoxib 50mg (n=98) vs 100mg (n=96) vs. 200mg BID (n=99) vs. 400mg QD (n=99) vs. diclofenac 75mg BID (n=94) vs. placebo (n=97) for 4 weeks	Follow up at 1, 2 and 4 weeks.	Patient assessments (baseline/4 weeks): lumiracoxib 50 BID (63.1±17.5/38.8±21.5) vs. L 100BID (62.0±18.5/ 37.8±22.2) vs. L200BID (64.0±17.3/ 37.5±24.0) vs. diclofenac (62.2±16.2/ 34.4±23.0) vs. placebo (62.5±18.1/50.0±23.0). Lumiracoxib and diclofenac superior to placebo.	"Throughout the study, all dosages of lumiracoxib were equally effective in lowering pain intensity, although at week 1 there was a modestly greater improvement in pain relief with the 400 mg once daily lumiracoxib dose when compared with the 50 and 100 mg twice daily doses."	Sparse details on randomization, allocation, and blinding. Efficacy comparable between lumiracoxib and diclofenac, however adverse effects higher with diclofenac.

Morgan 2001 (score=6.0)	NSAIDs	RCT	Sponsored by SmithKline Beecham Pharmaceuticals, Collegeville, PA. U.S.A. No mention of COI.	N = 335 Moderate to severe knee or hip OA	Mean age: 72 years; 99 male, 236 female	Nabumetone 1,000-2,000mg QD (n=167) vs. diclofenac 50mg BID-TID (n=168) for 12 weeks; doses titrated	Follow up at 1, 2, and 3 months.	Patient global assessments not different (nabumetone 75% vs. diclofenac 79%). Pain score changes: nabumetone -3.1±0.2 vs. diclofenac -3.7±0.2. No difference in Arthritis Impact Measurement Scales. More diclofenac patients on maximum dose (46% vs. 66%). Nabumetone group more acetaminophen 2nd week ($p<0.05$). More diclofenac than nabumetone patients ($p<0.05$) had ALT level 2 times or more than upper limit of normal (6 or 161 [3.7%] vs. 0 of 155 [0%]).	"Nabumetone was as effective as diclofenac in the treatment of elderly patients with moderate-to-severe osteoarthritis. However, the gastrointestinal safety profile of nabumetone was superior to that of diclofenac with respect to elevation of liver enzymes."	Blinding, randomization, compliance and co-intervention details missing.

Cannon 2000 (score=6.0)	NSAIDs	RCT	Sponsored by Merck Research Laboratories. No mention of COI.	N = 784 Hip or knee OA	Mean age: 63.6 ± 10.2 years; 255 male, 529 female.	Rofecoxib 12.5 QD (n=259) vs 25mg QD (n=257) vs. diclofenac 50mg TID (n=268) for 1 year	Follow up at 2, 4, 8, 12, 26, 39 and 52 weeks.	448/784 (57.1%) completed 1 year. No differences in discontinuation due to lack of efficacy or adverse effects. Mean response for primary end point of patient assessment of response to therapy similar among all treatment groups. Patient assessment comparing rofecoxib 25mg vs. diclofenac favored diclofenac (0.19, 95% CI 0.05-0.33). Rofecoxib 12.5mg also significant. Physician assessment of disease activity also favored diclofenac for both rofecoxib doses ($p < 0.05$). Only pain when walking WOMAC outcome did not demonstrate statistical superiority of diclofenac.	"In this 1-year study that included patients with cardiovascular risk factors (hypertension in 45%, angina in 3%, hypercholesterolemia in 16%, and diabetes in 7%), the incidence of thromboembolic cardiovascular events, such as myocardial infarction, stroke, transient ischemic attack, and peripheral arterial occlusions, was numerically lower in the rofecoxib groups (1.5%, 2.3%, and 3.4% in the 12.5 mg rofecoxib, 25-mg rofecoxib, and diclofenac groups). The specific inhibition of COX-2 with rofecoxib at a dosage of 12.5 mg and 25 mg once daily provided comparable clinical efficacy to that of the knee and hip. Rofecoxib was generally well tolerated."	Lack of details for compliance, blinding co-interventions. High dropout rate 42% at one year may reduce differences. Most data suggest comparable efficacy, however some data suggest diclofenac superior.

Alho 1988 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 252 Severe hip OA	Median age: 70 years; 71 male, 181 female	Piroxicam 20mg QAM (1st Control Visit: n=118. 2nd Control Visit: n=109) vs. naproxen 500mg QAM and 250mg QPM (1st Control Visit: n=115. 2nd Control Visit: n=100)). Trial length unclear (possibly 1 month), but observed for 5 months.	Follow up at 4-5 weeks and 1-4 months	Pain at rest at 4-5 weeks compared with baseline: piroxicam -1.5±1.7 vs. naproxen -0.9±0.6 (p = 0.056). Pain on movement/ impairment of daily activities improved, but not different between groups. Night pain piroxicam -2.0±2.1 vs. naproxen -1.3±2.1 (p = 0.01). Modified Harris hip score improved from baseline more for piroxicam than naproxen (p <0.01). No differences between groups at later follow-up visits.	"[I]t is profitable to continue a previous NSAID medication or re-establish such therapy while the patient waits for a planned operation for OA. The NSAIDs seem to be effective even in advanced OA where the mechanical joint incongruency component may be dominating. However, only 7% of the patients wanted to postpone the planned operation after regular medication."	Lack of study details-allocation, blinding. Data support equal efficacy, with a few data suggesting piroxicam superior to naproxen at 4 to 5 weeks.

Baumgartner 1996 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 61 Knee or hip OA	Mean age: 59.8 years; 15 male, 46 female.	Two SR tablets of ibuprofen 1,600mg (n=30) vs, diclofenac 100mg SR QPM (n=31) for 21 days.	Follow up at baseline, 7 and 21 days.	Investigator's opinion of much improved patients at Day 21: ibuprofen 37% vs. diclofenac 10%, p = 0.04. Patient severity of day pain was ibuprofen 1.2 vs. diclofenac 1.8, p = 0.006. Night pain (p = 0.048), quality of sleep (p = 0.03), ability to carry out normal activities (p = 0.01) all favored ibuprofen. No difference in adverse event reporting rates.	"[S]ignificant differences in favour of once-daily s-r ibuprofen (1600 mg) were demonstrated in terms of efficacy, indicating a potential therapeutic advantage for this formulation. Ibuprofen was also better tolerated than diclofenac sodium (100 mg/daily), the latter being associated with gastrointestinal side effects in a significant proportion of patients. Sustained-release ibuprofen thus represents an important addition to the available therapeutic armamentarium of once-daily NSAID formulation."	Lack of patient blinding. Data may suggest sustained relief ibuprofen superior to diclofenac, however the lack of blinding weakens conclusions although differences also included blinded investigator's assessments of change.
Shipley 1983 (score=6.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 36 Knee or hip OA	Mean age: 65 years; 12 male, 24 female.	Rhus Tox vs. placebo vs. fenoprofen 600mg TID. All patients received both treatments.	Follow up at 2, 4 and 6 weeks	VAS scores (baseline/ placebo/Rhus/fenoprofen): 53.4±25.1/61.0±27.6/58.2 ±25.5/41.5±29.0. Patients preferred fenoprofen. More adverse effects for fenoprofen.	"There was no significant difference between the effects of Rhus tox. and placebo. Fenoprofen produced highly significant pain relief compared with Rhus tox and placebo."	Rhus tox, 6X is poison ivy extract and appears not efficacious. NSAID efficacious vs. placebo or Rhus.

Brown 1986 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N =143 Hip and/ or knee OA	Mean age: 61.1 years; 51 male, 92 female.	Flurbiprofen 50mg BID (n=73) vs. sulindac 150mg BID (n=70) for 42 days.	Follow up at 0, 2, 4 and 6 weeks.	At 6 weeks, (knee/hip) 70.2%/82.6% flurbiprofen vs. 76.7%/66.7% sulindac improved. Weight-bearing pain not different. Pain with active movement: 72.3%/91.3% flurbiprofen vs. 76.7%/56.5%. Flurbiprofen superior to sulindac for hip OA regarding pain with movement (p = 0.002).	"Despite its half-life of 5.5 hours, flurbiprofen twice daily is as effective as twice-daily sulindac, which has a much longer half -life of 7.8 hours, for patients with osteoarthritis."	Comparable efficacy although flurbiprofen superior for hip pain with active movement.
Cardoe 1986 (score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 230 Hip and/or knee OA	Mean age: 62.7 years; 73 male, 157 female.	Isoxicam 200mg QD (n=113) vs. Naproxen 500mg BID (n=117) for 4 weeks. Double dummy.	Follow up at 3 days, 2 and 4 weeks	No apparent differences in most treatment outcomes including pain ratings. Isoxicam superior for night pain at 4 weeks (52% better vs. 36%, p <0.05). Comparable adverse effect profile (details sparse).	"[I]soxicam produced comparable benefits to naproxen and for some parameters was superior."	Study details are sparse. Second trial reported on rheumatoid arthritis (n = 249) with isoxicam more effective as rated by patients (p = 0.04).

Gordin 1984 (score=6.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 44 Hip or knee OA	Mean age: 61.7 years; 14 males, 28 females.	Slow-release formulation of indomethacin (50mg) vs. diflunisal (250mg); All patients received one of the two tablets at random daily for 6 weeks then the other for another 6 weeks.	6 weeks	Both treatments reduced pain, 22 preferred slow-release indomethacin; 7 diflunisal; 13 no preference. Patient overall evaluation of efficacy was indomethacin slightly more effective than diflunisal ($p < 0.01$). Total use of rescue analgesics: 540 tablets in indomethacin vs.711 with diflunisal.	"The indomethacin formulation alleviated pain slightly better than diflunisal in patients with arthrosis, and the patients preferred indomethacin to diflunisal in this respect. The tolerability of the drug was about the same."	Suggests indomethacin slightly superior to diflunisal.
Bianchi Porro 1998 (Score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 114 Arthritic disorders requiring indometh-acin, diclo-fenac, or keto-profen	Mean age: 52.4 years; 87 females, 16 males.	Omeprazole 20mg QD (n=57) vs. placebo (n=57) for 3 weeks. All patients given indomethacin 100mg, ketoprofen 150mg, and diclofenac 150mg.	No mention of follow-up.	26/57 (46%) of omeprazole vs. 20/57 (35%) of placebo group with normal gastroduodenal mucosa (score = 0). Clinically significant gastric lesions (score 3-4) in 6/57 (11%) omeprazole vs. 11/57 (19%) on placebo.	"Omeprazole 20mg once daily is significantly more effective than placebo in the prevention of gastric and duodenal ulcers due to chronic NSAIDs treatment and may provide clinical advantages, in terms of tolerability, over currently available prophylactic therapies."	Three weeks of treatment added to NSAID. Data support treatment.

Bergmann 1992 (Score=6.0)	NSAIDs	RCT	Sponsored by Houde Laboratories Paris La Defense. No mention of COI.	N = 12 Healthy volunteers	Age range: 22-32 years; 7 males, 5 females.	Lansoprazole 30mg QD (n=6) vs. placebo plus aspirin (n=6) for 1 week.	No mention of follow-up.	Mean Lanza scores 0.67±0.98 with lansoprazole vs. 2.25±1.1 with placebo (p <0.005).	"[I]t is possible to distinguish the functional and morphologic effects of a gastrotoxic drug such as aspirin during experimental studies in humans. Lansoprazole prevents hemorrhagic lesions without reinforcing the mucosal barrier."	Crossover study with small sample size (n = 12). Short experimental design of 1 week.
Graham 2002 (Score=6.0)	NSAIDs	RCT	Sponsored by TAP Pharmaceutical Products Inc. One or more authors have received or will receive benefits for personal or professional use.	N = 537 Patients without H pylori and long-term users of NSAIDs with history of gastric ulcer	Mean age: 60.4 years; 348 females, 187 males.	Placebo (n=134) vs. Misoprostol 200µg QID (n=134) vs. 15 mg of lansoprazole QD (n=136) vs. 30mg of lansoprazole QD (n=133) for 12 weeks.	Follow-up at 12 weeks.	Patients on NSAIDs. Either dose lansoprazole remained free from gastric ulcer longer vs. placebo (p <0.001).Misoprostol group remained free of gastric ulcers longer than placebo (p <0.001), 15mg lansoprazole (p = 0.01), or 30mg lansoprazole (p = 0.04).	"Proton pump inhibitors such as lansoprazole are superior to placebo for the prevention of NSAID-induced gastric ulcers but not superior to misoprostol, 800 microg/d. When the poor compliance and potential adverse effects associated with misoprostol are considered, proton pump inhibitors and full-dose misoprostol are clinically equivalent."	Not blinded to misoprostol. H pylori negative.
Elliott 1994 (Score=6.0)	NSAIDs	RCT	Sponsored by G.D. Searle & Co. No mention of COI.	N = 83 Arthritis patients on chronic NSAID therapy	Mean age: 65.5 years; 46 males, 37 females.	Misoprostol 200µg (n=40) vs. placebo tablets (n=43) for 12 months.	Follow-up at 3, 6, 12 months.	4/32 (12.5%) on misoprostol developed gastric ulcer vs. 11/38 (28.9%) on placebo (p <0.05); 6/11 with initial gastric ulcer developed further gastric ulcer vs. 9/58 without an initial ulcer (p <0.05).	"[M]isoprostol decreases the cumulative development of NSAID-induced gastric ulcers. Patients with a previous NSAID-ulcer have a higher risk of further ulceration."	Study suggests that misoprostol is effective.

Ehsanullah 1988 (Score=6.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 297 RA or OA without lesions in the stomach and duo-denum	Mean age: 58.4 years; 105 male, 158 females.	Ranitidine 150mg twice a day (n=137) vs. placebo twice a day (n=126).	Follow-up at 4 to 8 weeks.	Cumulative incidence of peptic ulceration at 8 weeks 10.3% (27/263); 2/135 (1.5%) developed duodenal ulceration in the ranitidine group vs. 10/126 (8%) taking placebo. Frequency of gastric ulceration same (6%) for the 2 groups at 8 weeks. Fewer gastric lesions in ranitidine group.	"Ranitidine 150 mg twice daily significantly reduced the incidence of duodenal ulceration but not gastric ulceration when prescribed concomitantly with one of four commonly used non-steroidal anti-inflammatory drugs."	RA or OA. Also treatments with naproxen, diclofenac, indomethacin or piroxicam. Suggests ranitidine prevents DU, not GU.
Bauer 1999 (score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 150 Knee or hip OA	Mean age: 57 years; 56 male, 68 female.	Oxaceprol 200mg TID (n=62) vs. diclofenac 25mg TID (n=62) for 20 days	Follow up at 1, 3, 6, 10, 15 and 20 days.	Pain at rest reduced: oxaceprol from 4.1 to 2.1 pts vs. diclofenac 4.3 to 2.5 pts (NS). Therapeutic equivalence also for changes in Lequesne index, weight-bearing pain, and pain-free walking time.	"[W]ith comparable therapeutic efficacy and a favorable spectrum of ADR, oxaceprol is a good alternative to standard NSAIDs, such as diclofenac, in the treatment of osteoarthritis."	Although author reports better tolerance, no significant differences were reported. Treatments appear comparable.
Ginsberg 1982 (score=5.5)	NSAIDs	Crossove r trial	No mention of sponsorship or COI.	N = 25 Hip or knee OA	Median age: 63 years old; 9 males, 16 females.	Nabumeto ne 1gm QHS (N=13) vs. naproxen 250mg BID (N=12) for 7 days each	No mention of follow-up.	Both treatments efficacious. Nabumetone better tolerated Among nabumetone first group, 7/13 considerably better vs. 10/13 naproxen. For naproxen first group, rates 5/12 vs. 5/12.	"Nabumetone (1g at night) appeared, thus, to be a good and very well tolerated anti-inflammatory drug in the treatment of osteoarthritis."	Submaximal naproxen dose used. Small sample size, groups tended to select their last treatment as best (p = 0.02), possibly a recall bias.

Adelowo 1998 (score=5.5)	NSAIDs	RCT	Sponsored by grant from Roche (Nigeria) Limited. No mention of COI.	N = 48 Knee or hip OA	Mean age: 12 males, 30 females	Tenoxicam 20mg QD (n=17) vs. piroxicam 20mg QD (n=25) for 6 weeks	6 weeks	Slight superiority of tenoxicam vs. piroxicam for pain. No difference in GI adverse effects. Excellent or good tolerability tenoxicam 88.2% vs. 60.0%, p = 0.06. All other measures of success/tolerability did not differ. Piroxicam and tenoxicam did not alter laboratory measures.	"Tenoxicam is an efficacious and well tolerated NSAID which proved useful among Nigerian osteoarthritis patients."	Study in Nigeria. Generally comparable efficacy, although trends tenoxicam may be superior but underpowered for those outcomes.
Makarowski 2002 (score=5.5)	NSAIDs	RCT	Sponsored by Pharmacia Corporation and Pfizer Inc. No mention of COI.	N = 467 Hip OA	Mean age: 62.3 years; 151 male, 316 female.	Valdecoxib 5mg QD (n=120) vs. 10mg QD (n=111) vs. naproxen 500mg BID (n-118) vs. placebo (n=118) for 12 weeks	Follow up at baseline, 2, 6 and 12 weeks.	Patient global assessment changes baseline to 12 weeks: valdecoxib 10mg (-1.29) vs. 5mg (-1.20) vs. naproxen (-1.18) vs. placebo (-0.87) (p <0.05 all arms vs. placebo). Physician global assessments similar. WOMAC score changes: valdecoxib 10mg (-2.83) vs. 5mg (-2.54) vs. naproxen (-2.94) vs. placebo (-1.25) (p <0.05 all arms vs. placebo). GI-related adverse effects lower compared with naproxen (11.0% vs. 4.5% vs. 4.2% vs. 1.7%).	"Single daily doses of valdecoxib 5 mg and 10 mg were similar to naproxen and superior to placebo, in treating symptomatic OA of the hip. Both doses of valdecoxib were well tolerated and demonstrated improved GI tolerability compared to naproxen."	High dropout rates although placebo was superior to naproxen for GI effects including constipation and dyspepsia. Suggests comparable efficacy for active treatments, but lower adverse GI symptoms for valdecoxib.

Marcolongo 1997 (score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 113 Hip OA	Mean age: 58.5 years; 17 males, 96 females	Ketoprofen controlled-release 200mg QD (n=57) vs. indomethacin 50mg BID (n=56) for 4 weeks	4 weeks	Daytime VAS scores with movement (baseline/final): indomethacin 6.15±2.08/ 3.85±2.07 vs. ketoprofen 6.25±2.34/3.84±2.38, p = 0.74. Other measures of rest pain, night pain, global scores not different. Willingness to or performance at work was (53.7%) in indomethacin and (58.7%) in ketoprofen (p = 0.67). No differences in GI adverse effects. Headache and dizziness in 10% of indomethacin vs. none in ketoprofen (p = 0.028). Indomethacin discontinued more frequently, 20% vs. 11%.	"Controlled-release ketoprofen may be preferred in indomethacin in the symptomatic treatment of osteoarthritis because of its better safety profile."	Open label trial. Sub-maximal doses. Some higher CNS adverse effects in indomethacin treated patients.
Kivitz 2001 (score=5.5)	NSAIDs	RCT	Sponsored by the Pharmacia Corporation a Pfizer Inc. No mention of COI.	N = 1,061 Hip OA	Mean age: 62.6 years; 361 male, 700 female	Celecoxib 100mg (n=216) vs. 200mg (n=207) vs. 400mg QD (n=213) vs. naproxen 500mg BID (n=207) vs. placebo (n=218) for 12 weeks	Follow up at baseline, 2-4 days, 2, 6, and 12 weeks.	Patient global assessments 12 weeks: placebo (-0.5) vs. celecoxib 100mg (-0.9) vs. 200mg (-1.1) vs. 400mg (-0.9) vs. naproxen (-1.1) (naproxen superior to 100 and 400mg doses, p <0.05). All medications favored over placebo. Patient withdrawl significantly higher in celecoxib 100mg a day vs. 400mg a day (p = 0.04) or naproxen (p = 0.02).	"Celecoxib doses of 200 and 400 mg/day were similarly efficacious and comparable to naproxen. The overall incidence of adverse events in patients receiving celecoxib 100-400 mg/day or naproxen 1000mg/day was comparable, and similar to those receiving placebo."	Dropout rate due to failure was high in placebo and treatment groups (52% vs treatment [25-35%]). Total number of adverse events was similar in all groups. Comparable efficacy shown for active treatments.

Telhag 1981 (score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 70 Knee or hip OA	Mean age: 62.3 years; 35 males, 35 females	Tolmetin sodium 400mg BID (n=34) vs. Naproxen 250mg BID (n=36) for 12 weeks	1, 2, 4, 8, 12 weeks	Patient overall assessment to responses (very good or good): tolmetin (15/34 = 44.1%) vs. naproxen (18/35/51.4%), NS. No differences in physician assessment, pain on active motion, pain at rest, localized tenderness. For patients evaluated at 12 weeks who had "pain symptomatology" initially, more tolmetin had reductions in severity of pain at rest and pain on active motion ($p < 0.05$).	"Tolmetin sodium given twice a day seems to be at least as effective as naproxen in relieving pain in osteoarthritis; tolerability for the two drugs was comparable."	Submaximal naproxen dose used. Overall responses were comparable over 12 weeks.
Yocum 2000 (score=5.5)	NSAIDs	RCT	Sponsored by a grant from Boehringer Ingelheim, Ridgefield, Conn. No mention of COI.	N = 774 Hip or knee OA flare	Mean age: 62.9 ± 10.3 years; 258 male, 516 female.	Meloxicam 3.75 (n=154) vs. 7.5 (n=154) vs. 15mg (n=156) a day vs. diclofenac 50mg BID (n=153) vs. placebo (n=157) for 12 weeks. Double dummy.	Follow up daily for 12 weeks	Discontinuation rates due to lack of efficacy at day 84 were 41% placebo vs. meloxicam 31/18/17% vs. diclofenac 12%. Rates of discontinuation at Day 84 due to adverse events were respectively 7/10/8/10/9%. Composite adverse events were comparable among 3 meloxicam groups and higher than placebo group (66.0%). No differences in GI adverse events between placebo and meloxicam groups. GI adverse events higher in diclofenac than placebo. Other adverse effects, e.g., headache, rash, edema, not different between any groups.	"For both patient's and investigator's final global assessment of efficacy, the 15-mg/d dosages of meloxicam and diclofenac were statistically significantly superior to placebo for all comparisons."	12 week trial with similar efficacy results for meloxicam 15mg/d vs. diclofenac 50mg BID. GI effects on diclofenac were higher for diarrhea and N/V, but overall pain improvement trended in favor of diclofenac.

Niwa 2008 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 10 Healthy subjects	Age range: 20-40 years; 10 males.	Rebamipide 300mg plus diclofenac 75mg plus omeprazole 20mg (n=2) vs. placebo plus diclofenac 75mg plus omeprazole 20mg QD (n=8) for 1 week.	No mention of follow-up.	Number of subjects with small-intestinal mucosal injuries significantly higher in placebo group (8/10) than rebamipide group (2.10) (p = 0.023).	"Rebamipide had significantly higher efficacy than placebo in preventing NSAID-induced small-intestinal mucosal injury."	Crossover trial with small sample size (n = 10). Evaluation of small intestine. 7 day treatment. Data suggest efficacy for small intestine.
Chandrasekaran 1991 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 90 Arthritic patients	Mean age: 39 years; 45 males, 45 females.	Patients with misoprostol intervention (n=45) vs. placebo group (n=45).	Follow-up at 4th week at the end of the study.	Patients on placebo with more post-therapy abnormal endoscopy findings; 24.4% of misoprostol group vs. 28.8% in placebo group had UGI symptoms during the trial (NS).	"Arthritic patients requiring long term NSAID therapy appear to benefit from misoprostol because of its cytoprotective effect on the gastrointestinal mucosa."	4 weeks RA, OA, and seronegative spondarthropathy. NSAIDs differed by diagnosis but results in aggregate.

Lanza Am J Gastroenterol 1988 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 30 Healthy volunteers	No mention of age or sex.	Misoprostol 200µg (n=10) vs. sucralfate 1g (n=10) vs. placebo, co-administered with 650mg of aspirin 4 times a day 7 days (n=10).	No mention of sponsorship or COI.	Misoprostol superior to sucralfate (p = 0.0001) and placebo (p = 0.00001). Differences in success rates between misoprostol and sucralfate and misoprostol and placebo (44%; 100%) and (61%; 100%), respectively.	"[M]isoprostol at a dose of 200µg, 4 times a day, when dosed concurrently with aspirin, was highly effective in protecting the gastroduodenal mucosae from aspirin-induced injury."	Suggests misoprostol is superior to placebo and sucralfate. Sucralfate not blinded.
Jiranek 1989 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 130 Healthy subjects	Age range: 18-40 years; 119 males, 11 females.	Misoprostol 50µg (n=30) vs. 100µg (n=29) vs. 200µg (n=30) vs. placebo plus aspirin 975mg (n=30) (given as three 325mg tablets) for 7 days.	No mention of specific follow-up.	Fewer endoscopic gastric ulcers in misoprostol vs. placebo (1% vs. 43%). No DU on 100 or 200µg misoprostol vs. 13% placebo (p <0.05). Fewer gastric and duodenal erosions in 3 misoprostol groups vs. placebo (p <0.01). Fewer gastric erosion (p <0.05) and duodenal erosion (p <0.05) in misoprostol 200µg vs. 50µg doses.	"[M]isoprostol can protect the normal gastroduodenum from acute ulceration and reduce the chance of erosion after 1 week of aspirin ingestion."	Data suggest reduced gastric duodenal erosions.

Chandrasekaran 1991 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 90 Arthritic patients	Mean age: 39 years; 45 males, 45 females.	Patients with misoprostol intervention (n=45) vs. placebo group (n=45).	Follow-up at 4th week at the end of the study.	Patients on placebo with more post-therapy abnormal endoscopy findings; 24.4% of misoprostol group vs. 28.8% in placebo group had UGI symptoms during the trial (NS).	"Arthritic patients requiring long term NSAID therapy appear to benefit from misoprostol because of its cytoprotective effect on the gastrointestinal mucosa."	4 weeks RA, OA, and seronegative spondarthropathy. NSAIDs differed by diagnosis but results in aggregate.
Averbuch 2004 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 206 Hip OA flare-up	Mean age: 63 ± 12 years; 73 females, 25 males.	Naproxen sodium 500mg BID (n=98) vs. placebo (n=108) for 12 weeks.	Follow-up at 6 months.	Results taken at screening, baseline, 2, 6, and 12 weeks. Visual analog and categorical scales appear similarly effective in determining average osteoarthritis pain.	"Looking at the OA pain model as an exemplar for chronic pain generally, we found a good correspondence between unconstrained VAS and 5-point CAT scale pain measurements." However, some variance likely "due to individual judgment differences as to how to relate to the VAS line."	Study of subjective pain assessment tools (outcome measurement) as comparison was not the variable randomized.
Stengaard-Pedersen 2004 (Score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 697 Knee or hip OA	Mean age: 66.9 years; 473 females, 224 males.	Celecoxib 200mg QAM (n=230) vs. celecoxib 200mg QPM (n=233) vs. celecoxib 100mg BID (n=234) for 12 weeks.	No mention of follow-up.	WOMAC composite scores were -11.19 vs. -12.23 and -11.69 for each group (NS). No differences in patient satisfaction with pain relief, ability to walk or bend, and willingness to continue medication.	"[R]egardless of the time of day at which celecoxib 200 mg q.d. is administered, patients are equally satisfied with the pain relief, ability to walk and bend, and willingness to continue medication."	Sparse methodology details. Data suggest timing of NSAID is not important.

Robinson 1989 (Score=5.5)	NSAIDs	RCT	Sponsored by Glaxo Inc. at Research Trangle Park, North Carolina. No mention of COI	N = 144 Patients with normal endo-scopic findings requiring NSAIDs	Mean age: 46.1 years; 51 males, 93 females.	Ranitidine 150mg twice a day (n=72) vs. placebo plus ibuprofen, indometha cin, naproxen, sulindac, or piroxicam (n=72) for 8 weeks.	Follow-up at baseline 1, 4, and 8 weeks.	47/57 (82%) of ranitidine had no mucosal damage in the duodenum by study end vs. 32/49 (65%) on placebo.	"[R]anitidine therapy (150mg bid) was effective in preventing duodenal, but not gastric injury resulting from eight weeks of NSAID treatment."	8 weeks treatment also included with NSAID (ibuprofen, naproxen, sulindac, indomethacin, piroxicam).
Bakshi 1996 (Score=5.5)	NSAIDs	RCT	Sponsored by BIOS (Consultancy and Contract Research) Limited Bagshot Surrey UK. No mention of COI.	N = 216 Hip or knee OA	Age range: 18-75 years; no mention of COI.	Diclofenac resinate capsules 75mg BID (n=105) vs. enteric-coated diclofenac sodium tablets 50mg TID (n=111). Double dummy.	No mention of follow-up.	VAS rest pain (baseline/ 12 weeks): diclofenac resinate (55.6/22.5) vs. diclofenac sodium (56.9/ 25.4), p = 0.34. Similar results for activity pain and stiffness. Patients much better/better: diclofenac resinate (75/85 = 88.2%) vs. diclofenac sodium (72/94 = 76.6%). Functional limitation improvements compared with baseline in 59% diclofenac resinate vs. 37% diclofenac sodium (p = 0.055).	"[T]he results of this trial confirm the well-established favourable tolerability profile of diclofenac sodium and also show that this NSAID administered once or twice daily at 75 mg as a resinate formulation is effective for controlling the symptoms of osteoarthritis."	No placebo comparisons. No baseline provided on comparability. Generally comparable medication preparations, however trends in favor of diclofenac residinate.
Berry 1992 (score=5.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 184 Hip or knee OA	Mean age 62.2; 63 males, 107 females.	Lornoxica m 6mg QD (n=42) vs. 4mg BID (n=42) vs. 6mg BID (n=44) vs. placebo (n=42) for 4 weeks	Baseline , 2 and 4 weeks.	Mean pain relief scores superior with lornoxicam 8mg daily (p <0.002) and lornoxicam 12mg daily (p <0.0001) vs. placebo. (Graphic data). Scores for lornoxicam 12mg daily greater than lornoxicam 6mg daily (p <0.02). No differences in adverse GI symptoms,	"Lornoxicam at doses of 8 mg and 12 mg daily was significantly more effective than placebo in the relief of joint pain associated with osteoarthritis of the hip and knee."	High dropout rate and possibility of effects from co-interventions. Data suggest ornoxicam effective.

								however trend towards higher adverse events at higher doses (placebo 9% vs. 7, 12, 17% lornoxicam doses).		
Hubault 1976 (score=5.5)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 9 Hip OA	No mention of age or gender of study population.	Ketoprofen 50mg TID vs. placebo; 2 week treatment each treatment. Each participant received both treatments in random order.	Follow up at baseline, 2 and 4 weeks.	Aggregate data not presented on pain ratings, etc. In 8 patients, ketoprofen preferred; in 1 case no preference.	"Nine cases were sufficient to produce a significant statistical results in favour of ketoprofen."	Very small sample. Limited data presented. Overall preferences suggest ketoprofen superior to placebo.

Petrick 1983 (score=5.5)	NSAIDs	2 RCTs	No mention of sponsorship or COI.	N = 757 Hip OA or Knee OA	Mean age: 54 years; 193 males, 564 females.	Meclo-fenamate sodium 100mg TID (n=366) vs. placebo for 4 weeks. Meclo-fenamate dose could be reduced (n=191).	No mention of follow-up.	Night pain (baseline/4 weeks): meclofenamate (1.24/-39%) vs. placebo (1.49/-25%), p <0.03. Similar results with pain on walking, starting motion, pain on passive motion (p <0.01). Meclofenamate sodium caused more GI symptoms.	"[T]he antirheumatic efficacy and favorable tolerance picture of meclofenamate sodium demonstrated that the drug is also clearly effective in the management of acute and chronic osteoarthritis of the hip and knee."	Blinding, randomization, unclear. Suggests meclofenamate superior to placebo.
Bingham 2007 (Score=5.0)	NSAIDs	2 identical RCTs	Sponsored by Merk & Co., Inc. One or more of the authors have received or will receive benefits for personal or professional use.	N = 1,207 (Study 1: N = 599; Study 2: N = 608) patients who were prior NSAID or aceta-minophe n users	Mean age: 62.1 years; 803 females, 404 males.	Etoricoxib 30mg QD (n=231) vs. celecoxib 200mg QD (n=241) vs. placebo (n=127) for 12 weeks.	No mention of follow-up.	WOMAC pain scores (baseline/12 weeks): etoricoxib 67.4±16.2/ 39.6±22.9 vs. celecoxib 67.5±16.3/42.8±22.9 vs. placebo 66.6±16.2/54.2 ±24.6 (p >0.05 comparing active treatments; p <0.001 compared with placebo). Safety and tolerability of etoricoxib and celecoxib appeared similar.	"Etoricoxib 30mg qd was at least as effective as celecoxib 200mg qd and had similar safety in the treatment of knee and hip OA; both were superior to placebo."	No significant differences in efficacy or side effects prolife of etoricoxib compared to celecoxib. 20% dropout at 12 weeks in both groups.

Kiff 1994 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 1,023 RA or OA	Mean age: 66 years; 636 females, 387 males.	Diclofenac 50mg misoprostol 200µg (n=507) vs. diclofenac 50mg (n=263) vs. ibuprofen 600mg (n=253). All BID or TID at physician discretion for 4 months.	Follow-up at 2 months.	Total good/very good patient ratings: 51, 50, 45% (graphic interpretations). Physician ratings of good/very good: 51, 49, 46% (graphic interpretations). Adverse effects in 336 (66.3%), 159 (60.5%) and 152 (60.1%). Dyspepsia in 11.0%, 6.5%, 6.3% respectively.	"Arthrotec…was as effective as diclofenac sodium 50 mg alone and more effective than ibuprofen 600 mg for the treatment of arthritis."	Some details sparse. High dropout rates. Submaximal ibuprofen dose and variable dosing frequency in all 3 arms precludes conclusion regarding more efficacious treatment.
Clarke 1975 (Score=5.0)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 50 Knee and/or hip OA	No mention of age or sex.	Naproxen First: (n=25) 250mg BID vs indometacin First: (n=25) [sic] 25mg QID for 4 weeks for each drug. Double dummy.	Follow-up at 2 weeks intervals.	Night pain changes: naproxen -0.53±1.01 vs. indometacin -0.48±0.85 (NS). Other measures of rest pain, pain on moving after rest, prolonged standing and walking not different between treatments. Sub-analyses suggest knee pain more difficult to treat. Objective assessments of stair climbing and walking times improved for knee and hip patients on both treatments, but not different between treatments. Indometacin adverse effects 128 vs. naproxen 85, p <0.01.	"In almost all parameters there was significant improvement from baseline on both drugs, the magnitude of improvement being statistically equivalent. Side-effects recorded during the naproxen treatment period were significantly fewer than during indometacin treatment."	No washout period prior to trial start. Comparable efficacy suggested. Quality evidence indomethacin has higher adverse effect profile.

Singer 2000 (Score=5.0)	NSAIDs	RCT	Sponsored by Forschungsforderungsfonds fur die Gewerbliche Wirtschaft and Federal state Tyrol. No mention of COI.	N = 174 Hip OA	Mean age: 55.2 years; 84 females, 90 males.	Dexibuprofen 400mg TID (n=58) vs. dexibuprofen 200mg TID (n=58) vs. ibuprofen 800mg TID (n=58) for 15 days	No mention of follow-up.	Improvements in WOMAC pain: ibuprofen 800mg (5.50±3.28) vs. dexibuprofen 400mg (6.30±3.95). Dexibuprofen 400mg failed to show superiority to racemic ibuprofen, but was borderline (p = 0.055). Dexibuprofen 200mg less effective than dexibuprofen 400mg (p = 0.023). Patient global efficacy (excellent and very good): Dex 200mg 56.7% vs. Dex 400mg 47.1% vs. IBU 40.6%.	"The active enantiomer dexibuprofen (S (+)-ibuprofen) proved to be an effective non-steroidal anti-inflammatory drug with a significant dose-response relationship in patients with painful osteoarthritis of the hip. Compared with racemic ibuprofen half of the daily dose of dexibuprofen shows at least equivalent efficacy."	Blinding, allocation, and compliance details are sparse. Suggests dexibuprofen at ½ dose is equivalent to racemic ibuprofen. However, there is no clear clinical advantage reported.
Davies 1980 (Score=5.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 21 Hip OA	Mean age: 65.4 ± 6.4; 11 males, 10 females.	Tolmetin sodium 400mg TID (n=11) vs. indomethacin 25mg TID (n=10) for 2 weeks. Double dummy.	Follow-up at 1, 3, 4, and 6 weeks.	Patients with severe limitations: 12 before tolmetin, 11 before indomethacin; decreased to 4 after each treatment. Tolmetin and indomethacin favored over placebo in all measures, but no difference between treatments.	"The degree of pain relief produced by both tolmetin sodium and indomethacin in the context of this clinical study was good."	Small sample size, low power led to general trends but few statistics significant.

Meurice 1983 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 60 Knee or hip OA	Mean age: 74 years; 12 males, 48 females.	Tiaprofenic acid 200mg TID (n=30) vs. indomethacin 33.3mg TID (n=30) for 3 months.	Follow-up at 14, 18.9, 26.4, 61.3, and 63 days.	Data mostly provided for knee patients. Both treatments efficacious at reducing pain scores, pain with movement, overall severity ratings ($p < 0.05$). Tiaprofenic acid scores for pain at rest lower at multiple time points (graphic data, $p < 0.05$). Mean time to achieve initial benefit was 18.9 days for tiaprofenic acid vs. 26.4 days for indomethacin ($p < 0.05$). Time to achieve maximum benefit similar (61.3 days for tiaprofenic acid vs. indomethacin 63.0 days).	"[T]his study has shown that tiaprofenic acid was better tolerated and at least as effective as indomethacin in the treatment over a 3-month period of elderly patients with osteoarthritis of the hips and knees."	Outcome differences favoring tiaprofenic acid over indomethacin of clinical uncertainty as no differences in overall severity and efficacy ratings.
Kriegel 2001 (Score=5.0)	NSAIDs	RCT	Sponsored by grant from Helsinn Healthcare. No mention of COI.	N = 370 Hip or knee OA	Mean age: 64.5 years; 144 females, 56 males.	Nimesulide 100mg BID (n=183) vs. naproxen 250mg QAM and 500mg QPM (n=187).	No mention of follow-up.	Equivalence for knee and/or hip OA (data not given). WOMAC pain scores (baseline/12 months): nimesulide (234.1±86.9/172.7± 116.0) vs. naproxen (240.4±94.4/ 177.7± 125.3); 152 (83.1%) on nimesulide and 160 (85.6%) on naproxen reported adverse events. Gastrointestinal adverse events reported with nimesulide (n = 77, 47.5%) vs. naproxen (n = 6, 54.5%), NS.	"This study demonstrates nimesulide to be as effective as naproxen in the long-term treatment of patients with OA of the knee and hip."	Study details lacking. Differences in GI side effects did not reach statistical significance. Results suggest comparable efficacy.

Corts 1991 (score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 85 Knee or hip OA	Mean age: 58.9 years; 27 males, 53 females	Droxicam 20mg QHS (n=40) vs. diclofenac 50mg TID (n=40) for 6 weeks	6 weeks	Weeks 1, 3, 6, 49 knee OA patients taking droxicam improved for severity of knee disease (p <0.0001), pain intensity (p <0.0001), duration of morning stiffness (p <0.0001), and range of maximal forced flexion (p <0.0001), and extension (p <0.05). Diclofenac had statistically significant results. More rescue paracetamol in diclofenac than droxicam at 3 (p = 0.0119) and 6 weeks (p = 0.0142). After 1, 3, 6 weeks, 31 hip OA patients treated by droxicam or diclofenac improved for hip disease (p <0.01) and pain intensity (p <0.0001). No differences between treatments. Fewer GI symptoms in droxicam at 6 weeks (p = 0.0258).	"Both oral droxicam and diclofenac are of benefit in reducing pain and improving joint motion and function in patients with osteoarthritis of the hip and knee.	Methodology details and some results sparse, especially for hip OA. Very high dropout (55.3%) precludes strong conclusions.
Car 1978 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 79 Hip OA	Mean age: 58.8 years; no mention of sex.	Diclofenac 50mg BID (n=39) vs. naproxen 250mg BID (n=40) for 2 weeks. Double dummy.	No mention of follow-up.	Percent of patients with improvement in joint pain severity: diclofenac 31/37 (83.8%) vs. naproxen 32/39 (82.0%). Patient opinion that they improved: diclofenac (81.6%) vs. naproxen (70.3%).	"[B]oth drugs provide effective symptomatic treatment for these patients."	Submaximal doses used with short trial. Baseline characteristics non-homogeneous. Data suggest comparable efficacy, but weaknesses preclude strong conclusions.

Keet 1979 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 35 Hip and/ or knee OA	Mean age: 52.5 years; 11 males, 24 females.	Diflunisal 250mg BID (n=17) vs. ibuprofen 400mg TID (n=18) for 8 weeks. Double dummy.	No mention of follow-up.	No symptoms or improvement at Week 8 in 16/17 (94.1%) diflunisal vs. 14/17 (82.4%) ibuprofen. All improved from baseline ($p < 0.01$) in multiple pain measures at Weeks 2, 4, and 8. Except for significant decrease ($p < 0.01$) in hemoglobin in ibuprofen group, no lab abnormalities.	"No significant differences between diflunisal and ibuprofen in the treatment of osteoarthritis of the hip and/or knee."	Allocation and baseline variables unclear. No differences in efficacy or safety profile. OTC ibuprofen dosage used.
Frank 1977 (Score=5.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 30 Hip OA	Age range: 30 to 79 years; 15 males, 11 females.	Flurbiprofen 50mg TID (n=14) vs. indomethacin 25mg TID daily (n=12) for 2 weeks intervals.	No mention of follow-up.	Not well-balanced distribution between those on flurbiprofen and those on indomethacin first. Pain severity scores: baseline 3.5, after flurbiprofen 1.4, after indomethacin 1.3 (NS). No differences between drugs in night pain or duration of morning stiffness.	"The results of this double-blind crossover study show that flurbiprofen in a dosage of 150 mg daily is effective in alleviating symptoms in patients with osteoarthrosis of the hip, the improvement from baseline values reaching statistical significance."	Sparse study details. Suggests comparable efficacy.
Valtonen 1979 (Score=5.0)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 53 Hip or knee OA	Mean age: 63 years; 9 males, 44 females.	Fenbufen 200mg TID (n=27) vs. aspirin 1.2g TID (n=26) for 8 weeks.	No mention of follow-up.	Pain at rest difference from baseline at Week 4 fenbufen 0.46 vs. aspirin 0.48. Week 8, differences aspiring 0.50 vs. fenbufen 0.39. Fenbufen preferred; 42.5% vs. 57.5% aspirin. Improvement better for knee than hip OA. No statistically significant differences between drugs. Adverse effects: 57% vs. 40% (significance not reported).	"It seems evident that the efficacy of 600 mg Fenbufen daily in the relief of symptoms and improvement in treating of osteoarthrosis of the knee or hip joints is equivalent to that of 3.6 g Aspirin daily. In addition to that Fenbufen was associated with fewer side effects during the trial period."	Allocation unclear. Blinding unclear. No significant differences exist based on information provided.

Hayllar 1996 (Score=5.0)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 19 Hip or knee OA	No mention of age; 12 males, 7 females.	Flosulide 20mg BID (n=13) vs. naproxen 500mg BID (n=7) each for 2 weeks.	No mention of follow-up.	Flosulide tolerated better than naproxen (90% vs. 47% good to excellent, p <0.005). Gastric Lanza damage scores (combined grades 2, 3, 4): flosulide (n = 5, 26%) vs. naproxen (12, 63%), p = 0.0006.	"The selective COX-2 inhibitor, flosulide, is significantly better tolerated and causes less gastric mucosal damage than naproxen when given for two weeks."	Small sample size. Endoscopic study suggests fewer mucosal (gastric) erosions with flosulide after 2 week treatment period compared with naproxen.
Becvár 1999 (Score=5.0)	NSAIDs	RCT	Sponsored by SmithKline Beecham Co. No mention of COI.	N = 394 Hip or knee OA	Mean age: 60.6 years; 92 males, 302 females.	Nabumetone 1,500mg QHS (n=202) vs. diclofenac retard 100mg QHS (n=193) for 12 weeks.	Follow-up at baseline, 30 days.	Complete and moderate pain relief nabumetone 103/177 (58.2%) vs. diclofenac retard 74/156 (47.4%). Fewer mucosal changes in esophagus (p = 0.007), stomach (p <0.001), but not duodenum among nabumetone compared with diclofenac. Data graphically interpreted, appear to be nabumetone 20% erosions at baseline and 16% after treatment and no ulcers vs. diclofenac 19% erosions at baseline, 17% at followup, but 9% ulcers.	"[N]abumetone and diclofenac retard have similar efficacy in the treatment of OA, but nabumetone has significantly fewer GIT side effects."	Diclofenac retard worse than nabumetone for mucosal erosions in the stomach and esophagus, but not in the duodenum. Drugs have comparable efficacy.

Rashad 1989 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 105 Hip OA awaiting arthro-plasty	Mean age: 66.4 years; no mention of sex.	Indomethacin 50mg QD or 75mg QD (n=55) vs. azapropazone 600mg QD or 900mg QD (n=46) for variable lengths of treatment followed to arthroplasty.	No mention of follow-up.	Initial day pain scores higher for azapropazone but not significant. Final day scores azapropazone higher ($p < 0.05$). Time to arthroplasty 50% longer in azapropazone (15.65, SE 1.63 months) vs. indomethacin (10.39, SE 0.84 months), $p < 0.01$. Overall reduction in joint space on x-ray trended slower in hips with azapropazone vs. indomethacin (NS).	"The patients receiving azapropazone, who had higher concentrations of synovial vasodilator prostaglandins, took longer than the indomethacin group to reach the arthroplasty end-point. Potent inhibitors of prostaglandin synthesis may be inappropriate in the management of osteoarthritis of the hip."	Some details sparse. Authors believe patients at similar pathophysiological end-point when they came to arthroplasty (determined by pain, x-ray findings).
Toft 1985 (Score=5.0)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 68 Hip and/ or knee OA	Mean age: 68.7 years; 24 males, 44 females.	Ketoprofen sustained-release formulation 200mg QD (n=35) vs. normal formulation 100mg BID (n=33) 3 weeks each.	Follow-up at baseline, 3 months.	Both treatments effective. No differences in preferences between preparations (SR preferred by 23 vs. 19, NS).	"No significant differences between the treatments were found."	No mention of compliance. Sparse data presented. Data suggest comparable efficacy.
Miyake 2005 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 194 RA in patients treated over a long term with NSAIDs	Mean age: 61 years; 135 females, 20 males.	Famotidine 20mg BID (n=13) vs. lansoprazole 15mg QD (n=13) for 24 weeks.	No mention of follow-up.	8% (1/13) peptic ulcer onset rate infamotidine vs. 2/13 (15%) lansoprazole (NS).	"In Japan, normal-dose H2RA is expected to be a new PU preventive treatment strategy in patients requiring long-term NSAID therapy."	RA patients on NSAIDs with peptic ulcers scars 24-week treatment; small sample (n = 26). Under-reported study.

Donnelly 2000 (Score=5.0)	NSAIDs	RCT	Sponsored by Searle, UK. No mention of COI.	N = 32 Healthy volunteers	No mention of age or sex.	Misoprostol 100µg plus aspirin 300mg (n=16) vs. placebo plus aspirin 300mg once daily (n=16) for 28 days.	No mention of follow-up.	Gastric erosion in 52% on aspirin plus placebo vs.17% on aspirin plus misoprostol (OR = 0.18, CI: 0.07-0.48), averaged over Days 5, 14, and 28. Percent gastric petechiae: 42% and 23% (OR = 0.42, CI: 0.17-0.97).	"Misoprostol 100 µg daily can prevent low-dose aspirin induced gastric mucosal injury without causing identifiable adverse effects."	Misoprostol 100QD vs. placebo plus ASA 300QD for 28 days. Data suggest misoprostol protects from gastric injury associated with ASA.
Silverstein 1986 (Score=5.0)	NSAIDs	RCT	Sponsored by G.D. Searle & Co, NIH training grant and program project grant, Fujinon instrument company. No mention of COI.	N = 60 Healthy male volunteers	Age range: 18-40 years; 60 males.	Misoprostol 200µg (n=30) vs. placebo (n=30) for 24 hours.	No mention of follow-up.	Mucosal protection in 20/30 on misoprostol (67%) vs.1/30 on placebo (3%) (p <0.001).	"[F]ive 200-micrograms doses of misoprostol given over 24 hr protects the gastric mucosa from the injurious effect of a single dose of aspirin."	Short-term experimental study. Suggests misoprostol reduces risk.
Miglioli 1996 (Score=5.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 107 Patients with arthritis	Mean age: 55.2 ± 9.7 years; 18 males, 89 females.	Diclofenac 200mg a day, or naproxen 1g a day plus sucralfate gel 1gm BID (n=53) vs. placebo (n=54) for 14 days.	Follow-up at 4 weeks.	More GU/DU ulcers in placebo group (p <0.05). More on placebo had heartburn and epigastric pain at final evaluation (51 vs. 30% and 49 vs. 28%; p <0.05).	"Sucralfate gel reduces both the incidence of acute gastroduodenal mucosal lesions and symptoms in patients with arthritis receiving short-term nonsteroidal anti-inflammatory drugs."	Data support efficacy in prevention.

Robinson 1991 (Score=4.5)	NSAIDs	RCT	Sponsored by grant from Glaxo Inc. at Research Triangle Park in North Carolina. No mention of COI.	N = 673 Patients receiving NSAIDs for arthritic or musculo-skeletal conditions	Mean age: 51 years; 261 males, 412 females.	Ranitidine 150mg twice daily (n=343) vs. placebo for 4 weeks or 8 weeks (n=330).	Follow-up at baseline, 5th week after treatment.	Protective effect against duodenal mucosal lesions including duodenal ulcers (3 studies) and gastric mucosal lesions including gastric ulcers (1 study) observed vs. placebo.	"[R]antidine is effective in preventing NSAID-associated duodenal ulcers and may be appropriate prophylaxis for certain high-risk patients."	4 RCTs for 4 weeks or 8 weeks treatment. Data suggest pro-tective for DU not GU.

Kogstad 1981 (Score=4.5)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 149 Hip or knee OA	Mean age: 67 years; 95 females, 54 males.	Piroxicam 20mg QAM (n=37) vs. naproxen (n=44) vs. placebo 250mg BID (n=46) for 4 weeks each.	No mention of follow-up.	Pain on movement: placebo 4.9, piroxicam 3.3, placebo 4.4, naproxen 3.5. Night pain, ability to walk similar findings. Reverse sequence with comparable findings. No differences in adverse effects.	"[P]atients' and investigators' preference for any of the three treatments, based on efficacy and toleration, significantly favoured piroxicam."	Sparse details. Washout at pre-study and crossover unclear. Overall assessment suggests comparable efficacy, although submaximal naproxen dose used.
Liyanage 1977 (Score=4.5)	NSAIDs	2 randomized crossover trials	Partially sponsored by Dr. Goulton of May & Baker Ltd. No mention of COI.	N = 24 N = 40 Hip and knee OA	Mean age: 64.8 years; 9 males, 15 females.	Tolmetin 400mg TID (n=12) vs. ketoprofen 50mg TID daily (n=12) vs. placebo (n=15) for 2 weeks. Double dummy.	Follow-up at baseline, 2 weeks after treatment.	Comparing doses of tolmetin, physician assessments: 13 better after 600mg vs. 12 better after 1,200mg. Other data comparable. Differences between active medication and placebo (1 week washout phase with a placebo) favored active treatment with either tolmetin or ketoprofen. Blood urea nitrogen levels increased on tolmetin and ketoprofen ($p < 0.05$).	"[N]o significant differences in any of the clinical parameters could be found between the 600 mg and 1200 mg tolmetin daily dose. This may have been due to the small numbers involved in this study. However, it was also considered that the methods used for monitoring the efficacy of treatment of osteoarthrosis were probably not sufficiently sensitive to validate subjective changes. The results of the comparative study revealed that both tolmetin and ketoprofen are effective analgesics."	Short trial periods, small sample size, sparse study details. Suggests no difference between 1200mg and 600mg a day tolmetin. Suggests tolmetin and ketoprofen equally effective.

Lund 1987 (Score=4.5)	NSAIDs	RCT Same trial as Jensen 1986	No mention of sponsorship or COI.	N = 108 Hip or knee OA	Median age: 66 years; 30 males, 78 females.	Tenoxicam 20mg QD (n=53) vs. piroxicam 20mg QD (n=55) for up to 24 months in this report.	Follow-up at 12 and 24 months.	Pain scores did not differ (graphic data). Excellent and good ratings were tenoxicam 81% vs. piroxicam 75% (NS). No differences in adverse effects.	"Both tenoxicam and piroxicam are effective in long-term treatment of osteoarthritis. No statistically significant differences between the efficacy and the tolerance of the drugs were seen. The fact that practically no withdrawals due to side-effects were seen after 12 months shows that the drugs once tolerated remain so despite long-term treatment."	Interim report (2 years) in an ongoing study. Suggests equivalent efficacy.
Chikanza 1994 (Score=4.5)	NSAIDs	Crossover trial	Partially sponsored by Ayerst Laboratories. No mention of COI.	N = 76 Knee and/ or hip OA	Median age: 62 years; 17 males, 59 females.	Etodolac 300mg BID (n=39) vs. naproxen 500mg BID (n=37) for 4 weeks each.	No mention of follow-up.	Patients favored naproxen (n = 18) more often than etodolac (7) (p = 0.044); most favored neither (47) for pain intensity. No differences in preferences for night pain or overall. Morning stiffness borderline favored naproxen (25 vs. 23, p = 0.09). More withdrawals for adverse events in etodolac (7) vs. naproxen.	"[N]aproxen and etodolac were equally effective in the management of pain and stiffness in osteoarthritis. However, a significantly higher proportion of patients preferred naproxen to etodolac for the relief of pain intensity. The incidence of adverse events caused by either drug was the same."	Lack of study details and lack of control for co-treatments. Data suggest etodolac may be slightly inferior to naproxen.
Gyory 1972 (Score=4.5)	NSAIDs	Crossover trials	No mention of sponsorship or COI.	Study 1: N = 46 RA Study 2: N = 42 hip OA	Mean age: 57 years; 18 males, 28 females.	Orudis 25mg QID (n=24) vs. Indomethacin 25mg QID (n=22).	No mention of follow-up.	OA patients: 8 preferred orudis vs. 15 indomethacin vs. 19, no difference (p = 0.21). Overall preference: orudis 17 vs. indomethacin 19 vs. 6 no difference (NS). Higher adverse effects for indomethacin (n = 55) vs. orudis (n = 34).	"The present studies suggest that in equal dosage clinical efficacy of Orudis is comparable with that of indomethacin."	Sparse details. Suggests comparable efficacy.

Levenstein 1985 (Score=4.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 309 Mostly hip or knee OA	Mean age: 59.4 years; 86 males, 223 females.	Isoxicam 200mg QD (n=155) vs. indomethacin 25mg TID (n=154) for 2 weeks. Double dummy.	No mention of specific follow-up time length.	Patient assessments (good/very good): isoxicam 113/155 (72.9%) vs. indomethacin 111/154 (72.1%). Patient tolerance (good/very good): isoxicam 134/155 (86.5%) vs. indomethacin 128/154 (83.1%) (NS). Significant improvements both groups after 7 days drug therapy (p <0.001).	"[I]ndomethacin treatment for up to 14 days reduced the pain and severity of the clinical symptoms of acute flare-up episodes of osteo-arthritis."	Lack of allocation and baseline details. Short trial period. No statistical analysis presented for adverse effects. Suggests equal efficacy.
Liyanage 1977 (Score=4.5)	NSAIDs vs. Other NSAIDs and Trials with Multiple Treatment Arms	2 randomized crossover trials	Partially sponsored by Dr. Goulton of May & Baker Ltd. No mention of COI.	N = 24 N = 40 Hip and knee OA	Mean age: 64.8 years; 9 males, 15 females.	Tolmetin 400mg TID vs. 200mg TID for 2 weeks. Tolmetin 400mg TID vs. ketoprofen 50mg TID daily for 2 weeks. Double dummy. All patients received both treatments.	Follow-up at baseline, 2 weeks after treatment.	Comparing doses of tolmetin, physician assessments: 13 better after 600mg vs. 12 better after 1,200mg. Other data comparable. Differences between active medication and placebo (1-week washout phase with a placebo) favored active treatment with either tolmetin or ketoprofen. Blood urea nitrogen levels increased on tolmetin and ketoprofen (p <0.05).	"[N]o significant differences in any of the clinical parameters could be found between the 600 mg and 1200 mg tolmetin daily dose. This may have been due to the small numbers involved in this study. However, it was also considered that the methods used for monitoring the efficacy of treatment of osteoarthrosis were probably not sufficiently sensitive to validate subjective changes. The results of the comparative study revealed that both tolmetin and ketoprofen are effective analgesics."	Short trial periods, small sample size, sparse study details. Suggests no difference between 1200mg and 600mg a day tolmetin. Suggests tolmetin and ketoprofen equally effective.

Knüsel 1982 (Score=4.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 50 Moderate to severe hip OA	Mean age: 59.2 years; 31 males, 19 females.	Carprofen 100mg TID (n=25) vs. diclofenac-sodium 50mg TID (n=25) for 21 days.	No mention of follow-up.	Pain in key joint and tenderness disappeared or relieved in nearly all patients in both treatment arms. Pain in general disappeared in 11/24 (45.8%) carprofen vs. 13/23 (56.5%) diclofenac (NS). Time to walk 20 meters and clinical efficacy did not differ (NS).	"The results indicate that in the treatment of moderate to severe coxarthrosis carprofen (300mg daily) and diclofenac-Na (150mg daily) display practically the same efficacy as anti-inflammatory agents."	Small sample size. Sparse details. Blinding unclear.
McIlwain 1988 (Score=4.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 38 Acute MSDs in athletes	Mean age: 24 years; 23 males, 11 females.	Piroxicam 40mg QD for 2 days then 20mg QD (n=16) vs. naproxen 500mg BID for 2 days then 375mg BID (n=18) for 7 days.	Follow-up at 3 and 7 days.	Measures of physical discomfort improved ($p < 0.001$) after 3 and 7 days both treatments. Mean reduction in spontaneous pain, swelling, tenderness statistically superior ($p < 0.05$) in piroxicam. Overall patient impressions of efficacy (excellent): piroxicam 11/16 (68.8%) vs. naproxen 7/18 (38.9%). No difference between treatments for days lost due to injury. Piroxicam larger mean reductions from baseline for spontaneous pain ($p = 0.047$), swelling ($p = 0.035$), and tenderness ($p = 0.017$) at 1st return visit compared to naproxen.	"Piroxicam and naproxen are effective and well-tolerated short-term treatments for acute musculoskeletal injuries in athletes."	Heterogeneity in disorders treated (e.g., sprains of ankle, AC, hand IP, soft tissue injuries of shoulder, knee or hip). No placebo group. Data suggest piroxicam superior to naproxen.

Molony 1971 (Score=4.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 33 Hip OA	No mention of age and sex.	Niflumic acid 200mg (n=8) vs. niflumic acid 250mg (n=7) vs. indomethacin 25mg (n=7) vs. phenylbutazone 100mg (n=9).	No mention of follow-up.	All 4 treatments had similar responses regarding pain on passive abduction of the hip and walking pain. No statistically significant differences between the treatments.	"Niflumic acid compared favourably with the two control drugs in the management of osteoarthritis of the hip. In the objective measurement of clinical response, niflumic acid 200mg tended to produce the greatest response. The incidence of side effects was similar in all treatment groups."	Suggests no significant advantages of one NSAID over another. Baseline comparability of study measures appears heterogeneous.
Manchester General Practitioner Group 1984 (Score=4.5)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 226 Hip, knee or spine OA	Mean age: 62 years; 69 males, 156 females (1 sex unrecorded).	Naproxen 500mg BID (n=105) vs. ibuprofen 400mg TID (n=69) for 6 weeks total.	Follow-up at baseline, 3 months.	Both drugs reduced inactivity stiffness, pain, interference with daily activities, overall disease severity ($p < 0.01$). At 3 weeks, naproxen superior to ibuprofen in relieving movement pain ($p = 0.009$), night pain ($p = 0.056$); 10 patients on naproxen, 5 on ibuprofen withdrew from trial because of side-effects.	"Naproxen and ibuprofen were both effective treatments for this group of osteoarthritics seen in general practice. Naproxen was more effective than ibuprofen and was preferred by more patients, but was associated with a larger number of side-effects."	Use of submaximal dose ibuprofen compared with full dose naproxen precludes an ability to assess which is more efficacious.

Kogstad 1981 (Score=4.5)	NSAIDs	Crossover trial	No mention of sponsorship or COI.	N = 149 Hip or knee OA	Mean age: 67 years; 95 females, 54 males.	Piroxicam 20mg QAM (n=37) vs. naproxen (n=44) vs. placebo 250mg BID (n=46) for 4 weeks each.	No mention of follow-up.	Pain on movement: placebo 4.9, piroxicam 3.3, placebo 4.4, naproxen 3.5. Night pain, ability to walk similar findings. Reverse sequence with comparable findings. No differences in adverse effects.	"[P]atients' and investigators' preference for any of the three treatments, based on efficacy and toleration, significantly favoured piroxicam."	Sparse details. Washout at pre-study and crossover unclear. Overall assessment suggests comparable efficacy, although submaximal naproxen dose used.
Liyanage 1977 (Score=4.5)	NSAIDs	2 randomized crossover trials	Partially sponsored by Dr. Goulton of May & Baker Ltd. No mention of COI.	N = 24 N = 40 Hip and knee OA	Mean age: 64.8 years; 9 males, 15 females.	Tolmetin 400mg TID (n=12) vs. ketoprofen 50mg TID daily (n=12) vs. placebo (n=15) for 2 weeks. Double dummy.	Follow-up at baseline, 2 weeks after treatment.	Comparing doses of tolmetin, physician assessments: 13 better after 600mg vs. 12 better after 1,200mg. Other data comparable. Differences between active medication and placebo (1 week washout phase with a placebo) favored active treatment with either tolmetin or ketoprofen. Blood urea nitrogen levels increased on tolmetin and ketoprofen ($p < 0.05$).	"[N]o significant differences in any of the clinical parameters could be found between the 600 mg and 1200 mg tolmetin daily dose. This may have been due to the small numbers involved in this study. However, it was also considered that the methods used for monitoring the efficacy of treatment of osteoarthrosis were probably not sufficiently sensitive to validate subjective changes. The results of the comparative study revealed that both tolmetin and ketoprofen are effective analgesics."	Short trial periods, small sample size, sparse study details. Suggests no difference between 1200mg and 600mg a day tolmetin. Suggests tolmetin and ketoprofen equally effective.

Lund 1987 (Score=4.5)	NSAIDs	RCT Same trial as Jensen 1986	No mention of sponsorship or COI.	N = 108 Hip or knee OA	Median age: 66 years; 30 males, 78 females.	Tenoxicam 20mg QD (n=53) vs. piroxicam 20mg QD (n=55) for up to 24 months in this report.	Follow-up at 12 and 24 months.	Pain scores did not differ (graphic data). Excellent and good ratings were tenoxicam 81% vs. piroxicam 75% (NS). No differences in adverse effects.	"Both tenoxicam and piroxicam are effective in long-term treatment of osteoarthritis. No statistically significant differences between the efficacy and the tolerance of the drugs were seen. The fact that practically no withdrawals due to side-effects were seen after 12 months shows that the drugs once tolerated remain so despite long-term treatment."	Interim report (2 years) in an ongoing study. Suggests equivalent efficacy.
Gordin 1985 (Score=4.5)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 21 Hip or knee OA	Mean age: 67.6 years; 2 males, 19 females.	Slow-release indomethacin 50mg (n=10) vs. naproxen 250mg (n=8), 2 tablets daily for 3 weeks.	No mention of follow-up.	Most patients pain-free at end of both treatment periods, 2 almost no change; 9 preferred slow-release indomethacin tablets; 6 naproxen; 4 no preference (NS).	"Analysis of results from 19 patients showed that both drugs effectively alleviated pain, and there was no difference between indomethacin and naproxen in this respect."	Small sample size. Sparse data. Suggests comparable efficacy.
Björkenheim 1985 (Score=4.5)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 75 Hip or knee OA	Age range: 36 to 70 years; no mention of specific numbers of sex.	Naproxen 1000mg QD (n=35) vs. Piroxicam 20mg QD (n=35) for 4 weeks each.	No mention of follow-up time length.	Global assessment disease activities (asymptomatic plus mild): naproxen (51/ 66 = 77.3%) vs. piroxicam (63.6%), p = 0.04. Treatment differences favored naproxen (p <0.05) for weight-bearing pain, physician/patient global assessments of patient response to therapy. Both groups chose naproxen.	"[N]aproxen 100 mg once daily was more effective than piroxicam 20 mg once daily for the treatment of osteoarthritis."	Sparse study details. Data suggest naproxen superior to piroxicam.

Medina Santillan 1999 (Score=4.5)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 38 Healthy volunteers	Mean age: 42 years; 25 males, 13 females.	Sodium diclofenac 75mg plus misoprostol 50µg (n=19) vs. diclofenac (n=19) for 14 days.	No mention of follow-up.	Misoprostol showed scores of 0-1 in 89% of cases versus 63% in diclofenac sodium/placebo group (p <0.05).	"[C]ombination of diclofenac and low-dose of misoprostol (50µg; bid) is associated with mucosal protection against NSAID-induced gastroduodenal damage."	Sparse data support misoprostol efficacy.
Gillgrass 1984 (score=4.5)	NSAIDs	Crossover Trial	Sponsored by Beecham Research Laboratories. No mention of COI.	N = 18 Hip or knee OA	Mean age: 61.1 years; 7 male, 11 female.	Nabumetone 1gm BID vs. placebo for 2 weeks each. Each participant received both treatments in a random order.	Follow up at baseline, 2 and 4 weeks.	Reduced pain (p <0.02). Intermalleolar straddle, intercondylar distance, knee flexion and extension showed little variation. Clinical assessment of response with 11/17 better on nabumetone, 3 were same on both, and 3 were better on placebo (p = 0.037).	"A 2-week, double-blind controlled crossover study in patients with osteoarthrosis has shown a statistically significant drug-related beneficial effect with respect to patient preference (P<0.001) and clinical response (P=0.037). Most clinical parameters assessed improved and no significant side-effects or drug-related adverse events were noted."	Small sample size, sparse study details. Few data.

Scheiman 1994 (Score=4.5)	NSAIDs	RCT	Sponsored partially by NIH grant MO1 RR00042, and Merck Sharpe and Dohme Research Laboratories. No mention of COI.	N = 20 Healthy volunteers	Mean age: 27 ±6 years; 11 males, 9 females.	Omeprazole 40mg QD (n=14) vs. placebo plus aspirin 650mg QID (n=6) for 2 weeks.	Follow-up at 6 months.	Omeprazole reduced PUD 55% vs. 10% (p <0.01). Endoscopic evidence of intraluminal bleeding or ulceration in 70% of placebo vs. 15% of omeprazole (p <0.001).	"Omeprazole 40mg/day significantly prevented both gastric and duodenal injury due to 2600mg aspirin/day over the two-week period of our study…Omeprazole 40mg/day prevented 95% of subjects from developing ulceration, 85% from having >15 erosions (all ≤3mm in size), and 55% from having >5 erosions. In the subjects given placebo, 25% developed gastric ulcers, 70% had grade 3 injury or worse, and all 95% had at least grade 2 injury."	Crossover, short 2 week study.
Verbruggen 1982 (Score=4.5)	NSAIDs	Crossover Trial	No mention of sponsorship and COI.	N = 21 Hip, knee or spine OA	Mean age: 64.3 years; 5 males, 16 females.	Nabumetone 1gm QHS (n=10) vs. naproxen 250mg BID (n=11) for 2 weeks each.	No mention of follow-up.	Patients improved both treatments. No patient preferences. Tolerance: 15 no preference, 6 preferred nabumetone, 0 preferred naproxen.	"Both drugs were considered to be equally effective and were both well tolerated… No evidence was found of changes in renal, hepatic or haematopoietic function with the two drugs tested."	Small sample size, scant statistical analysis provided.

Bacon 1990 (Score=4.5)	NSAIDs	Crossover Trial	Sponsored by Napp Laboratories Ltd., Cambridge. No mention of COI.	N = 80 patients with rheumatoid arthritis.	Mean age: 55 years; 29 males, 51 females.	Indomethacin controlled-release tablet 75mg QD (n=67) vs indomethacin immediate release capsule 25mg TID (n=66) for 4 weeks.	No mention of follow-up.	No difference in rescue paracetamol use between treatments. Pain on passive movement after treatments combining mild and none: controlled-release 43/66 (65.2%) vs. immediate-release indomethacin 37/66 (56.1%), both improved compared with baseline ($p < 0.01$). Patient assessment of global efficacy showed no statistically significant treatment differences; light-headedness significantly greater with immediate-release than controlled-release ($p < 0.05$).	"Both immediate-release and controlled-release indomethacin significantly reduced pain on passive movement of the worst affected joint compared to baseline. No treatment differences were found, however, for this or any of the other efficacy measures."	Lack of details. No baseline data of population although was a cross-over study, yet had significant dropouts. No clear differences or advantages of either treatment.
Koch 2000 (Score=4.0)	NSAIDs	RCT	No mention of sponsorship or COI.	N = 8,843 RA	Age range :> 52 years; no mention of sex.	Misoprostol plus NSAID (n=4404) vs. NSAID plus placebo (n=4404).	No mention of follow-up.	Relative risk reduction of gastrointestinal complications 40% with misoprostol. Number needed to treat to prevent 1 event 250 in 6 months or 125 when normalized at 1-year treatment.	"[M]isoprostol prevention of severe complications is effective."	Large study. All RA over a 6-month trial. Endoscope based on symptoms and signs. Study helpful for developing clinical risk estimates.
Blandino 2001 (score=4.5)	NSAIDs	Crossover Trial	No mention of sponsorship or COI.	N = 227 Hip or knee OA	No mention of age or gender distributions.	Diclofenac plus misoprostol vs. acetaminophen. No specific comparison group sample	No mention of follow-up.	WOMAC improved 12.2 points for diclofenac vs. 6.6 for acetaminophen. Second 6-week period improvement 12.9 vs. 2.1 points. MDHAQ scale improved more with diclofenac plus misoprostol 20.8 points vs. 13.1 acetaminophen period 1, and 24.6 points vs. 0.4 acetaminophen in period 2.	"The NSAID diclofenac was found to be more effective than acetaminophen in patients with moderate to severe arthritis."	Few study details. Results suggest diclofenac more effective than acetaminophen for pain and functional improvement.

						sizes reported.				

Pilotto 2000 (Score=4.0)	NSAIDs	RCT	Sponsored by Digestive Pathophysiology Center at department of geriatrics in Vicenza Italy and Department of Gastroenterology in Padova Italy. No mention of COI.	N = 69 H pylori positive patients with no severe gastro-duodenal lesions	Mean age: 75.4 years; 29 males, 40 females.	Pantoprazole 40mg QD plus amoxicillin 1g BID and clarithromycin 250mg BID for 1 week (n=34) vs. pantoprazole 40mg QD for 1 month (n=35).	Follow-up at 6 months.	Higher incidence of severe gastroduodenal damage in Group PAC vs. Group P (29% vs. 9%, p <0.05). Percent of patients worsened, unchanged, improved after 1 month Group PAC: 46%, 46%, and 9% vs. Group P: 7%, 65%, 29% (p <0.0008).	"One month of pantoprazole was more effective than a proton pump inhibitor-based triple therapy in the prevention of gastroduodenal damage in elderly H. pylori-positive NSAID users."	Triple therapy for 1 week pantoprazole for 1 month reduces strength of conclusion regarding what is efficacious vs. efficacy of 1 month when 1 arm still actively treated.

Høyeraal 1993 (Score=4.0)	NSAIDs	RCT	Sponsored by Roussel Nordiska AB Stockholm Sweden. No mention of COI.	N = 208 Hip and knee OA	Mean age: 66 years; 119 females, 61 males.	Tiaprofenic acid 300mg BID (n=71) vs. naproxen 500mg QAM and 250mg QPM (n=66) vs. placebo BID (n=61) for 3 weeks. Double dummy.	No mention of follow-up.	Twenty-eight drops, 17 discontinued for reasons related to treatment. Excellent or good responses: tiaprofenic acid 19/62 (30.6%) vs. naproxen 23/58 (39.7%) vs. placebo 12/60 (20.0%). Percentages of responders in 3 patient groups were 52, 59, and 30 respectively.	"[I]t appears that what characterizes a responder/nonresponder to one NSAID does not necessarily apply to another. These sets are related to dosage of the drug, assessment by patient/physician and objective measurements."	Suggests treatments better guided by predictive variables. Better responders to naproxen young females with high disease activity, low leisure physical activity, few affected joints. Responder to tiaprofenic acid tended to high disease activity, high leisure physical activity, high platelet count, little morning stiffness, few affected joints, gradual disease onset.
Famaey 1976 (score=4.0)	NSAIDs	Possible Crossover Trial	No mention of sponsorship or COI.	N = 20 Hip OA	Mean age: 66 years; 6 males, 7 females.	Ketoprofen 50mg TID (n=7) vs. placebo for 2 weeks (n=6).	No mention of follow-up.	Three of 20 (15%) did not complete. Patients favored treatment with ketoprofen ($p < 0.05$).	"[K]etoprofen was significantly better than placebo."	Small sample size. Lack of details and results. Study appears to be a crossover trial.

Evidence for the Use of Acetaminophen

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Geba 2002 (score=9.0)	NSAIDs vs. Other NSAIDs and Trials with Multiple Treatment Arms	RCT	Sponsored by Merck & Co, Inc. COI, Dr. Schnitzer has served as a consultant to AstraZeneca, GlaxoSmithLkine, Merck & Co, Novartis, Ortho-McNeil, McNeil Pharmaceuticals, and Wyeth-Ayerst.	N = 382 Knee OA	Mean age: 62.6 years; 121 male, 261 female.	Rofecoxib: (n=96) received 12.5mg a day vs. Rofecoxib: (n=95) received 25mg a day vs. Celecoxib: (n=97) received 200mg a day vs. Acetaminophen: (n=94) received 1gm QID for 6 weeks	Follow up at baseline, 2, 3 and 6 weeks.	Changes in night pain first 6 days: acetaminophen (-18.8) vs. celecoxib (-18.7) vs. rofecoxib 12.5mg (-22.0) vs. rofecoxib 25mg (-25.2), p <0.05 comparing rofecoxib 25mg to acetaminophen or celecoxib. Rest pain results: -12.5, -15.5, -18.6, -21.8. Walking pain after 6 weeks: -30.3, -36.2, -35.1, -42.0 (p <0.01 comparing rofecoxib 25mg to acetaminophen).	"Rofecoxib, 25 mg/d, provided efficacy advantages over acetaminophen, 4000 mg/d, celecoxib, 200 mg/d, and rofecoxib, 12.5 mg, for symptomatic knee OA."	More discontinued acetaminophen than other treatments. Rofecoxib appeared superior to other treatment arms.
Golden 2004 (score=8.5)	NSAIDs vs. Acetaminophen or Paracetamol	2 RCTs	Sponsored by F. Hoffmann-La Roche AG. No mention of COI	N = 465 Knee OA	Mean age 60.6 years; 284 males, 646 female.	Naproxen sodium: (n=158) received 220mg TID (BID if over 65 years) vs. Acetaminophen: (n=145) received 1gm QID vs. Placebo: (n=149) received QID	1, 2, 3, 4, 5, 6 and 7 days.	Nearly all measures improved for naproxen (rest pain, pain on passive motion, pain on weight bearing, stiffness, day pain, night pain), but only day pain relief improved for acetaminophen compared with placebo. Adverse effects in 17.4% of placebo vs. 20.9% acetaminophen vs. 24.2% naproxen.	"Nonprescription doses of naproxen sodium (440/660 mg) effectively relieve pain and other symptoms of osteoarthritis. Naproxen sodium is an alternative initial treatment of osteoarthritis and may be	Two very short term studies of 7 days each reported in pooled analyses. Submaximal naproxen dose vs. full acetaminophen dose. Acetaminophen appears inferior to naproxen, and not clearly superior to placebo.

									preferred to acetaminophen as first-line therapy in patients with moderate or severe pain."	
Temple 2006 (score=8.0)	NSAIDs vs. Acetaminophen or Paracetamol	RCT	Sponsored by McNeil Consumer and Specialty Pharmaceuticals. COI, Dr. Benson served as consultant for McNeil Consumer and Specialty Pharmaceutica	N = 581 Mild to moderate hip or knee OA	Mean age 59.3 years, 176 male, 395 female.	Acetaminophen: (n=287) received 1g Q4-6 hours vs. Naproxen: (n=284) received 375mg BID for up to 12 months. Single dummy.	1, 3, 6, 9, 12 months.	Few data on efficacy. WOMAC scores at 6 months improved in both groups; not significantly different. Adverse effects in 38.3% acetaminophen vs. 43.4% naproxen (NS). More constipation with naproxen (9.9% vs. 3.1%, p <0.002) and more peripheral edema (3.9% vs. 1.0%, p <0.033).	"With physician supervision, acetaminophen was found to be generally well tolerated in these patients for the treatment of osteoarthritis pain of the hip or knee for periods up to 12 months."	Maximal dose acetaminophen vs. submaximal dose naproxen likely biases in favor of acetaminophen. No significant differences in primary outcomes. Both groups had high dropouts.
Pincus 2001 (score=7.5)	NSAIDs vs. Acetaminophen or Paracetamol	Randomized Crossover Trial	Sponsored by Pharmacia. No mention of COI.	N = 227 Hip or knee OA	Mean age 61.4 years; 67 male 160 female	Diclofenac 150mg plus misoprostol 400µg: (n=112) vs. 4,000 mg Acetaminophen: (n=115) for 6 weeks	6 weeks	WOMAC scores for most-involved joint (baseline/6 weeks): diclofenac + misoprostol (42.5±2.1/ 30.3±2.0) vs. acetaminophen (37.4± 2.5/35.3±1.9) (p = 0.011). Acetaminophen first, results (baseline/6 weeks): 44.8±2.1/38.2 ±1.7) vs. diclofenac+ misoprostol (40.5±2.6/ 27.6±2.1) (p <0.01). Multidimensional Health Assessment	"Patients with osteoarthritis of the hip or knee had significantly greater improvements in pain scores over 6 weeks with diclofenac + misoprostol than with	No placebo arm. Data demonstrate diclofenac superior for pain relief and measures of function to acetaminophen, particularly for moderate to severe disease.

								Questionnaire VAS and SF-36 also favored diclofenac. Results comparing treatments by OA severity index [WOMAC total score estimate (p-values) for quartiles lowest to highest): 0.78 (0.86), -1.45 (0.70), -6.72 (0.63), -14.70 (p <0.001). Non-serious adverse GI events more common for diclofenac + misoprostol (p = 0.006). Diclofenac + misoprostol reported "better" or "much better" by 57%.	acetaminophen, although patients with mild osteoarthritis had similar improvements with both drugs. Acetaminophen was associated with fewer adverse effects."	
Boureau 2004 (score=7.5)	NSAIDs vs. Acetaminophen or Paracetamol	RCT	Sponsored by Boots Healcare, France. COI, some authors are affiliated with Boots healthcare (H Schneid & N Zeghari).	N = 222 Knee or hip OA	Mean age 66.5; 60 males, 162 females.	Ibuprofen: (n=111) received 400mg TID vs. Paracetamol: (n=111) received 1,000mg TID for 14 days. Double dummy.	Baseline, and every day for 2 weeks.	Pain intensity over hours or days reduced to greater extent with ibuprofen (p <0.05). Stiffness scores (baseline/final): ibuprofen 56.2±17.5/ 32.5±18.7 vs. paracetamol 56.2±17.5/ 43.7±20.0 (p = 0.002). Pain scores: ibuprofen 50.0±13.5/27.0±17.0 vs. 50.0±12.5/35.5±18.0 (p <0.001). Physical function scores: -19.8 vs. -12.8 (p = 0.002). Global efficacy higher for ibuprofen (67.5%) than paracetamol (37.8%), p = 0.001. Adverse effects did not differ (23.4% vs. 22.5%) (NS).	"[S]hows that a significant and a more marked reduction in pain was experienced by patients with OA of the hip or knee with ibuprofen 400 mg than with the paracetamol 1000mg."	Study used sub-maximal doses and demonstrated Ibuprofen 400 mg TID was more effective than paracetamol for OA of hip and knee at every time interval from hours to days 1 to 14.
Bradley 1991 (score=7.5)	NSAIDs vs. Other NSAIDs and Trials with	RCT	No mention of sponsorship or COI.	N = 184 Knee OA	Mean age: 59.6 years; 47	Ibuprofen: (n=61) received 600 mg QID vs.	Follow up at baseline, 3 to 7	Walking pain score changes: acetaminophen (0.13) vs. ibuprofen 1200mg (0.31) vs.	"[S]ymptomatic treatment of osteoarthritis	At baseline, trend towards more advanced disease in high-

	Multiple Treatment Arms acetaminophen				male, 137 female.	Ibuprofen: (n=62) received 300mg QID vs. Acetaminophen: (n=61) received 1gm QID for 4 weeks	days, and 4 weeks.	ibuprofen 2,400mg (0.45), p = 0.10. Rest pain scores were: 0.06 vs. 0.33 vs. 0.40, p = 0.05.	of the knee, the efficacy of acetaminophen was similar to that of ibuprofen, whether the latter was administered in an analgesic or an anti-inflammatory dose."	dose ibuprofen group. Walking pain score, rest pain both favored ibuprofen (some measures showed no difference).
Amadio 1983 (score=7.0)	Acetaminophen or Paracetamol vs. Placebo	Crossover Trial	No mention of sponsorship or COI.	N = 25 Knee OA	Mean age: 64 years; 3 males, 22 females.	Acetaminophen 1gm QID (n=14) vs. placebo (n=11) for 6 weeks.	No mention of follow-up.	Pain at rest better on acetaminophen (32 vs. 2 on placebo vs. 10 no difference, p = 0.0001). Pain on motion better on acetaminophen (29 vs. 4, p = 0.011). Tenderness better on acetaminophen (p = 0.0022). Swelling and heat not different (p = 0.5). Time to walk 50 feet 17.6s; after placebo 17.4± 1.2 vs. after acetaminophen 14.9±0.8, p = 0.05.	"Acetaminophen in a dose of 4000 mg/day is an effective alternative to salicylates in the treatment of osteoarthritic pain of the knees, with few adverse effects."	Suggests efficacy of acetaminophen.
Case 2003 (score=6.5)	NSAIDs vs. Acetaminophen or Paracetamol	RCT	Sponsored by a Specialized Center of Research osteoarthritis grant from the NIH and an intramural development	N = 82 Medial knee OA	Mean age: 62.21 years; 41 males, 41 females.	Diclofenac: (n=25) received 75mg BID vs Acetaminophen: (n=29) received 1000mg QID vs. Placebo:	Follow up was performed at 0, 2, and 12 weeks.	WOMAC pain scores (baseline/Week 2/Week 12): diclofenac (199.8± 101.5/139.6±105.2/146.0 ±101.2) vs. acetaminophen (310.8±86.3/206.1± 101.2/186.9±121.5) vs. placebo (198.6±110.9/	"Diclofenac is effective in the symptomatic treatment of OA of the knee, but acetaminophen is not."	Moderate sample size, lack of study details somewhat weaken results. Placebo arm strengthens conclusions that acetaminophen

			grant from the Rush Arthritis and Orthopedics Institute. COI, Author Baliunas received a Dean's Summer Research Fellowship from Rush Medical College.			(n=28) received for 12 weeks. Double dummy		197.1±118.8/183.4±122.9). Only diclofenac significant (p <0.002), while acetaminophen p = 0.13 for Week 0-12 differences and other pain changes negative. Acetaminophen never superior to placebo.		may be weakly effective or ineffective.
Pincus 2004 (score=6.5)	NSAIDs vs. Other NSAIDs and Trials with Multiple Treatment Arms	RCT	Sponsored by Pfizer Corporation. No mention of COI.	N = 1,080 Knee or hip OA	Mean age: 63.4 years; 385 male, 695 female.	Placebo: (n=172) vs. Acetaminophen: (n=171) received 1000mg QID vs. Celecoxib: (n=181) received 200mg QAM. 6 weeks each. Double dummy. Patients received 2 of 3 treatments.	Follow up at baseline, 1, 7, 8 and 12 weeks.	Percent improvement in WOMAC scores averaged over treatment: celecoxib 21.6% vs. acetaminophen 13.0% vs. placebo 7.9%. Similar VAS score results. Patient preference strongest for celecoxib, then acetaminophen, then placebo.	"[D]ata indicate a gradient of efficacy from celecoxib to acetaminophen to placebo"	Some variation in results in the two trial periods for acetaminophen vs. placebos. Patients generally reported preference for celecoxib over others.
Parr 1989 (score=6.5)	NSAIDs vs. Opioids	RCT	No mention of sponsorship or COI.	N = 846 Mostly hip or knee OA	Mean age: 54.79 years; 355 males, 400 females.	Diclofenac sodium slow release: (n=372) received 100mg QD vs. Dextro-	No mention of follow-up.	Dizziness, lightheadedness less common from diclofenac (14 vs. 30, p <0.05), as was CNS symptoms (48 vs. 93, p <0.01). Abdominal pain higher with diclofenac (40	"Pain as measured by a visual analogue scale (VAS) showed 8% greater pain	Study suggests greater efficacy of diclofenac vs. dextropropoxyphene plus acetaminophen. Benefits

						propoxyphene 180mg plus paracetamol: (n=381) 1.95gm QD		vs. 18, p <0.01) and diarrhea (14 vs. 2, p <0.01). Overall gastrointestinal effects not different (63 vs. 60). Pain ratings were (change in VAS): diclofenac -27.0 vs. dextropropoxyphene plus paracetamol -22.7, p <0.05. Physical mobility scores were -10.8 vs. -7.4 (p <0.01). Interference of work less common with diclofenac (3 vs. 11, p <0.05), and lost work time (3 vs. 16, p <0.05).	reduction with DSR as compared with D&P (P<0.05). Physical mobility as measured by the (Nottingham Health Profile) improved by 13% more with DSR as compared with D&P (P<0.05)."	suggested for working populations from diclofenac including lower incidence of problems at work and lost work time.
Miceli-Richard 2004 (score=6.5)	Acetaminophen or Paracetamol vs. Placebo	RCT	No mention of sponsorship or COI	N = 779 Knee OA	Mean age 70 years; 196 males, 583 females.	Paracetamol: (n=405) received 1gm QID vs. Placebo: (n=374) received for 6 weeks	Week 1 and 6	Changes in VAS scores at 1 week: paracetamol 16±21 vs. placebo 15±21, p = 0.40; 6 weeks: paracetamol 23±27 vs. 23±26, p = 0.66. WOMAC scores did not differ. Patient global assessments at 1 week: paracetamol 14± 21 vs. 12±22, p = 0.063; 6 weeks: 22±26 vs. 20±27, p = 0.23.	"A statistically significant symptomatic effect of oral paracetamol 4 g/day over placebo was not found, suggesting that paracetamol use in symptomatic OA of the knee should be further explored. The tolerability and safety of paracetamol, at the	Large sample size. Suggests paracetamol is not clearly effective for knee OA.

									recommended maximum dose of 4 g/day, was confirmed over 6 weeks"	
Morgan 2001 (score=6.0)	NSAIDs vs. Other NSAIDs and Trials with Multiple Treatment Arms	RCT	Sponsored by SmithKline Beecham Pharmaceuticals, Collegeville, PA. U.S.A. No mention of COI.	N = 335 Moderate to severe knee or hip OA	Mean age: 72 years; 99 male, 236 female	Nabumetone: (n=167) received 1,000-2,000mg QD vs. Diclofenac: (n=168) received 50mg BID-TID for 12 weeks; doses titrated	Follow up at 1, 2, and 3 months.	Patient global assessments not different (nabumetone 75% vs. diclofenac 79%). Pain score changes: nabumetone -3.1±0.2 vs. diclofenac -3.7±0.2. No difference in Arthritis Impact Measurement Scales. More diclofenac patients on maximum dose (46% vs. 66%). Nabumetone group more acetaminophen 2nd week ($p < 0.05$). More diclofenac than nabumetone patients ($p < 0.05$) had ALT level 2 times or more than upper limit of normal (6 or 161 [3.7%] vs. 0 of 155 [0%]).	"Nabumetone was as effective as diclofenac in the treatment of elderly patients with moderate-to-severe osteoarthritis. However, the gastrointestinal safety profile of nabumetone was superior to that of diclofenac with respect to elevation of liver enzymes."	Blinding, randomization, compliance and co-intervention details missing.
Blandino 2001 (score=4.5)	NSAIDs vs. Acetaminophen or Paracetamol	Crossover Trial	No mention of sponsorship or COI.	N = 227 Hip or knee OA	No mention of age or gender distributions.	Diclofenac plus misoprostol vs. acetaminophen. All patients received	No mention of follow-up.	WOMAC improved 12.2 points for diclofenac vs. 6.6 for acetaminophen. Second 6-week period improvement 12.9 vs. 2.1 points. MDHAQ scale improved more with diclofenac plus misoprostol 20.8 points	"The NSAID diclofenac was found to be more effective than acetaminophen in patients with moderate to	Few study details. Results suggest diclofenac more effective than acetaminophen for pain and functional improvement.

						both therapies.		vs. 13.1 acetaminophen period 1, and 24.6 points vs. 0.4 acetaminophen in period 2.	severe arthritis."	

Evidence for the use of cytoprotective medications

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cytoprotective agents, proton pump inhibitors, misoprostol, sucralfate, H2 blockers; hip osteoarthritis, hip degenerative joint disease, hip osteoarthritis, hip degenerative arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 18 in Scopus, 5 in CINAHL, 25 in Cochrane Library, 10 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for the Use of Analgesics

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Berti 1998 (score= 7.5)	Epidural Anesthesia and Analgesia for	RCT	No mention of sponsorship or COI.	N = 30	Mean age: 63.4 years; 15 males, 15 females	Post-operative anesthesia by continuous epidural infusion	1, 3, 6, 9, 12, 24 hours	"No differences in pain relief, sedation, or non-respiratory side effects were observed between the two groups. Rescue analgesics were required in three patients in the fentanyl	"Continuous epidural infusion of bupivacaine-morphine or bupivacaine-fentanyl mixtures provided similar pain relief. Patients receiving morphine showed a more marked decrease in SpO2 than those receiving	Equivocal results in pain management. Questionable clinical significance of oxygen saturation difference.

	Hip/Knee Arthroplasty					of bupivacaine 0.125% at 4ml/hour) in combination with either Fentanyl: (n=15) (0.005mg/ml) vs. Morphine: (n=15) (0.05mg/ml)		group (20%) and in two receiving morphine (13.3%) (P:NS). Two patients in the fentanyl group and three in the morphine group required oxygen due to SpO2 < 90% (P:NS).” Both opioid/ bupivacaine mixtures decreased hemoglobin oxygen saturation compared with pre-op values. Mean +/- SD SpO2 values measured at 3, 6, 12, 24 hours: 94.4 +/- 1, 92.6 +/- 0.9, 92 +/- 0.8, and 92.8 +/- 1 in morphine group, 95.3 +/- 0.5, 95 +/- 0.5, 94.6 +/- 1.2, and 95.6 +/- 1 in fentanyl group (p <0.05).	fentanyl. However, the average SpO2 remained > 90% in both groups.”	

Evidence for the use of Skeletal Muscle Relaxants

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Skeletal Muscle Relaxants, Neuromuscular Agents; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthritis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2 articles in PubMed, 3 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 87 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the use of Capsicum

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: capsicum patch, capsaicin patch; hip osteoarthritis, hip degenerative joint disease, hip osteoarthritis, hip degenerative arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 0 in Scopus, 0 in CINAHL, 2 in Cochrane Library, 169 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of NSAIDS

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: topical NSAIDs, lidocaine patches, eutectic mixture of local anesthetics, creams, ointments; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 82 in Scopus, 0 in CINAHL, 32 in Cochrane Library, 30 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.

Evidence for the Use of Lidocaine Patches

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: topical NSAIDs, lidocaine patches, eutectic mixture of local anesthetics, creams, ointments; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 82 in Scopus, 0 in CINAHL, 32 in Cochrane Library, 30 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.

Evidence for the use of Eutectic Mixture of Local Anesthetics

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: topical NSAIDs, lidocaine patches, eutectic mixture of local anesthetics, creams, ointments; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 82 in Scopus, 0 in CINAHL, 32 in Cochrane Library, 30 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.

Evidence for the use other creams/ointments

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: topical NSAIDs, lidocaine patches, eutectic mixture of local anesthetics, creams, ointments; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 82 in Scopus, 0 in CINAHL, 32 in Cochrane Library, 30 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.

Evidence for the Use of Tumor Necrosis Alpha-Factor

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: tumor necrosis factor-alpha blockers; hip osteoarthritis, hip degenerative joint disease, hip osteoarthritis, hip degenerative arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 articles in PubMed, 787 in Scopus, 2 in CINAHL, 2 in Cochrane Library, 812 in Google Scholar, and 1 from other sources. We considered for inclusion 0 from PubMed, 2 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 5 articles considered for inclusion, 1 randomized trial and 1 systematic study met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Schwarz 2003 (score=6.0)	Tumor Necrosis Alpha-Factor	RCT	Sponsored by Immunex Corp., VirtualScopics LLC, and research grants from the NIH, and the Orthopaedic Research and Education Foundation. No mention of COI.	N = 20 Arthroplasty patients with periacetabular osteolysis	Mean age: 63.9 years; 14 males, 6 females	Etanercept (25mg SQ, twice a week) (n=10) vs. placebo for 12 months (n=10)	6, 12 months	Mean change in periacetabular osteolysis: etanercept 3.40±3.61cm3 vs. placebo 3.00±3.90cm3 (p <0.038). Some reduction attributed to cup migration. Study not powered to detect clinical significance of treatment.	"Volumetric CT was able to measure progression of osteolysis over the course of a year. Varying results were found."	Small sample size. Low power. No difference demonstrated from treatment. Study proposes volumetric CT for assessment.

Evidence for the Use of Nerve Growth Factor Inhibitors

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Tanezumab; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis, nerve growth factor inhibitor, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 18 in Scopus, 6 in CINAHL, 14 in Cochrane Library, 197 in Google Scholar, and 2 from other sources. We considered for inclusion 5 from PubMed, 0 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 9 articles considered for inclusion, 6 randomized trials and 1 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/ Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Brown, 2014 (score=6.5)	Nerve Growth Factor Inhibitors	RCT	Sponsered by Pfizer Inc., COI Mark T. Brown, Michael D. Smith, Christine R. West, Kenneth M. Verburg are employees of and hold stock and/or stock options in Pfizer Inc. David N. Herrmann reports personal fees and other from Pfizer during the conduct of the study. Mark Goldstein has nothing to disclose. Aimee Burr is a paid contractor of Pfizer and holds stock in Pfizer Inc. Peter J. Dyck received financial support for services as a Neuro Care Laboratory for pharmaceutical studies of polyneuropathy which included Eli Lilly, Inc., Pfizer, Inc., ISIS, Inc., Alnylam, Inc., in the past and from other pharmaceutical companies in the distant past as well as support from Eli Lilly, Inc., Pfizer, Inc., ISIS, Inc., Alnylam, Inc. outside the submitted work.	N=219 Participants with knee of hip OA.	Mean age: 57.4; 97 males, 130 females.	Participant with intravenous injection of 5 mg tanezumab every 8 weeks over 24 weeks (n=73) vs. participants given intravenous injections of 10 mg tanezumab every 8 weeks over 24 weeks (n=74) vs. participants on placebo (vehicle) (n=72)	Follow up at baseline, and 24 weeks.	No significant difference from baseline to week 24 in Σ5NC + HRdb. Mean treatment difference for change from baseline to week 24 in IENF density was 0.61 with tanezumab 5mg vs placebo and -0.69 with tanezumab 10 mg vs. placebo.	"Tanezumab has a modulating effect on pain, does not appear to increase neurological safety signals, and offers a potentially promising, novel approach in treatment of pain."	Study interrupted due to Safety concerns and placed on hold June 2010.
Balanescu, 2014	Nerve Growth	RCT	Sponsored by Pfizer Inc. Christina McManus of UBC Scientific Solutions.	N= 604 Hip or Knee OA.	Mean age: 62.4;	Tanezumab 10 mg + Diclofenac sustain release (DSR) 75 mg	Follow-up at baseline,	Patients treated with tanezumab + DST (any dose) vs. Placebo + DSR	"Addition of tanezumab to DSR resulted in	Efficacy interrupted due to clinical hold at 23

(score=5.5)	Factor Inhibitors		COI: Andra Rodica Balanescu and Eugen Feist, Gernot Wolfram, Isabelle Davignon, Michael D. Smith, Mark T Brown and Christine R West		469 females, 135 males.	twice daily for 32 weeks (n= 145) Vs. Tanezumab 5mg + DSR 75 mg twice daily for 32 weeks (n=150) Vs. Tanezumab 2.5 mg + DSR75 mg twice daily for 32 weeks (n=157) Vs. Placebo + DSR: administered by intravenous infusion every 8 weeks for a total of three doses. (n=152)	2, 4, 8, 12, 16, 24 and 32 weeks.	experience ≥30%, ≥50%, ≥70% and ≥90% improvements in pain and were considered WOMAC Pain responders at week 16. Tanezumab treated patients had an improvements of two or more categories in PGA of OA at week 16 (tanezumab 2.5 mg+DSR: 5.8%; tanezumab 5 mg+DSR: 14.7%; tanezumab 10 mg+DSR: 16.6%; placebo +DSR: 4.6%) Adverse events was overall higher with tanezumab + DSR (45.2%-49.7%) than with placebo + DSR (34.9%)	significant improvements in pain, function and global assessments in patients with OA. Although no new safety signals were observed, the higher incidence of adverse events in the tanezumab+diclofenac group suggests that combination therapy is unfavourable. Further investigations of tanezumab monotherapy for OA pain treatment are required. "	weeks into study. Data suggest the addition of tanezument to DSR decreased hip OA pain but the combination therapy group of tanezumab + DSR had more adverse events, but results unlikely substantial due to clinical hold.
Schnitzer, 2014 (score=5.5)	Nerve Growth Factor Inhibitors	RCT	Sponsored by Pfizer Inc., and Christina McManus of Engage scientific solutions. COI, Abbott, Merck, Regeneron, Prizer Inc, Winston Laboratories; Genzyme, Eli Lilly, Nuvo research	N=2700 patients with diagnosis of hip or knee osteoarthritis.	Mean age: 61.6 years; 1904 females, 796 males.	Placebo + NSAID (n=539) vs. Tanezumab 5 mg (n=541) vs. Tanezumab 10 mg (n=542) vs. Tanezumab 5 mg+NSAID (n=536) vs. Tanezumab 10mg+NSAID (n=542).	16 weeks	Tanezumab 5 & 10 mg made greater improvement in WOMAC pain (p≤0.015), comparing with naproxen treatment and celexocib treatment (p≤0.007). Tanezumab monotherapy showed greater reduction in WOMAC pain score with ≥30%, ≥50%,≥70%,≥90% ,	"Subjects receiving partial symptomatic relief of OA pain with NSAIDs may receive greater benefit with tanezumab monotherapy. While only coadministration of tanezumab with NSAIDs met the definition of superiority, combination treatment did not provide	High dropouts as study termination caused almost 50% of participants to discontinue due to clinical hold.

								comparing with NSAID alone therapy (p≤0.044).	important benefits over tanezumab monotherapy."	
Ekman, 2014 (Score=4.5;Score=4.5)	Nerve Growth Factor Inhibitors	2 RCTs	Sponsored by Pfizer Inc. No mention of COI.	Study 1015: N=828 patients with knee or hip OA. Study 1018: N=840 patients with knee or hip OA.	Study 1015: mean age: 61.1 years; 499 females, 329 males. Study 1018: mean age: 59.9 years; 534 females, 306 males.	Study 1015: placebo (n=208) vs. Tanezumab 5mg (n=206) vs. Tanezumab 10mg (n=208) vs. Naproxen 500 mg BID (n=206). Study 1018: placebo (n=209) vs. Tanezumab 5 mg (n=211) vs. Tanezumab 10 mg (n=209) vs. Naproxen 500 mg BID (n=211).	16 weeks	Study 1015: tanezumab treatment indicated significant improvement in WOMAC pain score and physical function at 16th week (p≤0.021); 5mg tanezumab showed greater improvement at all levels (p≤0.017). Study 1018: tanezumab showed significant improvement in WOMAC pain and physical function at 16th week (p≤0.002); 5mg tanezumab showed greater improvement (p≤0.019) comparing with naproxen.	"Tanezumab provides efficacious treatment of knee or hip OA and may have therapeutic utility in patients with OA who experience inadequate analgesia with nonsteroidal antiinflammatory drugs."	No pain reduction with 10 mg tanezumab vs. naproxen. Data suggest 5 mg tanezumab may be beneficial for treating hip and knee OA if there are inadequate results from NSAIDs. Tanezumab 5 mg better for pain reduction than placebo but was associated with paresthesia, hyperesthesia, hypoesthesia, burning sensation, extremely pain, peripheral edema & arthralgia.
Brown 2013 (score=3.5)	Nerve Growth Factor Inhibitors	RCT								High dropout rates. Tanezumab placed on hold during this study due to excessive AEs.
Tive, 2015 (No score)	Nerve Growth Factor Inhibitors	Pool analysis								Tanezumab (TNZ) may be effective in relieving OA pain.

Evidence for the Use of Glucosamine

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis, 2-Amino-2-Deoxyglucose, 2 Amino 2 Deoxyglucose, Hespercorbin, Glucosamine Sulfate, Sulfate, Glucosamine, Dona, Dona S, Xicil, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 43 articles in PubMed, 0 in Scopus, 19 in CINAHL, 68 in Cochrane Library, 33 in Google Scholar, and 0 from other sources. We considered for inclusion 11 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 23 from other sources. Of the 34 articles considered for inclusion, 27 randomized trials and 7 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Chondroitin, Chondroitin Sulfate ; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 25 articles in PubMed, 77 in Scopus, 13 in CINAHL, 3 in Cochrane Library, 1150 in Google Scholar, and 7 from other sources. We considered for inclusion from 3 PubMed, 2 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 7 from other sources. Of the 17 articles considered for inclusion, 8 randomized trials and 9 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis Methylsulfonylmethane, methyl sulfone, Dimethyl sulfone controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 2 in Scopus, 0 in CINAHL, 3 in Cochrane Library, 330 in Google Scholar, and 1 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 1 from other sources. Of the 4 articles considered for inclusion, 2 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Uebelhart 2004 (score= 10.0)	Glucosamine	RCT	Sponsored by a grant from IBSA, Lugano, Switzerland. No mention of COI	N = 110 Knee OA	Mean age: 63.5 years; 21 males, 89 females	Chondroitin sulfate: (n=54) received 800mg QD vs. Placebo: (n=56) received for two 3-month periods during 1 year	3, 12 months	Chondroitin group improved vs. placebo at Months 9 and 12 ($p < 0.05$; $p < 0.01$). Pain intensity decreased 42% Month 9 and 12 in CS group vs. 25% in placebo ($p < 0.05$). Differences in VAS scores and physician and patient efficacy assessments favored CS at 6, 9, and 12 months ($p < 0.01$). CS treatment had a significant role upon variation of joint space surface area and mean joint space width ($p = 0.03$) but not on minimum joint space width vs. placebo.	"This study supports the evidence that oral CS of bovine origin and high pharmaceutical quality is a well-tolerated drug, which is effective in reducing pain and improving function in patients suffering from symptomatic knee osteoarthritis."	Dropout rate was 26% with no difference between the groups.
Clegg 2006 (score= 9.5)	Glucosamine	RCT	Sponsored by a contract from the National Center for Complementary and Alternative Medicine and the National Institute of Arthritis and Musculoskeletal and Skin Diseaseases. COI Drs. Bingham, Brandt, Clegg, Hooper, and Schnitzer report having received consulting fees or having served on advisory boards for McNeil Consumer and Specialty Pharmaceuticals.	N = 1,583 Knee OA	Mean age: 59 years; 568 males, 1015 females	Oral glucosamine hydrochloride: (n=317) received (500mg TID) vs. Chondroitin Sulfate: (n=318) received (400mg TID) vs. Glucosamine and Chondroitin Sulfate: (n=317) vs. Celecoxib: (n=318) received 200mg QD vs. Placebo: (n=313) in treatment of knee osteoarthritis in 6-month trial	24 weeks	Combined glucosamine and chondroitin sulfate was borderline vs. placebo in reducing WOMAC pain score 20% ($p = 0.09$). As compared with rate of response to placebo (60.1%), rate of response to combined treatment was 6.5% points higher ($p = 0.09$) and celecoxib response rate was 10.0% points higher ($p = 0.008$). For patients with moderate-to-severe pain at baseline, response rate significantly higher with combined therapy vs. placebo (79.2% vs. 54.3%, $p = 0.002$). OMERACT-OARSI response rates showed a similar result.	"Celecoxib was demonstrated to reduce pain effectively in the overall group of patients with osteoarthritis of the knee. The combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain."	Results showed combination glucosamine-chondroitin to have significantly better outcomes in subgroup of moderate-to-severe group (WOMAC pain score 301-400) in WOMAC pain reduction of 50% or more, WOMAC pain score change from baseline and WOMAC function score. Results with Celecoxib not significant in these categories. Study used non-conventional glucosamine preparation.

			Drs. Brandt, Moskowitz, Schnitzer, and Schumacher report having received consulting fees or having served on advisory boards for Pfizer. Dr. Brandt reports having equity interests in Pfizer. Drs. Moskowitz and Weisman report having received lecture fees from Pfizer; Dr. Brandt, lecture fees from McNeil Consumer and Specialty Pharmaceuticals; Drs. Bingham, Clegg, Hooper, Jackson, Molitor, Sawitzke, and Schnitzer, grant support from Pfizer; and Dr. Bingham, grant support from McNeil Consumer and Specialty Pharmaceuticals. Dr. Brandt reports having received royalties from books related to osteoarthritis. Dr. Moskowitz							

			reports having served as an expert consultant for Pfizer.							
Pavelká 2002 (score= 9.5)	Glucosamine	RCT	Sponsored by the Rotta Research/Rottapharm Group. No mention of COI.	N = 202 Knee OA	Mean age: 62.4 years; 45 males, 157 females	Oral glucosamine sulfate: (n=101) received (1,500mg once daily) vs. Placebo: (n=101) for knee osteoarthritis in 3-year trial of disease progression	3 years	After 3 years, average change in progressive joint space narrowing with placebo use -0.19mm (95% CI, -0.29 to -0.09mm) while no narrowing change with glucosamine sulfate use (0.04mm; 95% CI, -0.06 to 0.14mm), with a significant difference between groups (p = 0.001). Glucosamine sulfate significantly higher improvement in 20% on Lequesne index and 15% on WOMAC index joint stiffness (p <0.001 and p = 0.002, respectively) compared with placebo.	"Glucosamine sulfate is the first pharmacologic intervention that slowed the progression of knee osteoarthritis during the long-term treatment."	High dropout rate (81/202 = 41% dropout) over the 3 year study, although results reported by intent-to-treat.
Herrero-Beaumont 2007 (score= 9.0)	Glucosamine	RCT	Sponsored by the National Institutes of Health. No mention of COI.	N = 318 OA	Mean age: 63.9 years; 40 males, 278 females	Oral glucosamine sulfate: (n=106) received (1,500mg once daily) vs. Acetaminophen: (n=108) received (1,000mg TID) vs. Placebo: (n=104) received using double dummy technique in treatment of knee OA for 6 months	6 months	Glucosamine sulfate more effective than placebo in improving Lequesne score with decrease of 3.1 points, vs. 1.9 for placebo (mean difference =-1.2 [95% CI, -2.3 to -0.8]; p = 0.032); 2.7-point decrease with acetaminophen not significant vs. placebo (mean difference =-0.8 [95% CI, -1.9 to 0.3]; p = 0.18). Similar results observed for WOMAC. More responders to glucosamine sulfate (39.6%) and acetaminophen (33.3%) than placebo (21.2%) (p = 0.004 and p = 0.047 vs. placebo).	"The glucosamine sulfate at the once-daily dosage is an effective medication for knee osteoarthritis symptoms, compared with placebo. Although acetaminophen also had a higher responder rate compared with placebo, it failed to show significant effects on the algofunctional indexes."	Glucosamine appeared superior to acetaminophen as well as placebo.
Usha 2004 (score= 9.0)	Glucosamine	RCT	Sponsored by Healers Limited, Chennai, India. No COI.	N = 118 OA	Mean age: 51.3 years; 42 males, 76 females	Oral glucosamine: (n=30) (Glu) 500mg TID vs. Methyl-	6 months	Placebo showed insignificant change in mean pain index (mean difference = 1.57 [SD, ± 0.5]) to (mean difference = 1.16 [SD, ± 0.76]). Glu showed significant	"The therapy with Glu, MSM and their combination produced an analgesic, anti-inflammatory effect in	Unclear whether study medication was Glu sulfate or Glu hydrochloride. Combination of

						sulfonylmethane (MSM): (n=30) 500mg TID vs. Gluc and MSM: (n=30) vs. Placebo: (n=28) in osteoarthritis of knee for 12 weeks		decrease in mean pain index (mean difference = 1.74 [SD, ± 0.47]) to (mean difference = 0.65 [SD, ± 0.71]; p <0.001). MSM significantly decreased mean pain index from (mean difference = 1.53 [SD, ± 0.51]) to (mean difference = 0.74 [SD, ± 0.65]) and combination treatment highly significant decrease in mean pain index (mean difference = 1.7 [SD, ± 0.47]) to (mean difference = 0.36 [SD, ± 0.33]; p <0.001). After 12 weeks, mean swelling index significantly decreased with Glu and MSM, while decrease in swelling index with combination therapy greater (mean difference = 1.43 [SD, ± 0.63]) to (mean difference = 0.14 [SD, ± 0.35]; p <0.05).	patients with osteoarthritis. Combination therapy showed better efficacy in reducing pain, swelling and improving the functional ability of joints over individual therapy. All the treatments were well tolerated."	Glucosamine and MSM appears superior.
Maziéres 2007 (score= 9.0)	Glucosamine	RCT	Sponsored by the Pierre Fabre Company. COI BM was reimbursed by the Pierre Fabre Company for attending the Boston OARSI meeting. MZ and MH are employees of Pierre Fabre. PG was funded to perform the biochemical analyses.	N = 307 Knee OA	Mean age: 66 years; 167 males, 140 females	Chondroitin sulfate: (n=153) received 500mg BID vs. Placebo: (n=154) for 24 weeks for knee osteoarthritis	24 weeks	Decrease in pain was -26.2 (24.9) and -19.9 (23.5) mm and improved function was -2.4(3.4) (-25%) and -1.7 (3.3) (-17%) in chondroitin sulfate and placebo groups, respectively (0.029 and 0.109). OMERACT-OARSI responder rate was 68% in chondroitin sulfate and 56% in placebo group (p = 0.03). No significant difference observed for changes in biomarkers of inflammation.	"This study failed to show an efficacy of chondroitin sulfate on the two primary criteria considered together, although chondroitin sulfate was slightly more effective than placebo on pain, OMERACT-OARSI response rate, investigator's assessment and quality of life."	Baseline differences between groups on variable of stage of disease appear to be present 69% vs. 59% of chondroitin group rated as intermediate OA disease. No information on other percentage of groups.
Hughes 2002 (score= 8.5)	Glucosamine	RCT	Sponsored by a grant from Health Perception UK. COI Health Perception UK	N = 80 Knee OA	Mean age: 62. 28±9.12 years, 26	Oral glucosamine sulfate: (n=40) received (500mg TID) vs. Placebo:	6 months	Area under curve analysis revealed no significant difference between placebo [mean = 1065.45, SD=398.07] and	"As a symptom modifier in OA patients with a wide range of severities, glucosamine	Permitted co-treatment with NSAIDs may have confounded results.

			is a manufacturer of glucosamine sulphate.		males, 54 females	(n=40) with osteoarthritis of the knee for 6 months		glucosamine [mean = 1081.28, SD = 577.69]; p = 0.89 in primary outcomes measures. No differences between placebo and glucosamine for treatment response (x2 statistic 0.006, p = 0.94). No significant difference in use of rescue analgesia between glucosamine (mean paracetamol tablets taken 43, S.D. 63.92, range 0-252) and placebo (mean paracetamol taken 45, S.D. 75.64, range 0-264).	sulfate was no more effective than placebo."	Relatively small sample size.
McAlindon 2004 (score= 8.5)	Glucosamine	RCT	Sponsored by a grant from the Arthritis Foundation and the National Library of Medicine. No mention of COI.	N = 205 Knee OA	Mean age: 55-64 years; 73 males, 132 females	Oral glucosamine: (n=101) received (1,500mg once daily) vs Placebo: (n=104) in 12 week trial for knee osteoarthritis	12 weeks	At week 12 followed-up from baseline; no difference between glucosamine and placebo groups in terms of change in pain score (2.0±3.4 vs. 2.5±3.8, p = 0.41), and analgesic use (133±553 vs. -88±755, p = 0.12), after adjusting covariates.	"Although glucosamine appears to be safe, it is no more effective than placebo in treating the symptoms of knee osteoarthritis."	Baseline differences of comparison groups. Medication supplier changed during trial, resulting in initial use of glucosamine sulfate capsules replaced by glucosamine hydrochloride powder. Study completed through Internet.
Mehta 2007 (score= 8.5)	Glucosamine	RCT	Sponsored by Rainforest Nutritionals, Inc. COI KM is an employee of Vedic Lifesciences, Pvt, Ltd., a CRO that performed the study. ND is an employee of Vedic Lifesciences, Pvt, Ltd., a CRO that performed the study. MJSM is an advisor to Rainforest Nutritionals, Inc who	N = 95 OA	Mean age: 53.5 years; 24 males, 71 females	Oral glucosamine sulfate: (n=47) received (750mg BID) vs. Reparagen: (n=48) received (900mg BID) in mild to moderate osteoarthritis of knee for 8 weeks	1, 2, 4, 6, 8 weeks	Glucosamine sulfate and reparagen showed significant benefits in WOMAC and VAS outcomes (20% improvement from baseline) within 1 week of treatment (p <0.05) and over 8 weeks of treatment (p <0.001). Overall WOMAC score benefit was 60% reduction for glucosamine vs. 62% reparagen. Response rate of 50% reduction in WOMAC scores significantly greater for reparagen (58.3%) than glucosamine (38.2%) at Week 4 (p = 0.05). Rescue medication (paracetamol)	"Glucosamine sulfate and reparagen provided effective relief of mild to moderate osteoarthritis of the knee in this population, with continued improvements upon sustained treatment."	No placebo group. Data suggest reparagen may be superior to glucosamine

			supported the study and for these services has been compensated with equity but no other financial compensation.					significantly lower in reparagen group (p <0.01).		
Messier 2007 (score= 8.5)	Glucosamine	RCT	Sponsored by a grant from Rexall Sundown, Inc. No mention of COI.	N = 89 Knee OA	Mean age: 72.0 years; 26 males, 63 females	Glucosamine/Chondroitin: (n=45) received glucosamine hydrochloride 1,500mg chondroitin sulfate/1,200mg QD vs. Placebo: (n=44) for 6 months for knee OA. Both groups received exercise training and instruction.	12 months	Mean function did not vary significantly between groups at 6-month (p = 0.52) or 12-months (p = 0.50). However, mean WOMAC function combining both groups improved significantly over time (p = 0.005). There was no difference in pain measures, 6-minute walk distance, or knee strength at 6 or 12 months between the groups.	"Glucosamine hydrochloride/chondroitin sulfate group was not superior to the placebo group in function, pain, or mobility after both phases of the intervention (pill only and pill plus exercise)."	Allocation unclear with baseline differences in function present.
Noack 1994 (score= 8.5)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 252 Knee OA	Mean age: 55 years; 100 males, 152 females	Oral glucosamine sulfate: (n=126) received (500mg TID) vs. Placebo: (n=126) for knee osteoarthritis over 4 weeks	4 weeks	Lequesne index decreased to 7.45±0.5 points in glucosamine group (average 3.2) and 8.4±0.4 points in placebo group (average 2.2) (p <0.05). Proportion of responder patients was 52% with glucosamine and 37% with placebo in an intention-to-treat analysis (p = 0.016).	"The treatment with glucosamine sulfate resulted in a significantly higher improvement knee osteoarthritis in relation to placebo."	Blinding of assessor not clear. Results of per-protocol analysis similar to intent-to treat.

Reichelt 1994 (score= 8.5)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 155 Knee OA	Mean age: 56.5 years; 54 males, 101 females	Intramuscular injection glucosamine sulfate: (n=79) received (400mg twice a week) vs. Placebo: (n=76) for knee osteoarthritis over 6 weeks	2, 6 weeks	Intramuscular glucosamine sulfate vs. placebo showed improvement in symptoms of knee OA (pain and movement limitation) over 6-week therapeutic course ($p < 0.05$). Response rate 55% glucosamine (n = 73) vs. 33% (n = 69) placebo ($p = 0.012$). Local and systemic tolerability of intramuscular glucosamine sulfate were good and without significant difference compared to placebo.	"Intramuscular glucosamine sulfate reduced pain and improved functional in knee osteoarthritis patients."	Some details missing of randomization, allocation, and blinding.
Cibere 2004 (score= 8.5)	Glucosamine	RCT	Sponsored by grants from the Mary Pack Research Fund, Vancouver, British Columbia, Canada and by the Doris Alma Mary Anderson Fund for Geriatric Research, London, ON, Canada. COI: Dr. Cibere's work supported by a Canadian Institutes of Health Research Clinician Scientist Award and a Michael Smith Foundation for Health Research Postdoctoral Fellowship Award.	N = 137 Knee OA	Mean age: 64.5 years; 60 males, 77 females	Oral glucosamine sulfate: (n=71) received (up to 1,500mg a day) vs. Placebo: (n=66) for knee OA in 6 month trial. Randomized discontinuation trial (control was discontinuation of treatment) in patient group already using glucosamine sulfate with reported efficacy. Primary outcomes measures are disease flare-up and flare severity.	6 months	After 6 months, disease flares in intention-to-treat analysis were seen in 21 (45%) of 71 patients in glucosamine group and 28 (42%) of 66 patients in placebo group. Between-group difference not statistically significant (95% CI, -19 to 14; $p = 0.76$). After adjustments, no difference in risk of flare (Hazard ratio 0.8, (95% CI 0.5 to 1.4, $p = 0.45$) or use of acetaminophen and NSAIDs, mean changes in WOMAC pain scores on walking, pain, stiffness, or function scales, or adverse effects between glucosamine and placebo groups ($p > 0.05$).	"This study provided no evidence of symptomatic benefit from continued use of glucosamine sulfate over and above found with placebo."	Glucosamine group had more severe knee OA based on radiography at baseline providing an uncontrolled potential confounder. Cannot rule out possibility of long term benefit in the placebo (discontinuation group) from earlier use of glucosamine.

Houpt 1999 (score= 8.0)	Glucosamine	RCT	Sponsored by grant-in-aid of research from Wanpole Canada, Inc. No mention of COI.	N = 118 Knee OA	Mean age: 64.5 years; 45 males, 73 females	Oral glucosamine hydrochloride: (n=58) (500mg TID) vs. Placebo: (n=60) for osteoarthritis of the knee for 8 weeks	8 weeks	Glucosamine reduced WOMAC pain scores over 8 weeks (mean difference = 46.36 [SD, 13.1]) to (mean difference = 36.57 [SD, 19.5]) vs. placebo reduced WOMAC pain scores (mean difference = 42.42 [SD, 14.9]) to (mean difference = 38.57 [SD, 19.3]). Glucosamine hydrochloride has more than 2 times the improvement compared to placebo (21 vs. 9.1%). Between Week 5 and Week 8, knees of patients taking glucosamine appeared to show improvement vs. placebo (p = 0.026).	"There was no significant difference in pain reduction between the glucosamine hydrochloride and placebo group as measured by WOMAC. Secondary endpoints of cumulative pain reduction as measured by daily diary and knee examination were favorable, suggesting that glucosamine hydrochloride benefits some patients with knee OA."	The methods state pharmacists were blinded to treatment allocation, however, that seems impossible. Outcomes measures trend towards positive results.
Reginster 2001 (score= 8.0)	Glucosamine	RCT	Sponsored by research grant from Rotta Research Group, Monza, Italy. No mention of COI.	N = 212 Knee OA	Mean age: 65.8 years; 50 males, 162 females	Oral glucosamine sulfate: (n=106) received (1,500mg QD) vs. Placebo: (n=106) for knee OA in 3 year trial of disease progression	3 years	No average loss of joint-space width in patients receiving glucosamine sulfate (0.07mm, 95% CI, -0.17 to 0.32); placebo had significant mean and minimum joint-space narrowing (-0.31mm, 95% CI, -0.57 to -0.04). As assessed by WOMAC scores, symptoms worsened slightly in placebo vs. glucosamine sulfate (p = 0.016).	"The long-term effect of glucosamine sulfate was proved to benefit for both combined joint structure-modifying and symptom-modifying. No alteration in glycemic homeostasis was found."	High dropout rate (73/212 = 34%), although demographic data suggest a lack of bias. NSAIDs allowed during study.

Gruenwald 2009 (Score= 7.0)	Glucosamine	RCT	Sponsorship by Seven Seas LTD. No mention of COI.	N = 177 patients with moderate to severe hip or knee osteoarthritis.	Mean age 62.3 years: 65 males, 113 females	500 mg glucosamine sulfate 2 KCl; 444 mg fish oil; 200 mg omega-3-fatty acids; 120 µg vitamin A; 0.75 µg vitamin D; 1.5 mg vitamin E fatty acids (n = 90) vs glucosamine sulfate alone one capsule contained 500 mg glucosamine sulfate 2 KCl; 444 mg mixture of several oils [oils without EPA and DHA] containing palm oil [70%], rapeseed oil [15%], and sunflower oil [15%]; 120 µg vitamin A; 0.75 µg vitamin D; 1.5 mg vitamin E (n = 87) [DL α-tocopherol acetate])	13, and 26 weeks.	Minimal pain reduction of ≥20% the number of responders between groups (92.2% group A, 94.3% group B). At higher responder criterion (≥80% reduction in the WOMAC pain score) (group A 44%, group B 32%; P=0.044). OA symptoms (morning stiffness, pain in hips and knees) were reduced at end of the study: by 48.5%-55.6% group A and by 41.7%-55.3% in group B.	"This clinical trial has shown that both investigational products are highly efficacious and safe in the treatment of complaints of knee and hip OA. Both test products, glucosamine sulfate alone or in combination with omega-3 fatty acids, in the form of cod liver oil and fish oil, were well tolerated."	No placebo group. Data suggest comparable efficacy between groups, thus omega-3-fattyacids appear to have no additive value.

Rozendaal 2008 (score= 6.5)	Glucosamine	RCT	Sponsored by the Department of General Practice of the Erasmus Medical Center, Rotterdam, The Netherlands Stichting Anna Fonds, Leiden. No mention of COI.	N = 222 Hip OA	Mean age: 63.4 years; 68 males, 154 females	Oral glucosamine sulfate: (n=111) (750mg BID vs. Placebo (n=111) for hip osteoarthritis over 2 years	3, 12, 24 months	Change from baseline, WOMAC pain score for glucosamine sulfate (mean difference = -1.90 [SD, ± 1.6]) compared to placebo (mean difference = -0.30 [SD ± 1.6]). Joint space narrowing for glucosamine sulfate group (mean difference = -0.094 [SD ± 0.32]) compared to placebo (mean difference = -0.057 [SD ± 0.32]). Over 2 years daily therapy after adjusting for covariates, glucosamine sulfate no better than placebo in reducing WOMAC pain scores (mean difference = -1.54 [95% CI, -5.43 to 2.36]), or reducing WOMAC function scores (mean difference = -2.01 [95% CI, -5.38 to 1.36]). Joint space narrowing not significantly different between glucosamine sulfate and placebo (mean difference =-0.029 [95% CI, -0.122 to 0.064]).	"Glucosamine sulfate was no better than placebo in reducing symptoms and progression of hip osteoarthritis."	Data suggest non-statistically significant trends in symptoms and joint space narrowing in favor of glucosamine. Baseline disease was mild based on radiographic grading overall.
Müller-Fassbender 1994 (score= 6.5)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 199 Knee OA	Mean age: 54 years; 104 males, 95 females	Oral glucosamine sulfate: (n=100) 500mg. TID vs. Ibuprofen: (n=99) 400mg TID for 4 weeks treatment of knee osteoarthritis	4 weeks	Lequesne's index value progressively decreased in both groups, although no statistical significance was found between the groups. Ibuprofen treated patients experienced more prompt relief, mainly evident during first 2 weeks. GS exerted its main clinical effect from third week onward. GS group had significantly fewer adverse effects (p <0.001).	"This 200 patient comparative 4-week study demonstrated that oral glucosamine sulfate was as effective as ibuprofen (1200 mg/day) in controlling symptoms in patients with active OA of the knee. Conversely, glucosamine was better tolerated than ibuprofen."	Blinding and allocation unclear. No placebo control. No statistical difference in efficacy between OTC ibuprofen and GS in 4 week trial.

Yue 2011 (Score = 6.0)	Glucosamine	RCT	Sponsorship by Chinese National Science & Technology Pillar Program. No COI.	N= 251 Kashinbeck disease patient.	Mean age 51.88 years; 181 males, 70 females.	Chondroitin sulfate 600mg twice daily (n = 64) vs Glucosamine hydrochloride 480 three times a day. (n = 62) vs combination (n = 63) vs placebo (n = 62).	6 months	combination therapy of chondroitin sulfate and glucosamine hydrochloride reduced WOMAC pain by 20% (differences of 23.4%, P = 0.006) and 50% (differences of 15.7%, P = 0.016), WOMAC pain (P = 0.032), WOMAC stiffness (P = 0.043), and WOMAC total score (P = 0.035). Chondroitin sulfate used alone reduced WOMAC total score and stiffness score (P = 0.038 and P = 0.023, respectively). No positive effects in improving WOMAC Index scores observed with glucosamine hydrochloride alone.	"The findings of this study indicate that a combination of chondroitin sulfate and glucosamine hydrochloride was more effective than placebo in treating KBD."	Cluster randomized control trial. Data suggest continued chondroitin sulfate and glucosamine hydrochloride therapy reduced pain and joint stiffness in KBD patients.
Rindone 2000 (score= 6.0)	Glucosamine	RCT	No COI or sponsorship.	N = 98 Knee OA	Mean age: 63.5 years; 93 males, 5 females	Oral glucosamine sulfate: (n=49) (500mg TID) vs. Placebo (n=49) for knee OA over 2 months	2 months	No statistical difference between mean scores glucosamine and placebo while resting [mean (SD): 3.2 [2.5] glucosamine group vs. 3.4 [2.5] placebo, p = 0.81] or in mean scores walking [mean (SD): 4.9 [2.8] glucosamine vs. 4.9 [2.2] placebo, p = 0.90].	"Glucosamine was not better than placebo in reducing pain from osteoarthritis of the knee in this group of patients."	Study details are sparse.

Scroggie 2003 (score= 6.0)	Glucosamine	RCT	Sponsored by Surgeon General's Office of the US Air Force. No mention of COI.	N = 38 Type 2 diabetes mellitus	Mean age: 62.0 years; 18 males, 16 females	Glucosamine sulfate 1,500mg/chondroitin sulfate 1,200mg: (n=22) vs. Placebo: (n=12) for 90 days in patients with type 2 diabetes mellitus	90 days	HbA1c mean values changed very little in both treatment groups during the study. There were no significant differences between the baseline measures or between the groups. There were no changes in medical therapy in either group during the study period.	"This study demonstrated that oral glucosamine supplementation does not adversely affect glycemic control when administered to patients with type 2 diabetes mellitus at doses recommended by the manufacturer."	Study goal to assess glycemic control among diabetics prescribed GS/CS. Patients in placebo group had milder condition of diabetes. Allocation unclear.
Villacis 2006 (score= 5.5)	Glucosamine	Cross over Trial	Sponsored by Weider Nutrition Group and Technical Sourcing Inc. No mention of COI.	N = 15 Subjects with shrimp allergy and an ImmunoCAP class level of 2 or greater	Mean age: 26.7 years; 11 males, 4 females	Glucosamine hydrochloride 1,500mg chondroitin/ 1200mg using shell-fish derived vs. synthetic manufactured glucosamine in patients with confirmed shrimp/shell fish allergies. All patients received both treatments.	24 hours	Fifteen (15) subjects in crossover trial of one dose oral challenge with 24-hour follow-up. All subjects tolerated shell-derived glucosamine without incident or an immediate hypersensitivity response.	"Glucosamine supplements from specific manufacturers do not contain clinically relevant levels of shrimp allergen and therefore appear to pose no threat to shrimp-allergic individuals."	Small sample size. Randomization and allocation unclear. Results cannot be inferred to all manufacturers of shrimp/shell fish derived glucosamine.
Lopes Vaz 1982 (score= 5.0)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 40 Uni-lateral knee OA	Mean age: 57.8 years; 10 males, 28 females	Glucosamine sulfate: (n=18) received (1.5g) vs. Ibuprofen: (n=20) received (1.2g) daily over 8 weeks	1, 2 , 4, 8 weeks	Pain scores showed a significant decrease during both treatments. No significant differences were detected in the general symptoms which appeared during treatment. No significant variations were recorded in the hematological tests.	"The authors suggest that the best therapeutic results in osteoarthritis could possibly be obtained by giving glucosamine sulfate along with an anti-inflammatory agent during an initial period of about 2 weeks to ensure prompt reduction of pain and then to	Comparison is made with OTC strength ibuprofen. Allocation, baseline characteristics and blinding are unclear. There was no control for co-interventions.

									continue treatment for a further 6 to 10 weeks or longer with oral glucosamine sulfate."	
Vajaradul 1981 (score= 5.0)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 54 Gonarth-rosis	Mean age:52.6 years; 9 males, 45 females	Intra-articular injection of glucosamine sulfate: (n=28) (dose not reported) vs. saline Placebo: (=26) in affected knee	5 weeks	After 5 consecutive weeks of treatments, both treatments significantly improved pain scores, although pain reduction with glucosamine was greater (mean difference = 0.18, ±0.03; p <0.01) vs. placebo (mean difference = 0.69, ±0.18; p = 0.01).	"Glucosamine treatment provided a greater freedom from pain than that given by the mere injection of placebo into the joint. Moreover, glucosamine showed no resulting side effects."	Glucosamine group somewhat older. Details sparse, especially blinding.
Pujalte 1980 (score= 4.0)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 20 OA	Mean age: 61.7 years; 3 males, 17 females	Glucosamine sulfate: (n=10) (500mg TID) vs. Placebo: (n=10) for 6-8 weeks for non-specific OA	8 weeks	GS improved symptoms vs. placebo. Patients given glucosamine sulfate experienced earlier alleviation of symptoms compared with placebo. Glucosamine sulfate resulted in a significantly larger proportion of patients with lessening or disappearance of symptoms.	"Oral glucosamine sulfate treatment produced significant improvements in the symptoms of pain, joint tenderness and swelling, as well as in restriction of movement. Glucosamine sulfate is a drug of first choice for the basic treatment of patients with osteoarthritis."	Small sample size with a lack of study details. Study inclusion and exclusion criteria unclear. Body part (joint) being studied non-specific.

Drovanti 1980 (score= 4.0)	Glucosamine	RCT	No mention of sponsorship or COI.	N = 80 OA	Mean age: 60 years; 18 males, 62 females	Glucosamine sulfate: (n=40) received 500mg TID vs. Placebo: (n=40) received for 30 days for non-specific OA	30 days	Glucosamine sulfate demonstrated decrease in symptoms to a significantly larger extent in significantly shorter time than placebo. Patients treated with glucosamine sulfate had a 72% reduction (placebo 36%) during survey period. At end of treatment, significantly more patients treated with glucosamine sulfate experienced complete freedom from pain or restricted function.	"The positive effect of hospitalization on the symptoms of osteoarthritis may be significantly accelerated, and increased by a factor of almost two, with a simple oral treatment with glucosamine sulfate."	Lack of details. No control for co-interventions. Patients in hospital for unclear reasons. Multiple joint locations included (back, neck, generalized).
Norman 2010 (Score = 4.0)	Glucosamine	RCT	Sponsorship by grant to Dr. Heesch from the university of Queensland. No COI.	N = 36 low active participants with hip or knee OA	Mean age not stated. Age range 40-75; 11 male, 17 female	3-day walking group (n = 13) vs 5 day walking group (n = 15) Both groups walked 3000 step/day first 6 weeks then increased to 6000 step day 6 weeks. All participants took 750 mg each day.	Week 6, 12, 18, 24.	First 6 weeks of study (glucosamine supplementation only), physical activity levels, physical function, and total WOMAC scores improved ($P < 0.05$). (Week 6 - Week 24) improvement were seen in these outcomes ($P < 0.05$) No significant differences were found between walking groups.	"In people with hip or knee OA, walking a minimum of 3000 steps (~30 minutes), at least 3 days/ week, in combination with glucosamine sulphate, may reduce OA symptoms. A more robust study with a larger sample is needed to support these preliminary findings."	Small sample. Pilot study lower compliance in higher exercise group may have eliminated true differences if any.

Evidence for the Use of Chondroitin

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Uebelhart 2004 (score=10.0)	Chondroitin	RCT	Sponsored by a grant from IBSA, Lugano, Switzerland. No mention of COI	N = 110 Knee OA	Mean age: 63.5 years; 21 males, 89 females	Chondroitin sulfate 800mg QD (n=54) vs. placebo for two 3-month periods during 1 year (n=56)	3, 12 months	Chondroitin group improved vs. placebo at Months 9 and 12 ($p < 0.05$; $p < 0.01$). Pain intensity decreased 42% Month 9 and 12 in CS group vs. 25% in placebo ($p < 0.05$). Differences in VAS scores and physician and patient efficacy assessments favored CS at 6, 9, and 12 months ($p < 0.01$). CS treatment had a significant role upon variation of joint space surface area and mean joint space width ($p = 0.03$) but not on minimum joint space width vs. placebo.	"This study supports the evidence that oral CS of bovine origin and high pharmaceutical quality is a well-tolerated drug, which is effective in reducing pain and improving function in patients suffering from symptomatic knee osteoarthritis."	Dropout rate was 26% with no difference between the groups.
Clegg 2006 (score=9.5)	Chondroitin	RCT	Sponsored by a contract from the National Center for Complementary and Alternative Medicine and the National Institute of Arthritis and Musculoskeletal and Skin Diseaseases. COI Drs. Bingham, Brandt, Clegg, Hooper, and Schnitzer report having received consulting fees	N = 1,583 Knee OA	Mean age: 59 years; 568 males, 1015 females	Oral glucosamine hydrochloride (500mg TID)(n=317) vs. chondroitin sulfate (400mg TID) (n=318) vs. both glucosamine and chondroitin sulfate (n=317) vs. celecoxib 200mg QD (n=318) vs. placebo in treatment of knee osteoarthritis in 6-month trial (n=313)	24 weeks	Combined glucosamine and chondroitin sulfate was borderline vs. placebo in reducing WOMAC pain score 20% ($p = 0.09$). As compared with rate of response to placebo (60.1%), rate of response to combined treatment was 6.5% points higher ($p = 0.09$) and celecoxib response rate was 10.0% points higher ($p = 0.008$). For patients with moderate-to-severe pain at baseline, response rate significantly higher with combined therapy vs. placebo (79.2% vs. 54.3%, $p = 0.002$). OMERACT-OARSI	"Celecoxib was demonstrated to reduce pain effectively in the overall group of patients with osteoarthritis of the knee. The combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain."	Results showed combination glucosamine-chondroitin to have significantly better outcomes in subgroup of moderate-to-severe group (WOMAC pain score 301-400) in WOMAC pain reduction of 50% or more, WOMAC pain

			or having served on advisory boards for McNeil Consumer and Specialty Pharmaceuticals. Drs. Brandt, Moskowitz, Schnitzer, and Schumacher report having received consulting fees or having served on advisory boards for Pfizer. Dr. Brandt reports having equity interests in Pfizer. Drs. Moskowitz and Weisman report having received lecture fees from Pfizer; Dr. Brandt, lecture fees from McNeil Consumer and Specialty Pharmaceuticals; Drs. Bingham, Clegg, Hooper, Jackson, Molitor, Sawitzke, and Schnitzer, grant support from Pfizer; and Dr. Bingham, grant					response rates showed a similar result.		score change from baseline and WOMAC function score. Results with Celecoxib not significant in these categories. Study used non-conventional glucosamine preparation.

			support from McNeil Consumer and Specialty Pharmaceuticals. Dr. Brandt reports having received royalties from books related to osteoarthritis. Dr. Moskowitz reports having served as an expert consultant for Pfizer.							
Maziéres 2007 (score=9.0)	Chondroitin	RCT	Sponsored by the Pierre Fabre Company. COI BM was reimbursed by the Pierre Fabre Company for attending the Boston OARSI meeting. MZ and MH are employees of Pierre Fabre. PG was funded to perform the biochemical analyses.	N = 307 Knee OA	Mean age: 66 years; 167 males, 140 females	Chondroitin sulfate 500mg BID (n=153) vs. placebo for 24 weeks for knee osteoarthritis (n=154)	24 weeks	Decrease in pain was -26.2 (24.9) and -19.9 (23.5) mm and improved function was -2.4(3.4) (-25%) and -1.7 (3.3) (-17%) in chondroitin sulfate and placebo groups, respectively (0.029 and 0.109). OMERACT-OARSI responder rate was 68% in chondroitin sulfate and 56% in placebo group (p = 0.03). No significant difference observed for changes in biomarkers of inflammation.	"This study failed to show an efficacy of chondroitin sulfate on the two primary criteria considered together, although chondroitin sulfate was slightly more effective than placebo on pain, OMERACT-OARSI response rate, investigator's assessment and quality of life."	Baseline differences between groups on variable of stage of disease appear to be present 69% vs. 59% of chondroitin group rated as intermediate OA disease. No information on other percentage of groups.
Messier 2007 (score=8.5)	Chondroitin	RCT	Sponsored by a grant from Rexall Sundown, Inc. No mention of COI.	N = 89 Knee OA	Mean age: 72.0 years; 26	Glucosamine hydrochloride 1,500mg chondroitin sulfate/1,200mg QD (n=45) vs. placebo	12 months	Mean function did not vary significantly between groups at 6-month (p = 0.52) or 12-months (p = 0.50). However, mean WOMAC function	"Glucosamine hydrochloride/chondroitin sulfate group was not superior to the placebo group in function, pain, or	Allocation unclear with baseline differences in

					males, 63 females	for 6 months for knee OA (n=44). Both groups received exercise training and instruction.		combining both groups improved significantly over time (p = 0.005). There was no difference in pain measures, 6-minute walk distance, or knee strength at 6 or 12 months between the groups.	mobility after both phases of the intervention (pill only and pill plus exercise)."	function present.
Michel 2005 (score=8.0)	Chondroitin	RCT	No mention of sponsorship or COI.	N = 300 Knee OA	Mean age: 62.8 years; 146 males, 154 females	Oral chondroitin sulfate 800mg QD (n=150) vs. placebo for 2 years for knee OA (n=150).	2 years	Difference in joint space loss between the two groups was significant for the mean joint space width (0.14 +0.57 mm, p = 0.04) and for minimum joint space width (0.12 + 0.52 mm, p = 0.05) favoring the chondroitin sulfate group (no loss in chondroitin group). No difference in WOMAC pain or function scores.	"Chondroitin sulfate halted structural changes in osteoarthritis of the knee as assessed by radiographic follow-up over 2 years. There were no significant symptomatic effects in this study. The clinical relevance of the observed structural results has to be further evaluated."	Dropout was 26% at 2-years. Study population had relatively low pain severity scores to begin with, which may have contributed to lack of improvement of pain and function scores.
Scroggie 2003 (score=6.0)	Chondroitin	RCT	Sponsored by Surgeon General's Office of the US Air Force. No mention of COI.	N = 38 Type 2 diabetes mellitus	Mean age: 62.0 years; 18 males, 16 females	Glucosamine sulfate 1,500mg/chondroitin sulfate 1,200mg (n=26) vs. placebo for 90 days in patients with type 2 diabetes mellitus (n= 12)	90 days	HbA1c mean values changed very little in both treatment groups during the study. There were no significant differences between the baseline measures or between the groups. There were no changes in medical therapy in either group during the study period.	"This study demonstrated that oral glucosamine supplementation does not adversely affect glycemic control when administered to patients with type 2 diabetes mellitus at doses recommended by the manufacturer."	Study goal to assess glycemic control among diabetics prescribed GS/CS. Patients in placebo group had milder condition of diabetes. Allocation unclear.

Yue 2011 (Score = 6.0)	Chondroitin	RCT	Sponsorship by Chinese National Science & Technology Pillar Program. No COI.	(N= 251) Kashin beck disease patient.	Mean age 51.88 years; 181 males, 70 females.	Chondroitin sulfate 600mg twice daily (n = 64) vs Glucosamine hydrochloride 480 three times a day. (n = 62) vs combination (n = 63) vs placebo (n = 62).	6 months	combination therapy of chondroitin sulfate and glucosamine hydrochloride reduced WOMAC pain by 20% (differences of 23.4%, P = 0.006) and 50% (differences of 15.7%, P = 0.016), WOMAC pain (P = 0.032), WOMAC stiffness (P = 0.043), and WOMAC total score (P = 0.035). Chondroitin sulfate used alone reduced WOMAC total score and stiffness score (P = 0.038 and P = 0.023, respectively). No positive effects in improving WOMAC Index scores observed with glucosamine hydrochloride alone.	"The findings of this study indicate that a combination of chondroitin sulfate and glucosamine hydrochloride was more effective than placebo in treating KBD."	Cluster randomized control trial. Data suggest continued chondroitin sulfate and glucosamine hydrochloride therapy reduced pain and joint stiffness in KBD patients.
Villacis 2006 (score=5.5)	Chondroitin	Crossover Trial	Sponsored by Weider Nutrition Group and Technical Sourcing Inc. No mention of COI.	N = 15 Subjects with shrimp allergy and an ImmunoCAP class level of 2 or greater	Mean age: 26.7 years; 11 males, 4 females	Glucosamine hydrochloride 1,500mg chondroitin/ 1200mg using shell-fish derived vs. synthetic manufactured glucosamine in patients with confirmed shrimp/shell fish allergies	24 hours	Fifteen (15) subjects in crossover trial of one dose oral challenge with 24-hour follow-up. All subjects tolerated shell-derived glucosamine without incident or an immediate hypersensitivity response.	"Glucosamine supplements from specific manufacturers do not contain clinically relevant levels of shrimp allergen and therefore appear to pose no threat to shrimp-allergic individuals."	Small sample size. Randomization and allocation unclear. Results cannot be inferred to all manufacturers of shrimp/shell fish derived glucosamine.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Usha 2004 (score=9.0)	Glucosamine vs. Placebo	RCT	No mention of Sponsorship. No COI.	N = 118 OA	Mean age: 51.2 years; 42 males, 76 females.	Group 1: Oral glucosamine (Glu) 500mg TID (N=30) vs. Group 2: methyl-sulfonylmethane (MSM) 500mg TID (N=30) vs. Group 3: both Glu and MSM (N=30) vs. placebo (N=28)	Baseline, 2, 4, 8, and 12 weeks.	Placebo showed insignificant change in mean pain index (mean difference = 1.57 [SD, ± 0.5]) to (mean difference = 1.16 [SD, ± 0.76]). Glu showed significant decrease in mean pain index (mean difference = 1.74 [SD, ± 0.47]) to (mean difference = 0.65 [SD, ± 0.71]; p <0.001). MSM significantly decreased mean pain index from (mean difference = 1.53 [SD, ± 0.51]) to (mean difference = 0.74 [SD, ± 0.65]) and combination treatment highly significant decrease in mean pain index (mean difference = 1.7 [SD, ± 0.47]) to (mean difference = 0.36 [SD, ± 0.33]; p <0.001).	"The therapy with Glu, MSM and their combination produced an analgesic, anti-inflammatory effect in patients with osteoarthritis. Combination therapy showed better efficacy in reducing pain, swelling and improving the functional ability of joints over individual therapy. All the treatments were well tolerated."	Unclear whether study medication was Glu sulfate or Glu hydrochloride. Combination of Glucosamine and MSM appears superior.

								After 12 weeks, mean swelling index significantly decreased with Glu and MSM, while decrease in swelling index with combination therapy greater (mean difference = 1.43 [SD, ± 0.63]) to (mean difference = 0.14 [SD, ± 0.35]; p <0.05).		
Pagonis 2014 (score=5.0)	Methylsulfonylmethane (MSM) vs. placebo	RCT	No COI. No mention of sponsorship.	N=100 patients with Hip and Knee OA	Mean age 60.9 years; 46 male, 54 female.	Group 1: patients received daily dosage of 6 g MSM (N=50) vs Group 2: patients received placebo pills (N=50)	Baseline, 26 weeks.	Group 1 vs Group 2, WOMAC score change (26 weeks-baseline) for pain, stiffness, physical function, (Mean): -21.1 vs -3.9 (p<0.05), -21 vs -1.9 (p<0.05), -24.7 vs -0.6 (p<0.05). Group 1 vs Group 2, Patient GA, and Physician GA change (26 week-baseline) (0-4 Likert scale): -15.7 vs -2.8 (p<0.05) and -0.8 vs -0.2 (p<0.05). Group 1 vs Group 2, SF 36 Quality of life total score mean at 26 weeks: 31±21 vs 62±40 (p<0.05).	"Our results support anecdotal reports that intervention with MSM on elderly people suffering from OA is beneficial. A treatment approach based on current literature is to start off at 3 g/day, then to increase up to 6 g/day in two divided doses. Although large, long-term dose response studies are necessary, MSM should be considered in certain OA patient populations."	

Evidence for the Use of Complementary or Alternative Treatments or Dietary Supplements

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: completementary treatments, alternative treatments, homeopathic treatments, dietary supplements, vitamins, spiritual therapy, aromatherapy, neural therapy, craniosacral therapy; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 23 articles in PubMed, 22 in Scopus, 30 in CINAHL, 153 in Cochrane Library, 898 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 2 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 5 articles considered for inclusion, 3 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Beigert C, 2004 Score: score=8.0(OA) Score=6.5 (RA)	Complementary or Alternative Treatments or Dietary Supplements	Double blind RCT	No COI, sponsored by Tubingen University and Robugen GmbH	N = 127	Mean age: 62.16; 53 males, 74 females.	Group treated with willow bark extract (N = 43) vs treated with diclofenac (N = 43) vs placebo treatment (N=41)	Conducted at end of 6-week treatment period	WOMAC pain scores improved nearly across the entire board. Willow bark extract was not statistically significant: –2.8 mm; 95% CI –12.1 to 6.4 mm; p = 0.55, ANCOVA. Score between diclofenac and placebo was significant: –18.0 mm; 95% CI –27.2 to –8.8 mm; p = 0.0002, ANCOVA.	"The OA study suggested that the willow bark extract showed no relevant efficacy in patients with OA. Similarly, the RA trial did not indicate efficacy of this extract in patients with RA."	Placebo controlled data suggest lack of efficacy in both OA and RA.
Stebbings S 2015 (score=6.5)	Complementary or Alternative Treatments or Dietary Supplements	Small Sample (pilot study)	No COI for Dr. Stebbings or Dr. McNamara. Sponsored by Promisia Ltd., the manufacturer of the extract of Artemisia used in the study. S Hunt and E Beattie are employees of Promisia Ltd. Dr Hunt had input into the manuscript. Ms Beattie performed all statistical analysis and randomization.	N = 42	Mean age: 62.9; 22 males, 20 females	Treated with different doses of plant extract Artemisia annua (ART). ART low dose (n=14) vs ART high dose (n=14) vs Placebo (n=14).	Follow-up conducted at 6, 12 week marks of treatment.	Mean VAS pain score was statistically significantly reduced from baseline to 12 weeks in the ART low-dose group (mean change, −21.4mm; SD, 23.48 mm; p=0.0082). There were no statistically significant changes from baseline to 12 weeks in the ART high-dose group (mean change, −11.5mm; SD, 28.97mm; p=0.1757) or in the placebo (mean change, −6.7 mm; SD, 29.66 mm; p=0.3670) for VAS pain score.	"To summarize, in this randomized controlled trial, ART at a dose of 15o mg BD appeared to be safe and well tolerated. Treatment with ART was associated with a clinically relevant reduction in pain, stiffness, and functional limitation over a 12-week period in patients with an established diagnosis of hip or knee OA."	Data suggest Artmeisia annua may be associated with pain reduction at 12 weeks.
Maheu E 2012 (score=5.5)	Complementary or Alternative Treatments or Dietary Supplements	RCT	No COI, sponsored by Labratoires Expanscience, France.	N=345	Mean age: 62.2; 158 males, 187 females	Hip OA patients treated with Avocado-soybean unsponifiable-Expanscience (ASU-E). ASU-E treated (n=166) vs Placebo (n=179)	Follow-up conducted at end of 3-year treatment	There was no significant difference on mean JSW loss (−0.638 mm vs −0.672 mm, p=0.72, in the ASU-E and placebo groups, respectively) but there were 20% less "progressors" in the ASU-E than in the placebo group (40% vs 50%, respectively, p=0.040). No difference was observed on clinical outcomes	"3 year treatment with ASU- reduces the percentage of JSW progressors, indicating a potential structure modifying effect in hip OA to be confirmed, and the clinical relevance requires further assessment."	Significant dropout at 3 years. Data suggest 3-year treatment with Piascledine potentially may modify

										structure in hip OA.

Evidence for the Use of Herbal Preparations

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: diacerein, Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthritis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 26 articles in PubMed, 19 in Scopus, 2 in CINAHL, 19 in Cochrane Library, 541 in Google Scholar, and 10 from other sources. We considered for inclusion 2 from PubMed, 0 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 10 from other sources. Of the 17 articles considered for inclusion, 10 randomized trials and 7 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: herbal preparations, plant preparations, willow bark, Salix, ginger extract, rose hips, camphora molmol, maleluca alternifolia, angelica sinensis, aloe vera, thymus officinalis, menthe peperita, arnica montana, curcuma longa, tancaetum parthenium, zingiber officinicalis, avocado soybean unsaponifiables, oral enzymes, topical copper salicylate, S-Adenosylmethionine, diacerein harpagoside; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 22 articles in PubMed, 40 in Scopus, 0 in CINAHL, 4 in Cochrane Library, 456 in Google Scholar, and 18 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 4 from Google Scholar, and 18 from other sources. Of the 26 articles considered for inclusion, 19 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Maheu 1998 (score= 9.5)	Herbal Preparations	RCT	Sponsored by Pharmascience Laboratories, Courbevoie, France. No mention of COI.	N = 164 Knee or hip OA	Mean age: 64.1± 7.5 years; 46 males, 118 females	Avocado/Soy bean Unsaponifiables (ASU) 300mg daily for 6 months (n=85) vs. placebo for symptomatic efficacy (n=79)	2 months, 6 months	Significantly greater improvement in all outcome measures (Lequesne's Functional Index p <0.01, Pain on VAS p = 0.02, Functional disability p <0.001) in ASU group compared with placebo at 6 months.	"ASU treatment showed significant symptomatic efficacy over placebo in the treatment of OA, acting from month 2 and showing a persistent effect after the end of treatment."	The study does not have demonstrated changes in outcomes measures such as RTW.
Shackel 1997 (score= 9.5)	Herbal Preparations	RCT	Sponsored by F.H. Faulding & Co. Pty. Limited. No COI.	N = 116 Hip and/ or knee OA	Mean age: 60.7 years; 52 males, 64 females	Topical copper-salicylate gel (n=58) vs. placebo gel 1.5g to the forearm BID for 4 weeks (n=58)	28 days	Pain scores: (baseline/Week 4): CS 34.8±29.3/28.4±25.4 vs. placebo 30.5±29.7/24.9± 25.8, p = 0.94. Other out-comes NS. Number requiring paracetamol for adjunctive analgesia: 77% copper-salicylate, 71% for placebo. More skin rashes observed in C-S group (83%) vs. placebo (52%) (p = 0.002).	"Copper-salicylate gel applied to the forearm was no better than placebo gel as pain relief for patients with osteoarthritis of the hip or knee, but produced significantly more skin rashes."	Data suggest lack of efficacy of copper-salicylate gel applied on the forearm for hip/knee OA.
Najm 2004 (score= 9.0)	Herbal Preparations	Crossover Trial	Sponsored by Susan Samueli Center of Integrative Medicine (UCI). No COI.	N = 61 Knee OA	Mean age: 52.9 years; 17 males, 40 females	SAMe 600mg BID (n=28) vs. celecoxib 100mg BID for 8 weeks each (n=29) Double dummy.	4 months	Celecoxib superior for pain relief in first month (p = 0.024). During 2nd month, no differences in pain. Total COOP score: baseline 48.7±8.7 vs. SAMe 39.9±9.3 vs. celecoxib 39.8±11.3. SF-36 scores did not differ.	"SAMe has a slower onset of action but is as effective as celecoxib in the management of symptoms of knee osteoarthritis. Longer studies are needed to evaluate the long-term effectiveness of SAMe and the optimal dose to be used."	No placebo comparison. Data suggest SAMe is equally effective, although celecoxib 100mg BID has faster onset of pain.

Blotman 1997 (score= 9.0blit)	Herbal Preparations	RCT	Sponsored by Pharmascience. No mention of COI.	N = 164 Primary femoro-tibial or hip OA	Mean age: 64.1±7.5 years; 55 males, 108 females	Avocado/soybean unsaponifiables (ASU) 300mg daily for 3 months (n=80) vs. placebo for symptomatic efficacy (n=83)	3 months	Mean cumulative dose of NSAID used between Day 45 and 90 significantly lower in ASU group reflecting smaller proportion of patients in group who resumed NSAID use. For patients with hip osteoarthritis who went back on NSAID, cumulative dose, time spent back on drug significantly lower in ASU. No difference in knee OA. Algofunctional index score fell in both groups, but significantly larger in ASU group vs. placebo, p <0.01. No difference in VAS scores.	"Over 6 weeks, ASU reduced the need for NSAID in patients with lower limb OA. Further studies are needed to evaluate the duration of the persistence of this effect and its impact on patient care and on treatment costs."	Phase III trial. Unclear if this is preliminary report of same study (Maheu).
Winther 2005 (score= 9.0)	Herbal Preparations	Crossover Trial	No mention of sponsorship or COI.	N = 94 Knee or hip OA	Mean age: 65.6 years; 40 males, 54 females	Rose-hip powder 5g a day (n=47) vs. placebo for 3 weeks (n=47)	3 months	WOMAC pain scores (baseline/3 weeks/3 months): rose hips (33.7±19.4/29.4± 18.3/32.8±20.6) vs. placebo (33.7±19.4/35.3±21.5/35.6± 20.4), p = 0.014 at 3 weeks and p = 0.125 at 3 months. Stiffness, ALD and PGAD all statistically negative at 3 weeks.	"[T]he present herbal remedy can alleviate symptoms of osteoarthritis and reduce the consumption of 'rescue mediation.'"	Data are mixed with some outcomes positive and some not different. Crossover RCT. Data suggest Rosa canina may reduce pain and reliance on rescue meds.
Lequesne 2002 (score= 9.0)	Herbal Preparations	RCT	Sponsored by Pharmascience Laboratories, Courbevoie, France. No mention of COI.	N = 163 Hip OA	Mean age: 63.2±8.7 years; 102 males, 61 females	Avocado/soybean unsaponifiables (ASU) 300mg daily for 2 years (n=85) vs. placebo for joint space narrowing (n=78)	12 months	At 2-year follow-up, mean joint space width in ASU and placebo groups was 1.87±1.0mm and 1.90±1.33 (p = 0.90). However, in a subgroup of patients with initially more severe narrowing, joint space loss between initial and final radiograph in ASU group was half that in placebo group (-0.43±0.51mm vs. -0.86±0.62mm, p <0.01). No	"The clinical results concerning symptoms in this study were surprising. No difference on clinical parameters was observed between ASU and placebo groups, which contrasts with previous results significantly favoring ASU over placebo. ASU seemed to statistically significantly reduce progression of the narrowing of the joint space in a post-	High withdrawal rate over 2-year period (41%), although ITT and per-protocol analyses were similar.

								differences in regard to symptomatic effects in each of subpopulations, and NSAID use similar in both groups.	hoc analysis in the subpopulation of more severely affected patients, compared with those receiving placebo."	
Dougados 2001 (score= 9.0)	Diacerein vs. Placebo	RCT	Sponsored by grant from Negma Ltd. No mention of COI.	N = 507 Hip OA	Mean age: 62.6 years; 203 males, 304 females	Diacerein: (n=262) received 50mg twice daily vs. Placebo: (n=259) for 3-years	3 years	Radiographic progression of at least 0.5mm during study lower and occurred later in diacerein group vs. placebo. Cumulative radiographic progression rates of 0.5mm: 29.2% diacerein vs. 35.7% placebo at end of 1st year, and 42.5% diacerein vs. 50.2% with placebo at end of second year. No difference observed in use of analgesics and NSAIDs.	"This study confirms previous clinical findings indicating that the demonstration of a structure-modifying effect in hip OA is feasible, and shows, for the first time, that treatment with diacerein for 3 years has a significant structure-modifying effect as compared with placebo, coupled with a good safety profile."	Large sample size. Study suggests small benefit in delayed radiographic progression.
Rein 2004 (score= 8.5)	Herbal Preparations	Crossover Trial	Sponsored by Hyben Vital International, Langeland, Denmark. No mention of COI.	N = 112 OA in hip, knee, hand, shoulder, neck	Mean age: 68.1 years; 41 males, 71 females	Rose-hip powder 5g a day (n=50) vs. placebo for 3 months each treatment arm (n=47)	3 months	Pain reduction in placebo first group: 1.02±1.45 vs. 1.91±1.43, p = 0.008. Among those given rose hip first, pain reduction 1.45±1.28 vs. 1.72±1.37, p = 0.61. Consumption of rescue medication showed similar effects.	"Hyben Vital reduces the symptoms osteoarthritis. We interpret the marked differences in the response of the two groups as indicating a strong "carryover" effect of Hyben Vital."	Dropout rate high. Assumes lack of pain rebound in group given active medication first is due to carry forward effect of prior active treatment. No data to show wearing off over time.

Schmid 2001 (score= 8.0)	Herbal Preparations	RCT	Sponsored by grant from Alfried Krupp von Bohlen und Halbach Foundation and contribution by R.L. was sponsored b Karl und Veronica Carstens Foundation. No mention of COI.	N = 86 Hip or knee OA	Mean age: 53 years; 59 males, 19 females.	Willow bark extract (240mg salicin a day) (n=39) vs. placebo for 2 weeks (n=39)	2 weeks, 8 weeks	WOMAC pain indices (baseline/Day 14): willow bark 34.1±19.3/ 29.3) vs. placebo (44.1±26.5/45.1), p = 0.047. Patient assessments differed between the 2 groups (p = 0.0002) as did physicians (p = 0.0073).	"[W]illow bark extract showed a moderate analgesic effect in osteoarthritis and appeared to be well tolerated."	Pain scores somewhat worse in placebo at baseline, suggesting trial favored active treatment. Data suggest willow bark superior to placebo.
Glorioso 1985 (score= 7.5)	Herbal Preparations	RCT	No mention of sponsorship or COI.	N = 150 Hip or knee OA	Mean age : 57.6 years; 60 males, 90 females.	SAMe 400mg (n=75) vs. ibuprofen 400mg TID for 30 days (n=75)	30 days	"Pain pool" average symptoms: SAMe (10.32 ±2.8) vs. ibuprofen (10.29 ±2.9), NS. Rigidity in minutes: SAMe (19.45± 14.8 vs. ibuprofen 17.85± 15.20, NS). Patient and physician assessments not different between groups. Patient judgment (much better and better combined): SAMe (44/58.7%) vs. ibuprofen (40/75 = 53.3%), NS.	"The reported data confirmed that SAMe is effective in the treatment of symptoms of degenerative joint decreases; moreover SAMe exhibited a slightly more marked activity than the reference drug in particular."	No placebo control. Comparison to OTC dosage of ibuprofen with similar efficacy.

Lechner M 2011 (score= 7.5)	Herbal Preparations	RCT	No COI or mention of sponsorship	N=102 Hip and Knee OA	Age: 59.3 39 males, 66 females	Verum Group: (n=52) received individual herbal medication (n=52) vs Control Group: (n=50) received placebo (n=50)	At baseline, 20 weeks	Between the two groups there was little difference (p=0.783) , and no significant difference in functionality from SF-36 test.	"While the individual prescription consisting of medicinal herbs according to TCM diagnosis investigated in this trial tend to improve the osteoarthritis, the same effect was also achieved with the nonspecific prescription."	Compliance with treatments were variable. Data is inconclusive.
Bliddal 2000 (score= 7.5)	Herbal Preparations	RCT	Sponsored by Erovita A/S. No mention of COI.	N = 75 Hip or knee OA	Mean age: 66 years; 15 males, 41 females.	Ginger extract 170mg EV.ext-33 TID vs. ibuprofen 400mg TID vs. placebo TID. Double dummy.	3 weeks	Ranking of efficacy of 3 treatments: ibuprofen, ginger extract, placebo found for VAS (Friedman test: 24.65, p <0.00001) and Lequesne-index (p <0.00005). In crossover study, no difference between placebo and ginger extract. Explorative tests of differences for 1st treatment period showed better effect of ibuprofen and ginger extract than placebo (p <0.05).	"[A] statistically significant effect of ginger extract could only be demonstrated by explorative statistical methods in the first period of treatment before cross-over, while a significant difference was not observed in the study as a whole."	Ginger in the studied dosage not shown to provide relief. Comparative arm is OTC ibuprofen dose. OTC ibuprofen dose superior to other 2 arms.
Akhtar 2004 (score= 7.5)	Herbal Preparations	RCT	No mention of sponsorship or COI.	N = 96 Knee OA	Mean age: 56.6 years; 28 males, 70 females	Enteric-coated Phlogenzym® (bromelain 90mg, trypsin 48mg and rutosid 100mg) TID (n= 46) vs. diclofenac 50mg BID (n=52). Double dummy.	6 weeks	Lequesne's Algofunctional Index improved in 6 weeks among ERC 13.0 to 9.4 (26.3%) vs. DC from 12.5 to 9.4 (23.6%) (non-inferiority demonstrated). Index of severity/complaint indices did not differ, improved for each arm compared with baseline. Adverse events did not differ (27.5% v. 23.1%).	"ERC can be considered as an effective and safe alternative to NSAIDs such as diclofenac in the treatment of painful episodes of OA of the knee. Placebo-controlled studies are now needed to confirm these results."	Results suggest Phlogenzym equivalent to diclofenac.

Wigler 2003 (score= 7.0)	Herbal Preparations	Crossover Trial	Sponsored by Dalidar Pharma Israel. No mention of COI.	N = 29 Knee OA	Mean age: 61.9 years; 6 males, 23 females.	Zintona EC (n=14) vs. placebo QID for 3 months each treatment (n=15)	3 months, 6 months	Mean VAS on movement scores (baseline/post): ginger (76.1/41.0) vs. placebo (76.9/50.0), NS. Handicap scores also reduced both groups, but NS between groups. Reduction in knee circumference favored ginger (p = 0.15).	"Zintona EC was as effective as placebo during the first 3 months of the study, but at the end of 6 months, 3 months after crossover, the ginger extract group showed a significant superiority over the placebo group."	Data mostly negative for efficacy of ginger compared with placebo. Some data suggest some efficacy.
Altman 2001 (score= 6.5)	Herbal Preparations	RCT	Sponsored by GrängeMatic Ltd, Dublin, Ireland. No mention of COI.	N = 247 Knee OA	Mean age: 65.1 years; 95 males, 152 females	Ginger extract (255mg EV.EXT 77 extracted from 2.5-4.0gm dried ginger rhizomes plus 0.5-1.5gm dried galanga rhizomes) (n= 124) vs. placebo for 6 weeks (n= 123)	6 weeks	Pain after walking 50 feet (baseline/post): ginger (49.9 ±24.3/34.6±29.5) vs. placebo (53.1±25.1/44.2 ±28.3), p = 0.016. WOMAC pain favored treatment (p = 0.11) as did function (p = 0.13), while stiffness statistically positive (p = 0.018). More reductions in knee pain on standing with ginger (63%) vs. placebo 50%, p = 0.048.	"A highly purified and standardized ginger extract had a statistically significant effect on reducing symptoms of OA of the knee. This effect was moderate"	Somewhat greater advanced disease in ginger group at baseline (7.3% vs. 4.1% Stage 4) favors placebo. Adequacy of blinding unclear as placebo had coconut oil. Data suggest modest reduction in symptoms.
Klein 2006 (score= 6.5)	Herbal Preparations	RCT	No mention of sponsorship or COI.	N = 90 Hip OA	Mean age: 52.2 years; 59 males, 31 females	Enteric-coated Phlogenzym® 2 TID (n=45) vs. EC diclofenac 50mg BID. (n=45)Double dummy.	3 weeks, 6 weeks	Phlogenzym not inferior using multiple measures including pain, joint stiffness, physical function, and Lequesne's index.	"This study showed significant non-inferiority from 6 weeks treatment with PE in patients with OA…there was no real difference between PE and DC 100mg per day, implying an equal benefit-risk relation."	Study suggests comparable efficacy between phlogenzym and diclofenac.

Singer 2001 (score= 6.0)	Herbal Preparations	RCT	No mention of sponsorship or COI.	N = 63 Knee OA	No mention of age or sex.	Enteric-coated Phlogenzym® 6 per day (n=31) vs. Diclofenac 50mg TID for 1 week then BID for 3-week treatment. (n=32) Double dummy.	7 weeks	Lequesne indices improved in 93.6% of enzyme group vs. 87.5% diclofenac. Sum of Lequesne indices over 14 days: enzyme 12.27 vs. diclofenac 10.79 (NS). At Day 49, enzymes 9.81 vs. 12.77 (p = 0.0165). Pain on movement scores did not differ over active treatment, but favored enzyme group at Day 49, 28 days after 3-week treatment stopped.	"[S]hort-term evaluation indicates that Phlogenzym® as an oral enzyme formulation can be considered as an effective and safe alternative to non-steroidal anti-inflammatory drugs such as diclofenac in the treatment of active osteoarthritis of the knee."	Some details sparse. Data suggest comparable efficacy between Phlogenzym and diclofenac.
Vetter 1987 (score= 4.5)	Herbal Preparations	RCT	No mention of COI or sponsorship.	N = 36 OA knee, hip or spine	Mean age: 64.5 years; 15 males, 21 females.	S-Adenosylmethionine 400mg TID (n=18) vs. indomethacin 50mg TID for 4 weeks. (n=18)	28 days	Global clinical scores (baseline/post-treatment): SAMe (12.6/8.2) vs. indomethacin (11.1/5.9). Scores mostly improved for each diagnostic group: knee (p <0.02), hip (SAMe p = 0.043 vs. indomethacin p = 0.11) and spine (SAMe p = 0.11 vs. indomethacin p = 0.043).	"SAMe in the treatment of osteoarthritis does not seem to differ from that of indomethacin, but its tolerability appears to be better compared with that of indomethacin."	No placebo group. Small sample size and likely underpowered. Suggests SAMe may be effective in reducing symptoms.

Müller-Fassbender 1987 (score= 4.0)	Herbal Preparations	RCT	No mention of COI or sponsorship.	N = 36 OA of hip, knee or spine	Mean age: 54 years; 30 males, 6 females	S-Adenosylmethionine 400mg TID (n=18) vs. ibuprofen 400mg TID for 4 weeks. (n=18)	4 weeks	Global clinical scores (baseline/post treatment): SAMe (31.7/17.6) vs. ibuprofen (35.6/16.6). Scores also improved for knee, hip and spine with both treatments (p <0.01). Reductions in scores trended towards favoring ibuprofen.	"Both treatments were well tolerated and no patient from either group withdrew from the study."	Submaximal ibuprofen dose bias favors SAMe; no placebo. Small sample with study likely underpowered for detecting differences. Suggests SAMe equivalent to low dose ibuprofen.
Haghighi 2005 (score= 4.0)	Herbal Preparations	RCT	No mention of sponsorship or COI.	N = 120 Hip or knee OA	Mean age: 58.5 years; 89 males, 31 females.	Ginger extract 30mg BID (n=40) vs. ibuprofen 400mg TID (n=40) vs. placebo for 1 month (n= 40)	1 month	VAS pain (baseline/1 month): ginger (71.7±3.5/30±3.7) vs. ibuprofen (71.2±2.4/28±3.4) vs. placebo (64.2±2.8/ 56.5±3.6) (p <0.0001 but NS comparing ginger vs. OTC ibuprofen).	"Ginger extract and ibuprofen were significantly more effective than the placebo in the symptomatic treatment of OA, while there was no significant difference between the ginger extract and ibuprofen groups in a test for multiple comparison."	Methodological issues including blinding not well described. Baseline data demonstrate statistically significant differences in disease severity measures yet appear to represent these as "P>0.05." If methodological issues overcome, data suggest comparable efficacy between ginger and OTC ibuprofen and superiority to placebo.

Evidence for the Use of Diacerein

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Dougados 2001 (score=9.0)	Diacerein	RCT	Sponsored in part by a grant from Negma Ltd. No mention of COI.	N = 507 Hip OA	Mean age: 62.6 years; 203 males, 304 females.	Diacerein 50mg twice daily (n=255) vs. placebo (n=252)	Baseline, 6 months, 1, 2, and 3 years.	Radiographic progression of at least 0.5mm during study lower and occurred later in diacerein group vs. placebo. Cumulative radiographic progression rates of 0.5mm: 29.2% diacerein vs. 35.7% placebo at end of 1st year, and 42.5% diacerein vs. 50.2% with placebo at end of second year. No difference observed in use of analgesics and NSAIDs.	"This study confirms previous clinical findings indicating that the demonstration of a structure-modifying effect in hip OA is feasible, and shows, for the first time, that treatment with diacerein for 3 years has a significant structure-modifying effect as compared with placebo, coupled with a good safety profile."	Large sample size. Study suggests small benefit in delayed radiographic progression.
Pavelka 2007 (score=9.0)	Diacerein	RCT	Sponsored by a grant from TRB Chemedica International SA and Glynn Brother Chemicals AG. Sponsors reviewed and agreed with the contents of the manuscript before publication.	N = 168 Knee OA	Mean age 63.8±8.2; 34 males, 134 females.	50mg diacerein BID (n=82) vs. placebo (n=83)	Baseline, month 1, 2, 3, 4, 5, and 6.	WOMAC A scores (baseline/ Month 5): diacerein (261±87.3/ 144±105.7) vs. placebo (239± 80.2/191±108.3), p <0.0001. Total WOMAC scores p <0.0001. Acetaminophen consumption favored diacerein (1.0±1.11 vs. 1.5±1.34), p = 0.0018.	"[T]he findings of this study indicate that diacerein is an effective treatment for symptomatic knee OA. In addition, it has long carryover effect and an acceptable safety profile."	Allocation method unclear. Results suggest mild benefit of diacerein.
Lingetti 1982 (score=8.5)	Diacerein	RCT	No mention of sponsorship or COI.	N = 20 Hip or knee OA	Mean age 63.6; 9 males, 11 females.	Placebo x 2 weeks, diacerein 25mg BID x 4 weeks x 50mg BID for 8 weeks	Baseline, 2 4, and 8 weeks.	Total score (includes pain) baseline 9.25±1.17, 9.15±1.69 after placebo, 5.50±2.42, diacerein 50mg a day, and 1.90±1.77. Diacerein 100mg a day (p <0.001 for diacerein vs. placebo). Walking speed	"The results obtained confirm the therapeutic value of diacetylrhein in the treatment of osteoarthrosis of the hip and knee."	Crossover trial with small sample size. Unclear if treatment sequence completely randomized and blinded.

								significantly decreased on diacerein.		Comparisons with no/low dose intervals.
Leblan 2000 (score=8.5)	Diacerein	RCT	No mention of sponsorship or COI.	N = 122 Hip and knee OA	Mean age:61.7 years; 45 males, 77 females.	Group 1: Diacerein 50mg BID (n=60) vs. Group 2: harpagophytum (2,610mg a day) for 4 months.(n= 62) Double dummy.	Baseline, day 30, 60, and 120.	Mean pain score reductions on Day 20: harpagophytum – 30.6±3.3 vs. diacerein – 25.5±3.6. Cumulative doses of NSAID used at Day 20: harpagophytum 20.9 vs. diacerein 55.15, p <0.05.	"Harpagophytum was at least as effective as a reference drug (diacerhein) in the treatment of knee or hip osteoarthritis and reduced the need for analgesic and nonsteroidal anti-inflammatory therapy."	Data suggest harpagophytum at least as effective as diacerein and more effective by some measures. Adverse effects of diacerein appear greater.
Pham 2004 (score=8.5)	Diacerein	RCT	No mention of sponsorship or COI.	N = 301 Medial knee OA	Mean age: 64.8 years; 124 males, 177 females.	Group 1: Three courses of 3 intra-articular (IA) injections of 2.5mL hyaluronic acid (HA) +oral placebo vs (n=131) Group 2: IA injections of saline solution + diacerein 50mg BID (n=85) vs. Group 3: IA injections of saline solution + oral placebo, 1 year (n= 85)	Baseline, weeks 1,2,and 6, and Months 4, 6, 8, 10, 12.	VAS pain ratings: injections - 33.5±28.5 vs. diacerein - 33.9±25.7 vs. placebo - 34.5±27.4, p = 0.96. Patient's global assessments: -29.7±26.9 vs. -32.8±24.0 vs. -31.1±42.7, p = 0.82. Percentage patients' very good or good responses: 72% v. 65% v. 76%. No differences in adverse effects (p = 0.76)	"A weak but statistically significant structural deterioration occurred over 1 year, together with clinically relevant symptomatic improvement in patients receiving oral drug and iterative IA injections. Symptomatic and/or structural effects for both this new HA compound and diacerein were not demonstrated."	Study suggests no clear benefit of any treatment arm.
Chantre 2000 (score=8.0)	Diacerein	RCT	No mention of sponsorship or COI.	N = 122 Hip and knee OA	Mean age: 61.7 years; 45 males, 77 females.	Group 1: Diacerein 50mg BID (n=60) vs. Group 2: Harpadol (6 capsules a day, each containing 435mg of powder Harpagophytum procumbens) for 4 months (n=62). Double dummy.	Baseline, weeks 4, 8 and 16.	VAS pain scores (baseline/16 weeks): harpagophytum (63.6±13.2/31.3±22.9) vs. diacerein (61.6±11.1/35.8±22.8), p = 0.34. Lequesne functional indices were not different (p = 0.71). Diclofenac rescue tablets consumed at week 12 favored harpagophytum (20.9 vs. 55.51), p = 0.01.	"The results confirm that the two drugs are equally effective in the treatment of osteoarthritis of the knee or the hip. Improvements in all efficacy parameters were observed within each treatment group but there was no significant difference in the therapeutic response between the 2 groups for any efficacy parameters."	No placebo comparison group. Suggests harpagophytum at least comparable to diacerein, if not superior based on NSAIDs consumed.
Nguyen 1994	Diacerein	RCT	Sponsored by Negma	N = 288 Hip OA	Mean Age: 62.5	Group 1: diacerein placebo + tenoxicam	Baseline, 2, 4, 6,	Patient overall assessments rated good or very good:	"Both tenoxicam and diacerein appear to be	Allocation method unclear. Results

(score=7.5)			Pharma, Ltd. No mention of COI.		years; 124 Males, 164 Females.	placebo (n=71) vs. Group 2: tenoxicam 20mg and diacerein placebo (n=75) vs. Group 3: diacerein 50mg BID and tenoxicam placebo (n=75) vs. Group 4: diacerein 50mg BID and tenoxicam 20mg (n=67)	and 8 weeks.	placebo (41%) vs. tenoxicam (61%) vs. diacerein (49%) vs. combination (66%). Functional Lequesne impairment index ratings (8.4±4.1 vs. 6.9±4.6 vs. 7.7±4.6 vs. 6.3±3.8). Number needing analgesic rescue lower in tenoxicam than diacerein group. Tenoxicam began to differ from control after 2 weeks with persistent beneficial effects through trial. Diacerein differed from controls after 6 weeks for pain and functional impairment.	superior to placebo, and neither agent appears to significantly enhance or detract from the efficacy of the other when they are administered concomitantly. The onset of action of diacerein appears to be delayed (> or = 4 weeks)."	suggest tenoxicam modestly superior to diacerein for both speed of onset and magnitude of response. Diacerein has higher adverse effect of diarrhea (37% v. 4%).
Pelletier 2000 (score=6.0)	Diacerein	RCT	Sponsored by grant from Les Laboratories Negam, Toussusle-Noble, France. No COI.	N = 484 Knee OA	Mean age: 63.5±8.9 years; 98 males, 386 females.	Placebo BID (n=125) vs. diacerein 50mg a day (n=126) vs. diacerein 100mg a day (n=111) vs. diacerein 150mg a day (n=122) for 4 months	Baseline, 4, and 16 weeks for laboratory tests. And global tolerance assessment every week from 2-16.	VAS pain rating differences to Week 24: placebo -10.9±19.3 vs. 50mg a day -15.6±21.0 vs. 100mg a day -18.3±19.3 vs. 150mg a day -14.3±23.7 (p <0.05 100mg a day vs. placebo). WOMAC pain, stiffness scores significant for 100mg a day dose (p <0.05). Patient global efficacy assessments: placebo 52.9±30.9 vs. 50mg a day 62.7±28.1 vs. 100mg a day 61.1 ±24.6 vs. 150mg a day 61.0±29.3 (p <0.05 50mg a day vs. placebo). Significantly higher frequency of AEs observed for 150mg a day diacerein (18.9%) vs. other groups (11.2% placebo, 12.7% 50mg a day, 9.9% 100mg a day).	"The results of this dose-finding study confirm previous study findings that diacerein is an effective treatment for the signs and symptoms of knee OA, and that based on the results from ITT analysis, the optimal daily dosage is 100mg/day (50mg twice daily)."	High drop-out rate (28%-39%) in all groups. Compliance rate uncertain. Suggests mild benefit of diacerein.
Kay 1980 (score=5.0)	Diacerein	Crossover Trial	No mention of sponsorship or COI.	N = 12 Hip or knee OA	Mean Age 66.2 years;	Diacerein 50mg a day for 4 weeks preceded	Baseline and 12 weeks.	Data not in aggregate. Overall improvements on Diacerein marked in 3/12 (25%) and	"Improvement was not apparent for several weeks after starting active	Sparse details and limited analyses. Appears a

					2 males, 10 females.	and followed by 4 weeks of placebo		slightly improved in 3/12 (25%). Remainder 4/12 (33.3%) unchanged; 2/12 worse.	treatment and remission lasted for 2 weeks to 3 or more months after the drug was withdrawn."	crossover trial, however randomization and blinding unclear.

Evidence: for Orthotics, Shoe Insoles and Shoe Lifts

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: ambulatory devices, canes, shoe insoles, crutches, braces, orthotics; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 327 in Scopus, 7 in CINAHL, 57 in Cochrane Library, 68 in Google Scholar, and 7 from other sources. We considered for inclusion 0 from PubMed, 8 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 7 from other sources. Of the 17 articles considered for inclusion, 0 randomized trials and 17 systematic studies met the inclusion criteria.

Evidence for use of Magnets and Magnetic Stimulation

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Magnets, Magnetic stimulation; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 articles in PubMed, 86 in Scopus, 3 in CINAHL, 2 in Cochrane Library, 1600 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 3 articles considered for inclusion, 0 randomized trials and 3 systematic studies met the inclusion criteria.

Evidence for the Use of Physical Therapy and Occupational Therapy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Physical Therapy, Occupational Therapy; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 187 articles in PubMed, 5 in Scopus, 489 in CINAHL, 0 in Cochrane Library, 3670 in Google Scholar, and 2 from other sources. We considered for inclusion 16 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 19 articles considered for inclusion, 4 randomized trials and 1 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Bennell 2014 (score=7.5)	Physical Therapy	RCT	Sponsored by National Health Medical Research Council, and partly by Australian Research Council Future Fellowship, and partly by Australian National Health and Medical Research Council Practitioner Fellowship. COI: All authors submitted ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Bennell reported that she received royalties for educational DVD on knee osteoarthritis and from commercially available shoe from ASICS Oceania.	N=102 community volunteers with hip pain levels of ≥40 on VAS scale of 100 mm and hip osteoarthritis confirmed by radiograph	Mean age: 63.6 years; 40 males, 62 females	Active Group: (n=49) received education, advice, manual therapy, home exercise, and gait aid if appropriate for 10 treatment sessions over 12 weeks vs Sham Group: (n=53) received inactive ultrasound and inert gel for 10 treatment sessions over 12 weeks	13, 36 weeks	Change in pain score for active group was 58.8 to 40.1 mm and 58.0 to 35.2mm for sham group (95% CI -3.9-17.7). Change in function score for active group was 33.2 to 27.5 and 32.4 to 26.4 for sham group (95% CI -3.8-6.5). Active group improved in pain by a mean of 17.7 mm and sham group a mean of 22.9 mm. Function improved in active group by a mean of 5.2 units compared to sham group with 5.5 units.	"Among adults with painful hip osteoarthritis, physical therapy did not result in greater improvement in pain or function compared with sham treatment, raising questions about its value for these patients."	Data suggest lack of efficacy compared with sham for both pain and function in painful hip OA patients.
Holmich 1999 (score=7.0)	Physical Therapy	RCT	Sponsored by grants from Danish Research Council of Sport, the Danish Sports Federation, and the Scientific Commission of TEAM Denmark. No mention of COI.	N = 68 Male athletes with long-standing groin pain (median 40 weeks)	Mean age: 30 years; 68 males, 0 females	Active training program (12 exercises) with physical therapy (laser, friction massage, stretching TENS) (n= 34) vs. no active training for 8 to 12 weeks (n=34)	12 weeks, 4 months	23 AT patients vs. 4 in PT returned to sports without groin pain [OR = 12.7 (95% CI 3.4-47.2)]. Subjective global assessments of effect of treatments favored active training (p = 0.006). Treatment outcomes (excellent plus good): AT 25/34 (73.5%) vs. 10/34 (29.4%), p = 0.001. Per-protocol analysis	"AT with a programme aimed at improving strength and coordination of the muscles acting on the pelvis, in particular the adductor muscles, is very effective in the treatment of athletes with long-standing adductor-related groin pain. The potential preventive value of a short programme based upon the principles of AT should be assessed	Variable length of treatment course (8-12 weeks); numbers of treatments reduces ability to conclude efficacy of any one treatment intervention. Data suggest the active training plus physical therapy program superior to physical therapy alone.

								not appreciably different.	in future, randomised, clinical trials."	
Austin 2017 (score=6.5)	Physical Therapy	RCT	No sponsorship. COI: One or more authors checked 'yes' indicating that author had relevant financial relationship in biomedical arena outside submitted work.	N=120 patients undergoing primary, unilateral total hip arthroplasty	Mean age: 61.7 years; 61 males, 47 females	Formal Physical Therapy: (n=54) vs Home Exercise: (n=54)	10, 12 weeks, 6-12 months	Improvement in primary outcome at 1 month was 21.5 points (95% CI 16.2-26.9) for formal physical therapy group and 23.3 points (95% CI 18.3-28.4) for Home exercise group. At 6-12 months follow-up, improvement in outcome was 36.0 points (95% CI 30.9-41.2) for formal physical therapy group compared to 35.6 points (95% CI 30.9-40.4) for the home exercise group (p=0.82). WOMAC scores improved by 36.9 points (95% CI 32.2-41.8) for formal physical therapy compared to 36.4 points (95% CI 31.8-41.1) for home exercise.	"This randomized trial suggests that unsupervised home exercise is both safe and efficacious for a majority of patients undergoing total hip arthroplasty, and formal physical therapy may not be required."	Standard Care Bias. 28% of patients crossed over. Data suggest comparable efficacy between groups.
Neumayr 2006 (score=4.5)	Physical Therapy	RCT	Sponsored by National Institutes of Health Grants. No COI.	N = 46 patients with 46 hips Stages I, II, or III osteo-necrosis; all sickle cell anemia	Mean age: 26 years, 19 males, 19 females	Core decompression plus physical therapy (n= 17) vs physical therapy alone (limited weight bearing, stretching, adductor and	3 month intervals for 80 months	At mean 3 years, survival 82% of decompression vs. 86% PT (NS). Mean improvement in Harris Hip score 18.1 for coring vs. 15.7 PT (NS). No differences in hip survival across stages I-III (92, 82, 82%).	"[P]hysical therapy alone appeared to be as effective as hip core decompression followed by physical therapy in improving hip function and postponing the need for additional surgical intervention at a mean of	Less advanced disease PT group (stage III 33% vs. 59%) and non-study hips more disparate at baseline (19% vs. 47%) suggest randomization failure, thus conclusions difficult to draw. Generalizability from

						other muscle strengthening) (n=21).			three years after treatment."	sickle cell anemia to working populations or others unclear.

Evidence for the Use of Manipulation or Mobilization

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: manipulation, mobilization; hip osteoarthritis, hip osteoarthrosis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 340 articles in PubMed, 119 in Scopus, 23 in CINAHL, 34 in Cochrane Library, 1,620 in Google Scholar, and 2 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 4 articles considered for inclusion, 4 randomized trials and 0 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Chiropractic Treatment, Osteopathic Manipulative Treatment (OMT); Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 articles in PubMed, 7 in Scopus, 6 in CINAHL, 1 in Cochrane Library, 97 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Licciardone 2004 (score= 8.5)	Manipulation/Mobilization	RCT	Sponsored by the American Osteopathic Association, the Osteopathic Health System of Texas Foundation, and the carl Everett Charitable Lead Trust Fund. COI, Kimberly Fuda, MPH and David P. Russo DO, MPH.	N = 60 Hospitalized knee or hip OA surgery or hip fracture	Mean age: 69.2; 18 male, 42 female.	Osteopathic manipulative treatment protocol (OMT) (n=30) vs. sham treatment protocol (n=30). Manipulation was individualized (myofascial release, strain/counterstrain, muscle energy, soft tissue, high-velocity low amplitude mobilization, craniosacral). All received standard care.	Follow up from at least 3 weeks, but less than 6 months.	Functional Independence Measure total scores improved: OMT 26.5 points vs. sham 26.2 points, p = 0.86. Lengths of stay were OMT 15.4 days vs. sham 12.3 days (p = 0.09). All measures were not different except rehabilitation efficiency, which favored the sham group over OMT (2.0 vs. 2.6 for sham, p = 0.01).	"The (osteopathic manipulative treatment) protocol used does not appear to be efficacious in this hospital rehabilitation population."	Heterogeneous mixture of patients and individualization of treatments received preclude robust conclusions about indications for any one diagnosis. Inpatient rehabilitation population also might limit generalizability. At face value, OMT was not effective.
Hoeksma 2004 (score= 7.5)	Manipulation/Mobilization	RCT	No sponsorship and no COI mention	N = 109 Hip OA	Mean age: 72 years ; 18 males, 38 females	Manual therapy program (stretching, hip joint traction, traction manipulation in each limited position-high velocity thrust, repeated until optimal results) (n=56) vs. Exercise therapy program (n=53)	Follow up at baseline, 5 weeks, 17 weeks, and 29 weeks.	After 5 weeks, 81% manual vs. 50% exercise improved (p <0.05). Quality of life and hip function: manual vs. exercise therapy SF-36 bodily pain: baseline: 41.1±18 vs. 37.9±18 (NS); Week 29: 51.4±22 vs. 49.9±24 (NS). Harris hip score: baseline: 54.0±15 vs. 53.1±14 (NS); Week 29: 70.2±20 vs. 59.7±18 (p <0.05)	"The effect of the manual therapy program on hip function is superior to the exercise therapy program in patients with OA of the hip."	Data suggest manual therapy is better than exercise therapy to improve hip function and decrease hip pain.

Abbott, 2013 (score= 6.5)	Manipulation/Mobilization	RCT	Sponsored by Health research council of New Zealand (HRC 07/199 and 07/200) and the New Zealand Lottery Grant Board (MR212664), Lottery Grants Board, and Centre for Physiotherapy research. No COI.	N= 206 Participants with hip or knee OA	Mean age: 66 years, 92 males, 144 females.	Manual physiotherapy (n = 54): procedures to modify the quality and ROM of the target joint and associated soft tissue vs. Multi-modal exercise physiotherapy (n =51): procedure of warm-up/ aerobic, muscle strengthening and stretching, and neuromuscular control exercise. Vs. combined exercise and manual physiotherapy (n =50): mix of both manual and exercise therapy vs. or no trial physiotherapy (n = 51): consisted of nine treatment session of approx. 90mins.	Follow-up at baseline, 9 weeks, 6 months, and 1 year.	Baseline WOMAC score was 100.8 (53.8) on a scale of 0-240. WOMAC scores at 1 year compared with usual care group 28.5 (95% (CI) 9.2-47.8), for usual care plus manual therapy, 16.4 (-3.2 to 35.9)	"[M]anual physiotherapy provided benefits over usual care, that were sustained to 1 year. Exercise physiotherapy also provided physical performance benefits over usual care. There was no added benefit from a combination of the two therapies."	Data suggest at one-year post intervention, manual therapy and exercise were better than usual care for performance, but combination group was not superior to exercise groups or manual therapy groups alone.
Poulsen, 2013 (score= 6.0)	Manipulation/Mobilization	Pilot Study	Sponsored by the Danish Foundation for Chiropractic Research and	N = 118 Patients with clinical and	Mean age: 64.6; 63 males,	Patient Education (PE) program: (n= 37) vs.	Follow up at baseline, 6 weeks, 3 months, and 12 months	No significant differences were found between all three groups for mean pain severity (PE: 5.3 [SD 2.33], PE + MT: 3.4[2.4], MCI: 5.3 [1.7] P= 0.058)	"For primary care patients with OA of the hip, a combined	Data suggest a combination intervention of MT and PE is better than MCI. Also, PE

			Postgraduate education, Region of Southern Denmark, Danish Rheumatism association and University of Southern Denmark. No COI.	radiographic unilateral hip OA	48 females.	PE program plus Manual therapy (MT): (n=38) vs. Minimal Control Intervention (MCI): (n=36)		PE+ MT achieved a 1.9 greater pain reduction compared to MCI (95% CI 0.9-2.9)	intervention of MT and PE was more effective than a MCI. PE alone was not superior to the MCI."	alone not as good as MCI.
Beselga, 2015 (score= 3.5)	Manipulation/Mobilization	RCT								Small sample (n= 40) High dropout rates. No follow up duration. Confusing results from diagram vs. summary.
Blackman, 2014 score=(3.0)	Manipulation/Mobilization	Pilot study								Small sample (n=23). So underpowered, potential randomization failure at baseline, VAS scores different for groups.

Evidence for the use of Massage

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: massage; hip osteoarthritis, hip osteoarthrosis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 12 articles in PubMed, 28 in Scopus, 3 in CINAHL, 12 in Cochrane Library, 766 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Comments:

Evidence for the Use of Reflexology

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: reflexology; hip osteoarthritis, hip osteoarthrosis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 12 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 27 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Cryotherapy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cryotherapy, Heat-Cold Application; Hip Osteoarthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 10 articles in PubMed, 148 in Scopus, 40 in CINAHL, 16 in Cochrane Library, 1570 in Google Scholar (Went through first 100), and 1 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Cryotherapy, Heat-Cold Application; Hip Osteoarthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 10 articles in PubMed, 148 in Scopus, 40 in CINAHL, 16 in Cochrane Library, 1570 in Google Scholar (went through first 100), and 1 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Saito 2004 (score=4.5)	Cryotherapy	RCT	No COI, participation from assistance Mark Lourenz, Trevor Allen, Ewa Stendur, Barry Stilllman, and Janet Mckinney in developing this trail.	N = 46 with cementless THA	Mean age: 59.16 years; 9 males, 37 females.	Cryotherapy (cold compress) (n=23) vs. no cryotherapy for 4 days post-op (n=23)	Follow-up at 1, 4, and 7 days post-operation.	Half cryotherapy patients had no pain post-op Day 3 vs. 5 days in controls. Less mepivacaine used for anesthesia for cryotherapy group (295±99 vs. 489±160mg, p <0.001), but diclofenac doses did not differ (58 vs. 60mg, p = 0.53). Did not reduce blood loss or affect creatine kinase or C-reactive protein.	"Did not find a reduction in blood loss as a result of the cooling. The cryotherapy had no effect on the CK or CRP levels, indicating that it has no inhibitory effects on muscle damage or inflammation."	Suggests cryotherapy reduces pain scores first 4 post-op days. However, it is ineffective for reducing blood loss.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Saito 2004 (score=4.5)	Cryotherapy	RCT	No COI, participation from assistance Mark Lourenz, Trevor Allen, Ewa Stendur, Barry Stilllman, and Janet Mckinney in developing this trail.	N = 46 with cementless THA	Mean age: 59.16 years; 9 males, 37 females.	Cryotherapy (cold compress) (n=23) vs. no cryotherapy for 4 days post-op (n=23)	Follow-up at 1, 4, and 7 days post-operation.	Half cryotherapy patients had no pain post-op Day 3 vs. 5 days in controls. Less mepivacaine used for anesthesia for cryotherapy group (295±99 vs. 489±160mg, p <0.001), but diclofenac doses did not differ (58 vs. 60mg, p = 0.53). Did not reduce blood loss or affect creatine kinase or C-reactive protein.	"Did not find a reduction in blood loss as a result of the cooling. The cryotherapy had no effect on the CK or CRP levels, indicating that it has no inhibitory effects on muscle damage or inflammation."	Suggests cryotherapy reduces pain scores first 4 post-op days. However, it is ineffective for reducing blood loss.

Evidence for the use of Hot and Cold Therapies

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Diathermy; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 9 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 144 in Google Scholar, and 2 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic studies met the inclusion criteria.

Evidence for the sue of Infrared Therapy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Infrared therapy, Infrared rays; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2 articles in PubMed, 9 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 1300 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.

Evidence for the use of Ultrasound

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Ultrasound, ultrasonography; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 916 articles in PubMed, 1112 in Scopus, 8 in CINAHL, 15 in Cochrane Library, 2310 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 0 systematic studies met the inclusion criteria.

Evidence for the use of Low-Level Laser Therapy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: “laser therapy, low-level”, low level laser therapy, LLLT, low level light therapy; Hip Osteoarthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 6 articles in PubMed, 290 in Scopus, 14 in CINAHL, 44 in Cochrane Library, 5140 in Google Scholar (Went through first 100), and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the use of low-tech heat therapy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: heat therapy, local hyperthermia, thermotherapy; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 15 articles in PubMed, 374 in Scopus, 2 in CINAHL, 20

in Cochrane Library, 7290 in Google Scholar (Went through first 100), and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Electrical Stimulation Therapies

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Electrical stimulation therapy, TENS, iontophoresis, PENS, sympathetic electrotherapy, microcurrent therapy, interferencial therapy, h-wave stimulation, high voltage galvanic stimulation, transcutaneous electrical nerve stimulation, percutaneous electrical nerve stimulation, Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 19 articles in PubMed, 121 in Scopus, 5 in CINAHL, 90 in Cochrane Library, 10142 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Gremeaux 2008 (score=3.0)										Underpowered study (n=29). Unusual care bias, sparse methods.

Evidence for the Use of Transcutaneous Electrical Stimulation (TENS)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Transcutaneous Electric Nerve Stimulation, TENS, Neuromuscular Electrical Stimulation, NMES, Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip

Osteoarthritis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 8 articles in PubMed, 312 in Scopus, 2 in CINAHL, 55 in Cochrane Library, 336 in Google Scholar, and 1 from other sources. We considered for inclusion 0 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 2 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Lang 2007 (score=8.0)	TENS	RCT	No mention of sponsorship or COI.	N = 63 Hip fractures	Mean age: 80.4 years; 5 males, 58 females	TENS (n=30) vs. sham TENS during emergency transport (n=33)	No mention of follow up.	VAS pain (baseline/after transport): TENS (89±9/59±6) vs. placebo (86±12/79±11), p <0.01. Heart rate 67±11 vs. 99±8 (p <0.01). Blood pressure trended towards higher in placebo (e.g., diastolic 86±18 vs. 97±12, NS).	"TENS is a valuable and fast-acting pain treatment under the difficult circumstances of "out-of-hospital rescue." Because of its lack of side effects, it could also be a valuable tool in the hospital."	Post hoc excluded 9 from data analyses due to non-fractures. Baseline TENS group's pain trended towards shorter duration. Data suggest TENS reduces pain in emergency transport setting.

Evidence for the Use of Acupuncture

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms Acupunture, acupotomy, Electro acupuncture, acupressure, acupuncture therapy, warm needling, dry needling, needling, de-qi, warm, dry, pressure, electric current, needle; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 179 in Scopus, 7 in CINAHL, 12 in Cochrane Library, 191 in Google Scholar, and 7 from other sources. We considered for inclusion 10 from PubMed, 3 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 7 from other sources. Of the 21 articles considered for inclusion, 9 randomized trials and 6 systematic studies met the inclusion criteria

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Huguenin 2005 (score=7.5)	Acupuncture	RCT	No COI, participation from assistance Mark Lourenz, Trevor Allen, Ewa Stendur, Barry Stilllman, and Janet Mckinney in developing this trail.	N = 60 Male soccer runners	No mention of age; 59 males.	Therapeutic Treatment Group: (n=29) received dry needling of gluteal trigger points (most upper outer buttocks, 3-5 points each, 0.3mm diameter, 25mm long acupuncture needles) vs. Placebo Treatment Group: (n=30) received needling (blunted needle to 1 minute)	Follow up at baseline, 24 hours, and 72 hours.	VAS pain did not differ between groups (graphic data). No significant changes in ROM in either group. ROM with straight leg raise did not differ between groups.	'Neither dry needling nor placebo needling of the gluteal muscles resulted in any change in straight leg raise or hip internal rotation. Both interventions resulted in subjective improvement in activity related muscle pain and tightness."	Short-term trial of 3 days. No long-term outcomes data. Attempted blinding failed (p <0.001 between groups). Study also involves athletes from soccer clubs, thus applications to other populations unclear.
White 2010 (score=7.0)	Acupuncture	RCT	Sponsored by the Department of Health Postdoctoral research award, Rufford Maurice Laing Foundation, and the Southampton complementary Medicine Research Trust. No mention of COI.	N= 140 Hip or Knee OA	Mean age: 67.0±8.5 years; 56 males, 84 females.	Real Acupuncture (RA): (n=74) received 2 sessions (20 min) a week for 4 weeks. Needles were single use, blister packed 30 mm×0.3 mm and 40 mm×0.25 mm, depending on the area, needles and body size. vs Streitberger needle (SN): (n=73) received 2 sessions (20 min) a week for 4 weeks. Needle shaft moves into the handle rather than into the body	No follow up mention	No significant correlation between the strength of de qi and improvement in pain (p=.49) Real Acupuncture median pain reduction in mm (IQR):16.7 (28.2) vs. Streitberger Acupuncture median pain reduction in mm (IQR): 15.3 (31.7)	"[T]hese data suggest that the presence and intensity of *de qi* has no effect on the pain relief obtained for patients with OA. This result may have implications for both acupuncture treatment and for future trial methodology."	Data suggest needling sensation (de qi) has no effect on pain relief.

Witt 2006 (score=6.0)	Acupuncture	RCT	Sponsored by German social health insurance funds: Techniker Krankenkasse (TK); BKK Aktiv; Betriebskrankenkasse der Allianz Gesellschaften; Bertelsmann BKK; Bosch BKK; BKK BMW; DaimlerChrysler BKK; BKK Deutsche Bank; Ford Betriebskrankenkasse; BKK Hoechst; HypoVereinsbank Betriebskrankenkasse; Siemens-Betriebskrankenkasse; Handelskrankenkasse; Innungskrankenkasse Hamburg. members of the ARC advisory board, data management team, data acquisition team, and participation physicians and patients. No COI.	N = 712 Hip or knee OA	Mean age (SD): 61.8 ± 10.8 years; 331 males, 381 females.	Acupuncture Group: (n=322) received acupuncture up to 15 sessions over 3 months vs. Placebo Group: (n=310) received no acupuncture (delayed treatment for 3 months). Acupuncture individualized.	Follow-up at baseline, 3 months, and 6 months	WOMAC scores improved with acupuncture (17.6, SE 1.0; WOMAC 30.5±1.0) vs. controls (0.9, SE 1.0; WOMAC 47.3±1.0), p <0.001. All other WOMAC indices significantly improved (p <0.001). Quality of life scores also improved, p <0.001. Treatment success also occurred in those with delayed treatment.	"Acupuncture plus routine care is associated with marked clinical improvement in patients with chronic OA-associated pain of the knee or hip."	Large sample size; additional 2,921 received acupuncture, but not randomized. Individualized acupuncture treatments modestly weaken conclusion. Treatment made no difference. Non-randomized had almost identical results to those randomized to immediate acupuncture. Data support efficacy of acupuncture for intermediate-term symptom relief, but non-interventional control biases in favor of intervention.

Fink 2001 (score=6.0)	Acupuncture	RCT	Sponsored by PharmaMED Foundation Germany with participation from Dr. Adrian White, professor Edzard Ernst, Dr.Max Pittler, Professor Cao Xiadoding	N = 67 Hip OA	Mean age: 61.4 ± 8.6 years; 22 males, 43 females.	Treament Group: (n=33) received traditional needle placement and manipulation (20 minutes) vs. Control Group: (n=34) received needles away from classic positions, not manipulated. All needles within L2-L5 dermatomes; 10 treatments 3 weeks.	Follow-up at baseline, 2 weeks, 2 months, and 6 months.	All measures improved in both groups from Week 2 to 2 months, including patients' satisfaction, Lequesne index, quality of life, and VAS pain (graphic data). There were no differences between groups [e.g., VAS pain verum 54.6±18.9 vs. control 55.3±23.5 (NS)].	"Needle placement in the area of the affected hip is associated with improvement in the symptoms of osteoarthritis. It appears to be less important to follow the rules of traditional acupuncture techniques."	No observation or other control group. Patient blinding unclear. Suggests needle placement per traditional acupuncture is unnecessary and manipulation of needles is also not necessary.
Stener-Victorin 2004 (score=5.0)	Acupuncture	RCT	Sponsored by Research and Development Unit, Vastra Gotaland, Sweden. No COI mentioned.	N = 45 Hip OA	Mean age: 65.7 years; 18 males, 27 females.	Electro-acupuncture Group: (n=15) (most painful hip area, 4 of BL54, 36, GB29, 30, 31 and ST31; and distal points GB34, BL60) plus education (2x2-hour meetings) vs. Hydrotherapy Group: (n=15) (warm-up, mobility, strengthening) plus education vs. Education Group: (n=15) alone for 30 minute appointments, 10 times over 5 weeks.	Follow-up at baseline, after 10 treatments, 1 month, 3 months, and 6 months.	Pain related to motion and on load (baseline/after 10 treatments/3 months/6 months): EA (37/22/ 24/17) vs. hydrotherapy (55/35/ 25.5/28) vs. control (56/--/48.5/ 59), p <0.05 comparing EA and hydro at 3 months to baseline and EA vs. baseline at 6 months. Disability rating index: EA (36/28/ 33.5) vs. hydro (45/23.5/26.5) vs. control (43/--/45). Daytime ache improved in EA and hydrotherapy for 3 months. Night-time ache reduced 3 months with hydrotherapy vs. 6 months EA. Quality of life improved in EA and hydrotherapy groups up to 3 months after last treatment. No changes in education group alone.	"EA and hydrotherapy, both in combination with patient education, induce long-lasting effects, shown by reduced pain and ache and by increased functional activity and quality of life, as demonstrated by differences in the pre- and post-treatment assessments."	Small sample sizes and high dropouts by 6 months. Trial had multiple interventions, thus attribution of benefits to any one intervention difficult. Use of educational intervention as control might bias in favor of intervention.

Reinhold 2008 (score=5.0)	Acupuncture	RCT	Sponsored by German social health insurance funds: Techniker Krankenkasse (TK); BKK Aktiv; Betriebskrankenkasse der Allianz Gesellschaften; Bertelsmann BKK; Bosch BKK; BKK BMW; DaimlerChrysler BKK; BKK Deutsche Bank; Ford Betriebskrankenkasse; BKK Hoechst; HypoVereinsbank Betriebskrankenkasse; Siemens-Betriebskrankenkasse; Handelskrankenkasse; Tnnungskrankenkasse H No COI.	N = 489 Hip or knee OA	Mean age: 60.9; 189 males, 300 females.	Acupuncture Group: (n=246) received acupuncture treatment plus routine care (10-15 appointments) vs. Control: (n=243) received delayed acupuncture after 3 months and routine care for 3 months	Follow-up at baseline, and 3 months.	Costs higher for acupuncture over 3 months [mean cost-difference: 469.50 euros (95%CI 135.80-803.19). Overall ICER 17,845 euros per QALY gained. Cost effectiveness better for females.	"Acupuncture was a cost effective treatment strategy in patients with chronic osteoarthritis pain."	Acupuncture administered by multiple providers and relatively unstructured. Unclear if economic data from Germany applies to U.S.
Haslam 2001 (score=3.0)	Acupuncture	RCT								Small sample, sparse data. Unclear if controls already had same treatment, thus potentially biased to favor acupuncture. Controls wait listed for arthroplasty; likely biases in favor of intervention.

Martins, 2014 (score=3.0)	Acupuncture	RCT								Data suggest no difference between immediate vs delayed acupuncture
Fargas-Babjak 1989 (score=2.5)	Acupuncture	RCT								Intervention group instructed to use maximum intensity tolerated, thus true blinding absent. High dropouts. Pain tools had contradictory responses from same patients on same questions suggesting confusion or misinterpretation. No demonstrated improvements in functional outcomes.

Evidence for the Use of Intraarticular Glucocorticosteroid Injections

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: intra-articular steroid injections, corticosteroid, cortisone injections, injections, intraarticular; hip osteoarthritis, hip degenerative joint disease, hip osteoarthrosis, hip degenerative arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 47 articles in PubMed, 88 in Scopus, 36 in CINAHL, 3 in Cochrane Library, 376 in Google Scholar, and 2 from other sources. We considered for inclusion 23 from PubMed, 5 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 32 articles considered for inclusion, 6 randomized trials and 8 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Lambert 2007 (score=10.0)	Glucocorticosteroid Injections	RCT	Sponsored by a CHAR/Nycomed Development Award, the MSI Foundation, the University of Alberta Hospital Foundation, and the Arthritis Society of Canada. No COI.	N = 52 Hip OA	Mean age: 62.1 years; 21 males, 31 females	Triamcinolone hexacetonide 40mg plus bupivacaine 10mg (n=31) vs. bupivacaine. Fluoroscopy used (n=21).	2, 3, 6 months	WOMAC pain scores: (baseline/1 month/2 months): placebo (314.3±76.2/276.4± 129.0/306.5±121.2) vs. steroid (310.1±54.6/149.6± 113.0/157.4±127.2), p = 0.0005 and p <0.0001 respectively; 50% response rates for WOMAC differed (61.3% vs. 14.3%), p = 0.001.	"[C]orticosteroid injection can be an effective treatment of pain in hip OA, with benefits lasting up to 3 months in many cases."	Data suggest injections are efficacious for up to 3 months, although patients followed for 6 months and differences may be exceeded 3 months.
Qvistgaard 2006 (score=9.0)	Glucocorticosteroid Injections	RCT	Sponsored by the Oak Foundation and The Erna Hamilton Foundation. No mention of COI.	N = 101 Hip OA	Mean age: 66±12 years; 36 males, 65 females	Intraarticular Hyaluronic acid 3 2mL injections (n=33) vs. methylprednisolone 40mg (and 2 placebo injections) (n=32) vs. saline; 3 injections given at 14 day intervals; ultrasound-guidance (n=36)	14, 28, 90 days	Significant effect on walking pain (p = 0.044) due to improvement following corticosteroid vs. saline with effect-size 0.6 (95% CI, 0.1-1.1, p = 0.021). Effect size for HA vs. saline 0.4 (95% CI, -0.1 to 0.9, p = 0.13). Peak-effect after 2 weeks. No differences between treatments at endpoint. No significant adverse effects.	"Patients treated with corticosteroids experienced significant improvement during the 3 months of intervention, with an effect size indicating a moderate clinical effect. Although a similar significant result following treatment with HA could not be shown, the effect size indicated a small clinical improvement. A higher number of patients in future HA studies would serve to clarify this point."	Longest follow-up 90 days. Data suggest glucocorticosteroid injection may be superior to hyaluronic acid to saline. Most data suggest no benefits of either at 90 days.
Kullenberg 2004 (score=8.5)	Glucocorticosteroid Injections	RCT	No mention of sponsorship or COI.	N = 80 Hip OA	Mean age: 70 years; no mention of sex.	Triamcinolone acetonide 80mg (n=40) vs. mepivacaine 1% 2mL; fluoroscopy used (n=40)	3, 12 weeks	VAS total pain scores: (baseline/3 weeks/12 weeks): anesthetic (12.0±1.0/12.4± 1.8/--) vs. steroid (12.2±2.2/ 3.8±2.6/7.9±3.9). No complications.	"[I]ntraarticular corticosteroids might improve pain and range of motion of the affected joint in patients with hip OA."	Lack of anesthetic in glucocorticosteroid group could potentially unblind study. Data suggest injections are efficacious.

Atchia 2010 (score=6.5)	Glucocorticosteroid Injections	RCT	No mention of sponsorship. No COI.	N=77 hip osteoarthritis patients	Mean age: 69±8 years; 34 males, 43 females	Standard care: (n=20) received no injection vs Saline: (n=19) received 3 mL saline solution vs Durolane group: (n=19) received 3 mL/60 mg hylauronic acid injection vs Steroid Group: (n=19) received methylpresdnisolone acetate 3mL/120 mg	4, 8 weeks	NRS pain and WOMAC pain and function improved for steroid group only. Effect size was 1.5, 1.0, 0.5 for NRS pain, 1.9, 1.1, 0.6 for WOMAC pain, and 1.3, 0.9, 0.4 for WOMAC function respectively for weeks 1, 4, and 8. Synovitis was only predictor of steroid response at weeks 4 and 8 ($p<0.05$, OR 16.7, 95% CI 1.4-204).	"Ultrasound-guided corticosteroid injections are highly efficacious; furthermore synovitis on ultrasound is a biomarker of response to injection."	Standard care bias. Data suggest US may be of benefit for treatment of hip OA. The steroid group maintained response over an 8 week period.
Flanagan 1988 (score=5.0)	Glucocorticosteroid Injections	RCT	No mention of sponsorship or COI.	N = 36 Hip OA awaiting THA	Mean age not stated, range 46-79 years; 7 males, 28 females	Triamcinolone 20mg (n=12) vs. bupivacaine 0.5% 10mL (n=12) vs. saline; fluoroscopy used (n=11)	1, 2, 6, 9, 12 months	Percentages of patients improving (1/2 months): steroid (75/33.3) vs. bupivacaine (58.3/75/) vs. saline (63.6/60).	"The majority of patients had good pain relief for 1 month but in general this was not maintained and some patients were much worse after the injection."	Small numbers in each group. Limited data provided. Data do not clearly support injections.
Cunningt on 2010 (score=5.0)	Glucocorticosteroid Injections	RCT	Sponsored by Arthritis Research Campaign. COI: Dr. Platt received consulting fees, speaking fees, and/or honoraria from Abbott and SonoSite.	N=184 patients with inflammatory arthritis and an inflamed joint	Mean age: 58.2 years; 51 males, 133 females	US-guided corticosteroid injections group: (n=92) vs CE-guided corticosteroid injections group: (n=92)	2, 6 weeks	Of the US-guided injections, 83% were accurate compared to 66% of CE-guided injections. A greater improvement in VAS score was observed for accurate injection compared to inaccurate injection at 6 weeks (30.6 mm vs 21.2 mm; $p=0.03$). Clinicians using US were able to reliably assess accuracy ($p<0.001$) compared to those who used CE ($p=0.29$).	"US Guidance significantly improves the accuracy of joint injection, allowing trainee to rapidly achieve higher accuracy than more experienced rheumatologists. US guidance did not improve the short-term outcome of joint injection."	Data suggest accuracy of injection is significantly improved with US, but short-term outcomes of the joint injections did not improve.

Evidence for the Use of Intraarticular Hip Viscosupplementation Injections

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: hyaluronic acid injection, viscosupplementation, intra-capsular acid salt; hip osteoarthritis, hip degenerative joint disease, hip osteoarthrosis, hip degenerative arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 55 articles in PubMed, 0 in Scopus, 17 in CINAHL, 3 in Cochrane Library, 595 in Google Scholar, and 2 from other sources. We considered for inclusion 15 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 20 articles considered for inclusion, 7 randomized trials and 4 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Qvistgaard 2006 (score= 9.0)	Intraarticular Injections	RCT	Sponsored by the Oak Foundation and The Erna Hamilton Foundation. No mention of COI.	N = 101 Hip OA	Mean age: 66±12 years; 36 males, 65 females	Intraarticular Hyaluronic acid 3 2mL injections (n=46) vs. methylprednisolone 40mg (and 2 placebo injections) vs. saline; 3 injections given at 14 day intervals; ultrasound-guidance (n=55).	14, 28, 90 days	Significant effect on walking pain (p = 0.044) due to improvement following corticosteroid vs. saline with effect-size 0.6 (95% CI, 0.1-1.1, p = 0.021). Effect size for HA vs. saline 0.4 (95% CI, -0.1 to 0.9, p = 0.13). Peak-effect after 2 weeks. No differences between treatments at endpoint. No significant adverse effects.	"Patients treated with corticosteroids experienced significant improvement during the 3 months of intervention, with an effect size indicating a moderate clinical effect. Although a similar significant result following treatment with HA could not be shown, the effect size indicated a small clinical improvement. A higher number of patients in future HA studies would serve to clarify this point."	Longest follow-up 90 days. Data suggest glucocorticosteroid injection may be superior to hyaluronic acid to saline. Most data suggest no benefits of either at 90 days.

Gramajo 1989 (score= 7.0)	Intraarticular Injections	RCT	No mention of sponsorship or COI.	N = 62 Hip or knee OA	Mean age: 57.7 years; 4 males, 26 females	Glycosaminoglycan-peptide complex (GPC) ("Rumalon") injections (n=32) vs. placebo injections. 3 injections a week for 8 week course, 3 courses per year (n=30).	2 years	Night pain (before/after treatment): GPC 2.4±2.9/0.4± 0.69 vs. placebo 2.1±1.58/1.9 ±0.83, p <0.001. Results comparable for day pain (p <0.01) and joint mobility (p <0.005). Time to walk 10 meters: GPC 21.8±6.88/ 18.0±4.86 vs. 24.1±7.31/ 23.9±3.3 seconds, p <0.001. No adverse effects reported.	"[G]lycosaminoglycan-peptide complex ('Rumalon') offers not only an effective but also a well-tolerated form of treatment which can be used to replace or supplement non-steroidal anti-inflammatory drugs, particularly in long-term therapy."	Co-interventions uncontrolled. Therapy requires 72 injections per year.
Dallari 2016 (score= 6.5)	Intraarticular Injections	RCT	No COI. No mention of sponsorship.	N=111 patients with hip osteoarthritis	Mean age not stated, range 18-65 years; 58 males, 53 females	PRP Group: (n=44) received 3 weekly consecutive injections of 5 mL platelet-rich plasma vs HA Group: (n=36) received 3 weekly consecutive injections of 2 mL hyaluronic acid vs PRP+ HA Group: (n=31) received 3 weekly consecutive injections of 7 mL platelet-rich plasma and hyaluronic acid	2, 6, 12 months	At 6 month follow-up, PRP group showed higher WOMAC scores (mean=72; 95%CI 67-76), lower VAS score (mean=21; 95%CI 15-28), compared to HA group (WOMAC mean=59 [95% CI 54-65], VAS score mean=44 [95% CI 36-52], p<0.0005) and compared to PRP+HA group (WOMAC mean=59 [95% CI 54-66], VAS mean=35 [95% CI 26-45], p=.007). The trend was not observed in WOMAC score for PRP group at 12 month follow up.	"Results indicated that intra-articular PRP injections offer a significant clinical improvement in patients with hip OA without relevant side effects. The benefit was significantly more stable up to 12 months as compared with other tested treatments. The addition of PRP+HA did not lead to a significant improvement in pain symptoms."	Persons performing treatment and patients not blinded to treatment. Limited baseline data on group. No placebo group. Data suggest PRP may be beneficial for hip OA.

Atchia 2010 (score= 6.5)	Intraarticular Injections	RCT	No mention of sponsorship. No COI.	N=77 hip osteoarthritis patients	Mean age: 69±8 years; 34 males, 43 females	Standard care: (n=20) received no injection vs Saline: (n=19) received 3 mL saline solution vs Durolane group: (n=19) received 3 mL/60 mg hylauronic acid injection vs Steroid Group: (n=19) received methylpresdnisolone acetate 3mL/120 mg	4, 8 weeks	NRS pain and WOMAC pain and function improved for steroid group only. Effect size was 1.5, 1.0, 0.5 for NRS pain, 1.9, 1.1, 0.6 for WOMAC pain, and 1.3, 0.9, 0.4 for WOMAC function respectively for weeks 1, 4, and 8. Synovitis was only predictor of steroid response at weeks 4 and 8 ($p<0.05$, OR 16.7, 95% CI 1.4-204).	"Ultrasound-guided corticosteroid injections are highly efficacious; furthermore synovitis on ultrasound is a biomarker of response to injection."	Standard care bias. Data suggest US may be of benefit for treatment of hip OA. The steroid group maintained response over an 8 week period.
Migliore 2009 (score= 6.0)	Intraarticular Injections	RCT	No mention of sponsorship. COI: Fidia Farmaceutici S.p.A. (Padova, Italy) is currently financing the article-processing charge.	N=42 patients with hip OA	Mean age:70±8.9 years; 22 males, 20 females	Hyalubrix Group: (n=22) vs Carbocaine group: (n=20)	6 months	Both treatment groups improved at the 3 and 6-month follow-up ($p<0.001$). Hyalubrix group showed better improvement than mepivacaine at 3 months ($p<0.001$) and at 6 months ($p<0.05$).	"This comparative study suggests a beneficial effect and safety of intra-articular HA in the management of hip OA."	No placebo group (anesthetic injected). Small sample. Data suggest IAHA may be beneficial for treating hip OA.

Tikiz 2005 (score= 6.0)	Intraarticular Injections	RCT	No mention of COI or sponsorship.	N = 48 patients with 56 hips Hip OA	Mean age: 59.5 years; 9 males, 34 females	Lower molecular weight hyaluronan (LMW HA) (Ostenil) 2mL (n=25) vs. higher molecular weight viscosupplement (hylan G-F 20, Synvisc) 2ML; 1 intra-articular injection Q week for 3 weeks (n=18)	1, 3, 6 months	VAS, WOMAC, Lequesne scores reduced in both groups; lasted 6 months; % reduction (LMWHA vs. HMWHA): 38 vs. 40% (p <0.001) VAS pain, 43 vs. 40% WOMAC (p <0.001), 47 vs. 49% Lequesne (p <0.001). No difference between 2 groups; 3 dropouts due to pain. Local adverse effects pain and/or swelling in 3/32 hips (9%) with LMW HA vs. 3/24 hips (12.5%) with hylan G-F 20 (NS).	"[B]oth types of viscosupplementation produced a significant clinical improvement during the 6-month follow-up period. However, no significant difference was found in outcomes between higher and lower molecular weight hyaluronan."	Data suggest either equal efficacy or equal lack of efficacy as there was no placebo control, however magnitude of reductions and duration of effect suggests efficacy.
Battaglia 2013 (score= 5.0)	Intraarticular Injections	RCT	No mention of sponsorship. No COI.	N=100 patients with chronic unilateral symptomatic hip OA	Mean age: 53±12 years; 63 males, 37 females	PRP Group: (n=50) received 3 consecutive (once every 2 weeks) intra-articular ultrasound-guided injections of 5 mL autologous platelet-rich plasma vs HA Group: (n=50) received vial (30 mg/2 mL) of high-molecular-weight (1500 kD) hyaluronic acid	1, 3, 6, 12 months	Improvement was observed between 1 and 3 month follow-up for both groups. At 6-12 month follow-up showed slightly progressive worsening. PRP group showed functional improvement and pain reduction, but was not superior to HA group at 12 months.	"Intra-articular PRP injections are as safe and efficacious as HA at 12-month follow-up in terms of functional improvement and pain reduction. However, efficacy is temporary, as demonstrated by gradual worsening of clinical scores toward the end of follow-up, even if these findings cannot be extended to all of the different PRP preparations available."	Baseline differences between groups (group A had higher NSAID use with lower age), grades of OA at baseline dissimilar.

No COI. No mention of sponsorship.	N=111 patients with hip osteoarthritis	Mean age not stated, range 18-65 years; 58 males, 53 females	PRP Group: (n=44) received 3 weekly consecutive injections of 5 mL platelet-rich plasma vs HA Group: (n=36) received 3 weekly consecutive injections of 2 mL hyaluronic acid vs PRP+ HA Group: (n=31) received 3 weekly consecutive injections of 7 mL platelet-rich plasma and hyaluronic acid	2, 6, 12 months	At 6 month follow-up, PRP group showed higher WOMAC scores (mean=72; 95%CI 67-76), lower VAS score (mean=21; 95%CI 15-28), compared to HA group (WOMAC mean=59 [95% CI 54-65], VAS score mean=44 [95% CI 36-52], p<0.0005) and compared to PRP+HA group (WOMAC mean=59 [95% CI 54-66], VAS mean=35 [95% CI 26-45], p=.007). The trend was not observed in WOMAC score for PRP group at 12 month follow up.	" Results indicated that intra-articular PRP injections offer a significant clinical improvement in patients with hip OA without relevant side effects. The benefit was significantly more stable up to 12 months as compared with other tested treatments. The addition of PRP+HA did not lead to a significant improvement in pain symptoms."	Persons performing treatment and patients not blinded to treatment. Limited baseline data on group. No placebo group. Data suggest PRP may be beneficial for hip OA.
No mention of sponsorship. No COI.	N=100 patients with chronic unilateral symptomatic hip OA	Mean age: 53±12 years; 63 males, 37 females	PRP Group: (n=52) received 3 consecutive (once every 2 weeks) intra-articular ultrasound-guided injections of 5 mL autologous PRP (150 mL of venous blood was taken from each patient and collected in a bag containing 21 mL of sodium citrate, and 2 centrifugations were performed) vs HA Group: (n=52) received 3 consecutive (once every 2 weeks) intra-articular ultrasound-guided injections of (30 mg/2mL) of high-molecular-weight (1500 kD)	1, 3, 6, 12 months	Improvement was observed between 1 and 3 month follow-up for both groups. At 6-12 month follow-up showed slightly progressive worsening. PRP group showed functional improvement and pain reduction, but was not superior to HA group at 12 months.	"Intra-articular PRP injections are as safe and efficacious as HA at 12-month follow-up in terms of functional improvement and pain reduction. However, efficacy is temporary, as demonstrated by gradual worsening of clinical scores toward the end of follow-up, even if these findings cannot be extended to all of the different PRP preparations available."	Baseline differences between groups (group A had higher NSAID use with lower age), grades of OA at baseline dissimilar.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Dallari 2016 (score=6.5)	Platelet-Rich Plasma Injections	RCT								
Battaglia 2013	Platelet-Rich	RCT								

(score=5.0)	Plasma Injections									

Evidence for the use of Prolotherapy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: prolotherapy injections; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 260 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 160 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.

Evidence for the use of Botulinum Injections

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: botulinum injection, botox; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 2 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the use of glucosamine sulfate intra-muscular injections

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Glucosamine Sulfate Intra-Muscular Injection; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 17 in Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for use of glucosamine sulfate intra-articular injections

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Glucosamine Sulfate Intra-articular Injections; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 4 articles in PubMed, 5 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 3 in Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Pre-Operative Autologous Blood Donations

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: pre-operative autologous blood donation; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 397 in Google Scholar, and 1 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Billote 2002 (score=7.0)	Pre-Autologous Blood Donation	RCT	Sponsored by one or more of the authors received grants or outside funding from Northwestern Memorial Hospital Intramural Fund. No COI.	N = 96 Patients scheduled for primary THR	Mean age: 59.7 years; 61 males, 35 females	Autologous blood donation (2 units, last donation at least 2 weeks before surgery) (n=42) vs. no donation pre-arthroplasty(n=54). All treated with FeSO4 325mg BID.	6 weeks	Hemoglobin levels lower on admission (129±13g/ L vs. 138±12g/L, p <0.05) as well as different in the recovery room; 54/54 (100%) non-donors no transfusions vs. 13/42 (31.0%) donors.	"Preoperative autologous donation provided no benefit for nonanemic patients undergoing primary total hip replacement surgery."	Results suggest autologous blood donation ineffective as conducted in this trial and costs were $758 higher per patient for this population.

Evidence for the Use of Hip Arthroplasty

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hip Arthroplasty, Hip Replacement, Total Hip Arthroplasty; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1,611 articles in PubMed, 158 in Scopus, 633 in CINAHL, 2 in Cochrane Library, 4,890 in Google Scholar, and 3 from other sources. We considered for inclusion 31 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 3 from other sources. Of the 40 articles considered for inclusion, 80 randomized trials and 13 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/ Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Karnezis 1994 (score=10.0)	Hip arthroplasty	RCT	No sponsorship or COI.	N = 92 THR and TKR patients, 88% OA	Mean age: 65.9 years; 42 males, 50 females	Desmopressin group (n=43) vs. placebo (n=49).	No mention of follow-up.	Higher volume transfused blood in desmopressin group (1944±738 vs. 1015±515mL). No significant differences between groups with regard to coagulation.	"[D]esmopressin does not reduce blood loss or transfusion requirements after total joint arthroplasty."	Study suggests Desmopressin does not provide benefit for hip and knee arthroplasty patients.
Rosenlund 2017 (Score=8.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N=77 patients with hip osteoarthritis	Mean age: 61 years; 52 males, 25 females.	Posterior approach group (n=39) vs. lateral approach group (n=38).	Follow-up at 3, 6 and 12 months.	No significant difference was found in Hip Disability and Osteoarthritis Outcome Score-Physical Function Short Form (HOOS-PS) score in two groups (-3.3, 95% confidential interval: -8.7 to 2.1). Posterior treatment did not improve physical function better than lateral treatment. However, significant improvement in HOOS-PS was found within the two groups: posterior group 39 (95%CI: 35 to 44) and lateral group 36 (95%CI: 30 to 42).	"We found no superior efficacy of using the PA compared with LA, as evaluated from patient-reported physical function, pain, physical activity, and quality of life. However, patients operated using the PA had less self-reported limping at 12 months."	Data suggest comparable efficacy between surgical approaches with more post-operative lumping observed in the lateral surgical approach.

Lavigne 2010 (score=8.5)	Hip arthroplasty	RCT	Sponsored by one or more of the authors (ML) have received funding from Zimmer, Warsaw, IN. No COI.	N = 48 All with OA and <65yrs, included 14 healthy controls	Mean age: 48.5 years; 37 males, 25 females	Hip resurfacing (Durom) (n=24) vs. large-head total hip arthroplasty (CLS stem) (n=24). Durom acetabula both groups; 1 year follow-up.	3, 6, 12 months	Fast walking speed (m/s) (baseline/3/6/12 months): HR (1.58/ 1.62/1.71/1.82) vs. THA (1.50/1.65/1.68/ 1.73) (NS). No difference in walking speed, step length, cadence, postural balance. Functional reach favored HR.	"(Hip Resurfacing) did not provide better clinical function over large-head THA."	Younger, active population. Data suggest comparable efficacy.
Nayak 1996; Rorabeck 1994; Rorabeck 1996; Laupacis 1993 (score=8.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 250 1º or 2º OA, N=16	Mean age: 61.1 years; 132 males, 118 females	Femoral Mallory-Head plasma spray-coated titanium or cobalt-chromium implants (n=113) vs. smooth implants for cement fixation. 28mm modular titanium cobalt-chrome heads used. Used canal lavage, restrictor and cement gun (n=111).	3 months, 6 months, 12 months, and yearly thereafter	Progressive acetabular osteolysis evidence in 9% (n = 10) cementless group. None received revision surgery for acetabular osteolysis; no evidence of acetabular component migration or shift. Acetabular osteolysis evident in 5% (n = 6) of cemented group. No significant difference between groups for prevalence of acetabular osteolysis p = 0.46.	"This study found no difference in the prevalence of acetabular osteolysis between the two groups."	Study mixed titanium and cobalt-chrome heads, limiting interpretation of results. Acetabular osteolysis higher 9% vs. 5%, for cementless, but not stat. significant and apparently nearly all had titanium.

Ogonda 2005 (score=8.0)	Hip arthroplasty	RCT	Sponsored by one or more of the authors received grants or outside funding from DePuy International. No COI.	N = 219 Unilateral THA	Mean age: 66.6 years; 107 males, 112 females	Surgery through a short incision of ≤10cm (n=109) vs. standard incision of 16cm (n=110).	6 weeks post-operation	Estimated intra-operative blood loss (ml) mini-incision vs. standard-incision group (mean ± SD): 314±162 vs. 366±190 (p = 0.03). Morphine usage [507] 42.9±97.4 vs. 45.0±96.8 (p = 0.89); pain scores not significantly different. Harris hip score 84.15±10.56 vs. 83.36±8.33 (p = 0.54).	"Minimally invasive total hip arthroplasty performed through a single-incision posterior approach by a high-volume hip surgeon with extensive experience in less invasive approaches to the hip…offers no significant benefit in the early postoperative period compared with a standard incision of 16cm."	Modestly reduced EBL, otherwise no apparent benefit of minimal incision. Patients not well described. Presumably mostly osteoarthrosis.
Usichenko 2005 (score=8.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 61 THA	Mean age: 67.1 years; 24 males, 30 females	Auricular acupuncture (hip joint, shenmen, lung, thalamus) (n=31) vs. sham (4 helix points) up to 3 post-op days (n=30).	3 days post-operation	Auricular acupuncture 32% less piritramide vs. control 1st 36 post-op hours (37 vs. 54mg, p = 0.004). Total dose 36% lower (0.54 vs. 0.84 mg/kg, p = 0.002). Time to 1st request lower (40 vs. 25 minutes, p = 0.04).	"(Auricular acupuncture) could be used to reduce postoperative analgesic requirement."	No differences in rates of belief of receipt of real acupuncture.
Rasquinha 2004 (score=8.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 237 88.2% OA	Mean age: 70.0 years; 245 males, 340 females	Ranawat-Burstein prosthesis with smooth (n=119) vs. rough finish for cemented femoral stems (n=118). Over 60 years, cemented	Yearly follow-up for 20 years	Mean lateral inclination p >0.05. Heterotopic ossification p >0.05. 5 hips with smooth femoral stems and 6 hips with rough femoral stems with cemented acetabular components demonstrated zone 1A interface lucency with	"As an isolated variable, surface finish does not appear to significantly influence results at mean follow-up of 6.5 years."	Results suggest no significant differences between rough and smooth prostheses.

						and under age 60 hybridized prostheses (more criteria in article). Single surgeon. Post-erolateral approach; 3rd generation cement.		1 in each cohort showing interface lucency in entire zone 1 (p >0.05). Cement mantle A smooth/rough: 50.9%/49.5%, p = 0.18.		
Devane 1997 (score=7.5)	Hip arthroplasty	RCT	No sponsorship or COI.	N = 250 1º or 2º OA	Mean age: 64 years; 71 males, 68 females	Same population and study as above, but only 148 available	6 weeks, 3 months, 6 months, yearly for minimum for 4 years	Rate of linear wear 0.152 with cement vs. 0.246mm a year (p = 0.0002). Rate of 3-dimensional displacement significant (p = 0.0000008). Rate of volumetric wear also lower at 98.5 vs. 155.1mm^3 a year p = 0.000008).	"Osteolysis was associated with an increased rate of polyethylene wear only in the hips in which the prosthesis had been inserted without cement."	Suggests cemented prostheses wear less rapidly.
Schouten 2012 (Score=7.5)	Hip arthroplasty	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=77 patients with degenerative and no inflammatory joint disease.	Mean age: 62.6 years; 45 males, 32 females.	Ceramic-on-metal bearing surfaces group (n=41) vs. metal-on-metal bearing surfaces group (n=36).	Follow-up at 6 and 12 months.	Serum Co levels increased in the two groups after 12 months: ceramic-on-metal group from 0.31 to 1.77 µg/l; metal-on-metal group from 0.35 to 1.57 µg/l; but the change was not significant (p=0.76). Serum Cr levels increased in two groups too: ceramic-on metal from 0.62 to 1.84µg/l; metal-on-	"[C]oM and MoM couplings are associated with an equivalent increase in serum cobalt and chromium levels, and comparable functional outcome scores at six and 12-months follow-up."	Data suggest at both 6 and 12 months follow-up, both groups showed similar serum cobalt and chromium levels and comparable functional outcome scores.

								metal from 0.57 to 1.73 µg/l; the change was not significant too (p=0.76).		
MacDonald 2010 (score=7.5)	Hip arthroplasty	RCT	Sponsored by one or more of the authors has received funding from Physicians Services Inc, Smith and Nephew Inc, Memphis, TN, and DePuy Inc, Warsaw, IN. COI: One or more authors certifies that he has or may receive payments or benefits from a commercial entity related to this work.	N = 388 OA	Mean age: 60.5 years; 219 males, 169 females	Proximally porous-coated tapered cementless femoral component (Synergy) (n=198) vs. fully porous-coated cementless femoral component (Prodigy) (n=190). All 28mm head. Acetabulum usually Reflection and Duraloc respectively. Minimum 2 years follow-up (mean 6.7 years).	Pre-operation, 6 months, 1 year, 2 years	Harris hip scores (baseline/1/2 years): synergy (43.2/85.6/86.4) vs. prodigy (43.1/84.5/86.7), NS. No differences in WOMAC, SF-12 mental or physical, UCLA scores and contralateral hip bone density. Prevalence of thigh pain and severity measures also not different over 2 years. Net average bone densities all Gruen zones (0.5, 1, 2 years): Synergy (1.5/1.48/1.48) vs. Prodigy (1.3/1.31/1.31), p <0.001, p = 0.002 and p = 0.002.	"Both fully and proximally coated stems performed well, with no clinical differences at 2 years' follow-up, except in bone mineral density evaluations."	Data mostly suggest comparable efficacy. Greater bone density measures in several Gruen zones, at 0.5, 1, 2 years in the Synergy group.

Usichenko 2006 (score=7.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 64 THA	Mean age: 67.5 years; 28 males, 19 females	Auricular acupuncture (lung, shenmen, forehead, hip) (n=33) vs. sham (4 helix points) (n=31).	No mention of follow up.	21% less fentanyl (3.9±1.4 vs. 4.9±1.2, p = 0.005) in acupuncture group vs. sham. 6 in acupuncture group required intraoperative atropine vs. 3 (NS).	"Auricular acupuncture reduced fentanyl requirement compared to sham procedure during hip arthroplasty."	Data suggest mild reduction in fentanyl. No other differences. Considering quality evidence, traditional acupuncture not superior to sham for LBP, arthritis. Study requires replication.
Östgaard 2001 (score=7.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 123 OA	Mean age: 72 years; 55 males, 68 females	Original (n=61) vs. new Charnley stem instrumentation (n=62).	10 years	Original instrumentation with AP x-ray views showed 23% of stems in varus and 7% valgus position. New instrumentation 10% varus (p = 0.03) and 24% valgus (p = 0.03). Posterior angling on lateral views 43% vs. 37%. Cement mantle quality not different (p = 0.6).	"The femoral stems were less often in the varus position with the new instrumentation. However, the worst malposition, with implant-inner cortex contact, especially seen on the lateral radiograph, was not addressed at all."	Authors suggest manufacturer should respond to the problem. Long-term implications vis-à-vis clinical outcome are unclear, but suggest suboptimal results with new instrumentation.
Widman 2001 (score=6.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 74 OA	Mean age: 72 years; 26 males, 48 females	Lateral position (n=30) vs. supine position for surgery (n=44).	24 hours post-operation	Intraoperative blood loss (ml) mean/SD Supine: 723±316. Lateral: 508±316, p = 0.005. Adjusted value supine/lateral: 775 vs. 509, p <0.001. Adjusted value after 24 hour accumulated blood loss supine/lateral: 1472 vs. 1273, p = 0.043.	Lateral position in hip replacement surgery is advantageous over supine position in regards to reducing perioperative blood loss.	Suggests lateral position results in lower blood loss.

Kim 2002 (score=6.5)	Hip arthroplasty	RCT and crossover for simultaneous	No sponsorship or COI.	N = 156 50 bilateral simultaneous; 106 unilateral	Mean age: 52.0 years ;100 males, 56 females	Cemented (Elite Plus, Simplex-P cement) (n=100) vs. uncemented (Profile) hip arthroplasty (n=106). All cups Duraloc cementless.	1 min, 3 min, 5 min, and 10 minutes after implantation, 24 hrs post-op, 48 hrs post-op	Number of fat globules per high-power field from right atrium total/mean (% affected): cementless stem: 220/2.2. Cementless stem: 331/3.1 (NS). 49% unilateral vs. 54% bilateral with fat globules in right atrial blood samples (NS). No hemodynamic differences (p = 0.14).	Bilateral simultaneous and unilateral total hip arthroplasty and cemented and cementless stems showed similar fat and bone-marrow-cell embolization.	Majority had osteonecrosis. Korean study; authors question generalizability to U.S. Crossover trial for simultaneous arthroplasties is study strength. Suggests simultaneous arthroplasties are reasonably safe.
Salemyr 2015 (Score=6.5)	Hip arthroplasty	RCT	Sponsored by Åke Wibergs Stiftelse, Ulla and Gustaf Ugglas Stiftelse, Sven Norén Foundation, Loo and Hans Ostermans Stiftelse, the DePuy Johnsson and Johnsson Foundation for Clinical Research, and Stockholm County Council and Karolinska Institutet. No mention of COI.	N=51 patients with primary hip osteoarthritis.	Mean age: 62 years ; 22 males, 29 females.	Ultra-short stem group (n=26) vs. conventional stem group (n=25).	Follow-up at 1 and 2 years.	Both Harris hip and WOMAC scores improved in two groups. Harris hip score: ultra-short stem group increased from 42 to 95 points; conventional stem group from 38 to 92 points; but no significant difference was found between the two groups (p=0.2). WOMAC score: ultra-short stem increased from 48 to 95 points,; conventional stem from 42 to 94 points; but the differences was not significant either (p=0.09).	"Up to 2 years after total hip arthroplasty, compared to the conventional tapered stem the ultra-short uncemented anatomical stem induced lower periprosthetic bone loss and had equally excellent stem fixation and clinical outcome."	Data suggest at 2 years post-surgery, there was less periprosthetic bone loss in ultra-short stem group with equal stem fixation to conventional stem group.

Chiu 1993 (score=6.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 120 Acute hip fractures	Mean age: 77.2 years; 28 males, 92 females	Drape group (operative site was covered with plastic adhesive drape after operation) (n=65) vs. no-drape group (operation site was left uncovered) (n=55).	6 months	No difference in post-op wound infection rates. Five swaps (4.2%) taken at wound closure positive for bacterial growth; 4 drape group, 1 no-drape group. Difference not statistically significant (X2 = 0.53, p >0.25).	The use of plastic adhesive drapes did not affect the wound infection rate after acute hip fracture operations.	Study suggests adhesive drapes do not provide advantage over no-drape at incision site.
Garbuz 2010 (score=6.5)	Hip arthroplasty	RCT	Sponsored by Zimmer, Inc, Warsaw, In. No mention of COI.	N = 104 Patients required to be suitable for hip resurfac-ing	Mean age: 51.8 years; 93 males, 11 females	Hip resurfacing (Durom) (n=48) vs. large-head arthroplasty (Metasul) (n=56). Durom acetabula both groups; 2 years follow-up.	2 months, 1 year, 2 years	WOMAC pain (pre/mean 1 year): Resurface (48.9/91.5) vs. large head THA (52.4/90.0), NS. Serum cobalt levels rose 46-fold with THA vs. 3.9-fold with resurfacing THA (5.09 vs. 0.51µg/L, p <0.001).	"Due to these excessive high metal ion levels, the authors recommend against further use of this particular large-head total hip arthroplasty."	Ions measured in subset. Data suggest greater wear with large head arthroplasty.
Kim 2005 (score=6.5)	Hip arthroplasty	Randomized Crossover Trial	No mention of sponsorship. No COI.	N = 52 All osteo-necrosis, all bilateral arthroplasties	Mean age: 53 years; 54 males, 5 females	Zirconia femoral head (n=47 hips) vs. cobalt-chromium head (n=47 hips).	10-16 years	Mean polyethylene wear rate was 0.08 mm/year with zirconia vs. 0.17 mm/year with cobalt-chromium (p = 0.004). Mean volumetric polyethylene wear was 350.8 mm3 with zirconia heads vs. 744.7 mm3 with cobalt-chromium (p = 0.004). Two zirconia	"The mean amount and rate of polyethylene wear were significantly lower in the hips with a zirconia head than they were in the hips with a cobalt-chromium head, presumably because the zirconia heads had a smoother articulating surface."	Volumetric wear data support the zirconia implant vs. cobalt-chromium, but only revisions were 2 zirconia stems. Loosening observed to have occurred in those who were not active vs. others doing farm work or playing tennis

								stems revised due to loosening vs. no other stems/cups revised. Roughness Ra values of 2 explanted zirconia heads 15.87 and 17.35nm vs. unimplanted zirconia heads of 5.31 and 5.48nm.		(despite advice to avoid high impact).
Glyn-Jones 2008 (Score=6.5)	Hip arthroplasty	RCT	Sponsored by Royal College of Surgeons and Zimmer Inc. No mention of COI.	N=52 patients underwent total hip arthroplasty.	Mean age: 67.5 years; 26 males, 26 females.	Standard UHMWPE Trilogy liner group (n=26) vs. Longevity HXLPE liner group (n=26).	No mention of follow-up.	Total penetration rates in HXLPE group was 0.31±0.18 mm and UHMWPE group was 0.39±0.21 mm. No difference was found significantly between the two groups after two years (p=0.16).	"[H]XLPE has a 40% lower wear rate as compared with UHMWPE, suggesting that it will perform better in the long term."	Data suggest HXLPE has about a 40% lower wear rate compared to UHW
Laupacis 2002 (score=6.5)	Hip arthroplasty	RCT	Sponsored by Medical Research Council of Canada (currently Canadian Institutes of Health Research). No COI.	N = 250 Hip OA	Mean age: 64 years; 130 males, 120 females	Same population and study as above	Yearly follow-up for 10 years	Thirteen revisions if cemented; 6 if uncemented (p = 0.11). More femoral components revised if cemented (12 vs. 1, p = 0.0002). Post-op scores 6-minute-walk test (m): 3 months: 327; 6 months: 363; 1 year: 386; 2 years: 408. Western Ontario and McMaster University Osteoarthritis Index (points): 3 months: 0.9; 6 months: 0.8; 1 year: 0.6; 2 years: 0.7.	"[T]he group that had the cemented Mallory-Head hip prostheses required more revisions of the femoral component than did the group with the cementless Mallory-Head prostheses, which was perhaps related to the titanium-alloy femoral stem."	Results may be confounded by titanium stems that may have produced failures.

Onsten 1994 (score=6.5)	Hip arthroplasty	Crossover trial	Sponsored by The Malm City Research Foundations, The Lund University Foundations. and the Greta and Johan Kock Foundations. No COI.	N = 21 OA	Mean age: 69 years; 6 males, 15 females	Charnley acetabular components inserted with cement (n=21 hips) vs. porous Harris-Galante acetabular components inserted without cement, one in each hip (n=21 hips).	23-48 months	No significant difference between two designs in regards to migration; 0.2mm for both (p = 0.98) along transverse avis, 0.3mm for both (p = 0.75) along longitudinal axis, 0.3mm for Harris-Galante and 0.2mm for Charnley (p = 0.06) along sagittal axis.	"After short to medium-term follow up, there no major difference between the two designs for skeletal fixation."	No differences, but small sample size.
Flivik 2006 (score=6.5)	Hip arthroplasty	RCT	Sponsored by Swedish Medical Research Council, Stiftelsen för bistånd åt rörelsehindrade i Skåne, Region Skåne and the Medical Faculty of Lund University. No mention of COI.	N = 50 OA	Mean age: 68 years; 29 males, 21 females	Removal of at least 75% of subchondral bone plate (n=25) vs. retained other than ream to slight bleeding surface (n=25). All Opticup, Palacos with gentamicin cement, Optivac vacuum mixing system, and cement gun.	3, 6 months, 1 year, 2 years	Polyethylene wear proximal penetration 0.33±0.14 vs. 0.36±0.18mm (p = 0.42). Cups rotated more horizontally in the retention group.	"Removing the subchondral bone plate, where possible, improves the cement-bone interface without jeopardizing the stability, implying better long-term cup survival. However, it is a more demanding surgical technique."	Suggests subchondral bone removal may be superior, but long term outcomes lacking.

Kim 2003 (score=6.5)	Hip arthroplasty	RCT	No sponsorship or COI.	N = 98 Osteonecrosis of the femoral head; simul-taneous bilateral THA and unilateral THA	Mean age: 47.3 years; 80 males, 18 females	Simultaneous bilateral total hip arthroplasty with cemented stem in 1 hip and cementless stem in other (n=50) vs. unilateral total hip arthroplasty with cementless stem (n=48)	preoperatively; 6 weeks; 3, 6, and 12 months; and yearly thereafter	Linear wear cemented 1.15±0.6 vs. cementless 0.69±0.57mm. Volumetric wear 438.77±228.08 vs. 262.98±218.17mm3. Wear per year 0.22±0.12 vs. 0.14±0.12mm (p = 0.23). Radiolucent lines <1mm in 14% vs. 5%.	"Although there was no aseptic loosening of the components, a high rate of linear wear of the polyethylene liner and a high rate of osteolysis in these high-risk young patients remain challenging problems."	Appears to be subset of Kim 2002 population. Suggests long term outcomes may be poorer than other studies, possibly young age and/or other osteonecrosis-related factors.
Flivik 2004 (score=6.5)	Hip arthroplasty	RCT	Sponsored by the medical faculty of Lund University, The Swedish Medical Research Council (Vetenskapsrådet), and Stiftelsen fo¨r bistånd åt ro¨relsehindrade i Skåne. No mention of COI.	N = 14 Primary coxarthrosis	Mean age: 70 years; 7 males, 7 females	Pressurized cement with conventional pressurizer (n=7) vs. sequential method including individual pressurization of each anchorage hole (n=7).	No mention of follow up.	An average peak pressure of 858mm Hg for sequential technique, while 478mm Hg for subsequent compressor. Cement tap penetration wider with sequential (14.6 vs. 10.3mm, p = 0.03). Penetration depth superior as well (2.8 vs. 0.65mm, p <0.001).	"Conventional methods for cement pressurization in the acetabulum may not be optimal."	Suggests pressurizing each anchorage hole is superior. Only an immediate post-operative study and no short of long term clinical follow-up.
Hallan 2006 (score=6.5)	Hip arthroplasty	RCT	Sponsored by Biomet Merck. COI: One or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article. In addition, benefits have been or will be directed to a	N = 57 64.9% OA, 21.1% post-trauma, 15.8% RA	Mean age: 74 years; 12 males, 46 females	Palamed G (n=27) vs. Palacos R cements (n=30); all Charnley prostheses	Post-operation, 3, 6, 12, 24 months	Mean subsidence Palamed G 0.18mm vs. Palacos R 0.21mm and mean internal rotation 1.7º vs. 2.0º at 2 years. No statistically significant differences.	"Both bone cements provided good initial fixation of the femoral component and good clinical results at two years."	No differences between the 2 cements.

			research fund, foundation, educational institution, or other non-profit organisation with which one or more of the authors are associated.							
Schauss 2006 (score=6.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 130 THA due to hip OA	Mean age: 73 years; 40 males, 90 females	Degradable cement restrictor (Biostop G) (n=60) vs. non-degradable cement restrictor (Allopro) (n=62).	3 months	Median cement plug length 27mm in biodegradable restrictor group vs. 15mm non-degradable restrictor group. 53% non-degradable restrictors and 64% degradable restrictors graded normal sized. 26% of non-degradable restrictors classified as undersized vs. 15% of degradable restrictors.	"The results indicate insufficient intramedullary plug fixation of the degradable restrictor probably due to the elastic material properties which also may lead to inferior precision in restrictor size choice."	Pressurizing is important to cement quality and migration of restrictors reduces quality.
Freund 2003 (score=6.5)	Hip arthroplasty	RCT	No sponsorship. No mention of COI.	N = 70 Primary cemented hip replacement	Mean age: 67 years; 40 males, 29 females	Polyethylene (n=35) vs. Shuttle Stop (degradable) (n=34)	2 years	At 3 months, Shuttle Stop with 8 distortions or plug displacements and 13 cement leakages vs. 0 distortions/plug displacements and 3 with cement leakage in polyethylene group ($p < 0.01$). At 3 years, 2 failures and 1 probable loosening in Shuttle stop vs. no failures and 1 loosening in polyethylene group.	"We cannot recommend the Shuttle Stop for femoral canal sealing in total hip replacement."	Suggests biodegradable inferior.

Faris 2006 (score=6.0)	Hip arthroplasty	RCT	No sponsorship or COI.	N = 407 Unclear diagnoses	Mean age: 73.5 years; 128 males, 279 females	Acetabular cups (Biomet) with cement spacers made from polyethylene (n=198) vs acetabular without polyethylene spacers (n=209).	1, 3, 5, 7, 9 years	Radiographic failures with 12.6% vs. without spacers 7.2% (p<0.038). Cup revisions in 2 (1%) versus 1 (0.5%) (NS). Radiolucency in any zone in 48 vs. 35.	"Acetabular cups with polyethylene spacers were found to have a significantly higher initial rate of failure (p<0.038) when compared with cups without cement spacers. Yet, polyethylene spacers resulted in a significantly thicker and more uniform cement mantle in zones 1, 2, and 3 (p<0.0001)."	Unclear whether spacers result in superior outcomes as results conflict within this study.
Baad-Hansen 2011 (Score=6.0)	Hip arthroplasty	RCT	Sponsored by Zimmer, Warsaw, Indiana. No mention of COI.	N=60 patients with primary osteoarthritis.	Median age: 62 years; 34 males, 26 females.	Intervention Monoblock cup group (n=30) vs. intervention Trilogy cup group (n=30).	Follow-up at 2 years.	Significant difference was found between Monoblock cup group and Trilogy group with transverse axis (p=0.04); the mean value for Monoblock was -0.01 (95%CI:-0.11 to 0.12) and Trilogy -0.6 (95%CI: -0.72 to -0.48).	"[P]romising early results concerning fixation of trabecular metal components to the acetabular host bone."	Data suggest preliminary results of study warrant further investigation but are promising.
Röhrl 2004 (score=6.0)	Hip arthroplasty	RCT	Sponsored by Smith & Nephew, Memphis, TN. No mention of COI.	N = 81 OA	Mean age: 56 years; 42 males, 39 females	Press-fit only (PF) (n=21) vs. press-fit and HA coating (PF+HA) (n=22) vs. press-fit and 3 screws (PF+screws) (n=22) vs. press-fit and 3 pegs placed similar to	2, 12, 24, 60 months	HA-coated cups had fewer radiolucent lines (p <0.003) than other groups. Most lines were in zones II and III. Cups augmented with screws and pegs had lines in 19% of the interfaces versus 9% in cups with no holes (PF and PF +HA).	"Screws or pegs did not improve the fixation of press-fit hemispherical cups. Sealed cups and HA coating resulted in fewer radiolucencies and better interface without any tradeoffs."	Suggests hydroxyapatite-coated cups superior than others for cementless fixation with 5 years follow-up.

						screws (PF+pegs) (n=22). All Reflection cups.				
Motobe 2004 (score=6.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 35 OA, RA and femoral neck fracture, all <55 years	Mean age: 77.7 years; 8 males, 27 females	Femoral component inserted with or without cement; Endogenous cannabinoids inserted using a conventional cementing technique (n=16) vs. insertion without cement (n=19).	No mention of follow-up.	Sixteen patients in cemented group had a sudden decrease in systolic blood pressure of more than 20% at 2 minutes after prosthetic insertion vs. none in non-cemented group ($p = 0.0015$). Sudden decrease in diastolic blood pressure also differed significantly at 2 minute interval ($p < 0.05$). Significant difference in anandamide (ANA) and 2-arachidonylglycerol (2-AG) levels ($p < 0.05$).	"We have demonstrated for the first time significant increases in levels of ANA and 2AG, members of a newly identified class of neurohumoral vascular mediators, in the course of cemented hip cement arthroplasty. This observation strongly suggests that ANA and 2AG are mediators of the hemodynamic variables associated with bone cement implantation shock. Therefore, targeting of the biosynthesis of, specific receptors for and biological degradation systems of endocannabinoids might be useful as new strategies for the prevention and clinical management of BCIS."	Study suggests endogenous cannabinoids are important vascular mediators, released by bone cement. A preventive therapy is unclear.

Girard 2006 (score=6.0)	Hip arthroplasty	RCT	No mention of sponsorship. No COI.	N = 104 Unilateral or mild bilateral OA, also had 16 patients with dysplasia or Perthe's disease	Mean age: 47.5 years; 65 males, 39 females	Total hip arthroplasty (CLS Spotorno, Metasul, Allofit, Zimmer) (n=55) vs. hip resurfacing (Durom, Zimmer) (n=49).	No mention of follow-up.	Horizontal center of rotation reconstructed in 60% THA vs. 84% SRA groups to within ±3mm of contralateral side. Mean vertical location not different (p = 0.74). Mean post-op femoral offset increased 5.1mm in TWH vs. decreased 3.3mm SRA groups (p = 0.0001). Leg length increased in THA vs. SRA groups with 60% normalized in THA vs. 86% in SRA (p = 0.002).	"The radiological parameters of acetabular reconstruction were similar in both groups. Restoration of the normal proximal femoral anatomy was more precise with SRA (surface replacement arthroplasty)."	Baseline BMI higher in THA group (p = 0.06). Data suggest comparable immediate post-surgical results, however no intermediate or long term follow-up.
Repantis 2015 (Score=6.0)	Hip arthroplasty	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=90 patients with unilateral hip osteoarthritis.	Mean age: 67.3 years; 20 males, 70 females.	Zweymuller-Plus total hip arthroplasty with minimally invasive approach group (n=37) vs. Zweymuller-Plus total hip arthroplasty with conventional approach group (n=43).	Follow-up at 4 years.	After the surgery, visual analog scale scores improved in the two groups: minimally invasive approach group showed significant lower pain score VAS=0.97±1.4 (p=0.013). The Bicon cup inclination angle showed no difference in the two groups (p=0.517).	"The present prospective randomized study revealed no significant mid-term clinical and functional benefit for patients who underwent a THA through an MIS in comparison with those who were managed with a conventional open approach."	Data suggest no benefit from minimally invasive approach vs. standard approach.

Thanner 2000 (score=5.5)	Hip arthroplasty	RCT	Sponsored by Swedish Medical Research Council; Ingabritt and Arne Lundbergs Research Foundation; and Zimmer International. No mention of COI.	N = 62 Hip replacement	Mean age: 56 years; 32 males, 30 females	Trilogy cup with 3 cluster holes (n=30 hips) vs. Trilogy cup without 3 cluster holes (n=34 hips).	7 days post-op, 3, 6, 12, 24 months	Cups without screw fixation had fewer radiolucent lines on the AP radiographs (p = 0.04) at 1-2 years. There were no differences at 2 years.	"Our results confirm earlier reports that screws are not necessary for additional cup fixation. Additional screw fixation may be considered in cases with poor bone stock."	Screws for acetabular fixation appear unnecessary.
Lachiewicz 2008 (score=5.5)	Hip arthroplasty	RCT	Sponsored by one or more of the authors received, in any one year, outside funding or grants in excess of $10,000 from Zimmer, Inc. COI: one or more of the authors or a member of his or her immediate family received, in any one year, payments or other benefits in excess of $10,000 or a commitment or agreement to provide such benefits from a commercial entity (Zimmer). Also, a commercial entity (Zimmer) paid or directed in any one year, or agreed to pay or direct, benefits in excess of $10,000 to the Department of Orthopaedics, University of North Carolina, with which one or more of the authors, or a member of his or her immediate family, are affiliated or associated.	N = 201 patients withTHA	Mean age: 71.5 years; no mention of sex.	Polished (Ra, 0.18 to 0.3 nanometer) (n=113 hips) vs. precoated roughened (Ra, 1.8 to 2.3 nanometer) cemented femoral component with similar geometry (n=106 hips).	1, 2, 3, 4, 5, 6, 7 years	No significant differences (log rank p = 0.66) in survival. Three hips with polished component had periprosthetic fractures; 2 precoated roughened components revised due to loosening. No significant differences in Harris hip scores.	"Kaplan-Meier survival analysis showed no significant difference between two types of cemented femoral components with similar geometry but substantially different surface finished at seven years."	No evidence favoring smooth vs. rough finishes.

Smolders 2011 (Score=5.5)	Hip arthroplasty	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=71 patients underwent hip arthroplasty	Median age: 58.5 years; 42 males, 29 females.	Resurfacing hip arthroplasty group (n=38) vs. conventional metal-on-metal hip arthroplasty (n=33).	Follow-up at 12 and 24 months.	Before the surgery, conventional metal-on-metal group showed lower UCLA activity score. Postoperatively, the median UCLA activity score of resurfacing group was better in 6, 12 and 24 months (p=0.01; p=0.002; p=0.04).	"R patients scored higher on UCLA, OHS, and satisfaction at some time points; however, as for the UCLA, preoperative levels were already in favor of R. The differences, although statistically significant, were of minor clinical importance."	Data suggest minor clinical differences between hip resurfacing group versus metal-on-metal hip arthroplasty group at 6,12, and 24 months post-operatively.
Garellick 1999 (score=5.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 410 hips underwent THA	No mention of age or sex.	Charnley (n=206) vs. Spectron prosthesis (n=204)	1, 3, 5 to 6, and 10 years	17% of Charnley stems in varus positions. On lateral view, 73% angled posteriorly, resulting in high frequencies of implant-bone contact in zones 3, 8; 12. 45% of Spectron stems angled posteriorly. At every follow-up, significantly ($p < 0.001$) increased calcar resorption for Spectron vs. Charnley. 23 Spectron Metal-Backed cups considered radiographically loose. 10 Charnley stems classified as mechanical failures and four cups radiographically loose. Cement mantle quality only variable associated with stem loosening ($p = 0.007$).	"[U]se of a cemented metal-backed cup should be avoided, at least when combined with larger femoral heads. We found a decreased failure rate for the longer and collared Spectron stem compared with the uncollared and shorter Chanley."	High dropouts with 154 patients deceased at 10 year follow-up. Suggests Charnley inferior.

Pitto 1999 (score=5.5)	Hip arthroplasty	RCT	Sponsored by Doktor Robert Pfleger Foundation, Bamberg, Germany. No COI.	N = 60 OA	Mean age: 65 years; 24 males, 36 females	Arthroplasty without cement (Group 1) (n=20) vs. conventional cementing (plus bone plug) (Group 2) (n=20) vs. bone vacuum cementing (methyl-methacrylate plug) (Group 3) (n=20). Palacos R cement used.	No mention of follow-up	Shorter duration of surgery in uncemented (58±12 vs. 71±22 vs. 77±16 minutes, p <0.05). Embolic events in 15% vs. 10% in group 2 had grade 2 embolic events. Duration of embolic events also shorter in uncemented (Grade 1: 4±3 vs. 8±6.5 vs. 7±3 sec, p <0.05. Grade 2: None vs. 11±4 vs. 4).	"…[S]evere embolic events and intraoperative pulmonary impairment are common when a femoral component is fixed with use of a conventional cementing technique. The results clearly demonstrated a low risk of embolism during total hip arthroplasty when the femoral component was fixed without cement and when it was fixed with the bone-vacuum cementing technique."	More embolic events with conventional cementation versus bone-vacuum or no cementing. Used different plugs.
Garneti 2004 (score=5.5)	Hip arthroplasty	RCT	No sponsorship. No mention of COI.	N = 50 OA	Mean age: 68.6 years; no mention of sex.	Bolus 10mg/kg of intravenous tranexamic acid (n=25) vs normal saline at anesthesia (n=25).	48 hours	No significant difference in blood loss from femoral canal, peri-operative bleeding, and post-op hemoglobin. Tranexamic acid group required more transfusions.	"The results of this study do not support the routine use of tranexamic acid in primary total hip arthroplasty."	Tranexamic acid appears unhelpful. Blinding not well described.
Nelissen 2005 (score=5.5)	Hip arthroplasty	RCT	Sponsored t by Stryker, Howmedica, Kalamazoo, MI. No mention of COI.	N = 39 THA	Mean age: 71± 5.8 years; no mention	Simplex P cement (n=22 hips) vs. Simplex AF cement (n=19); all Exeter prostheses	1, 6 weeks, 3, 6 months, 1 year, 2 years	No differences in translation or rotation migration. Subsidence of stem at 2-year follow-up was 1.1 +/ - 0.56 mm for Simplex AF cement vs. 1.5 +/- 1.00 mm for Simplex P (NS). No significant	"2 acetabular cups in the Simplex AF group (almost 10%) were revised because of mechanical loosening. Because of these findings, we suggest caution before using this new high-viscosity	Methods details sparse. Suggests very high viscosity may result in loosening, though results are not significant.

					of sex.			correlation between minimum and maximum cement mantle thickness around components.	bone cement for fixation of acetabular components."	
Nysted 2014 (Score=5.5)	Hip arthroplasty	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=90 hips with osteoarthritis.	Mean age: 54 years; 33 males, 57 females.	ABG-I anatomical stem group (n=43) vs. unique femoral stem group (n=47).	Follow-up at 5 years.	Mean Merle d'Aubigne score increase from 11 to 17 points in ABG-I group and 10 to 17 points in unique group after 5 years. Mean pain score decreased from 6.5 to 1.1 in ABG-I group and 6.5 to 1.0 in unique group after 5 years..	"No improvement in long-term stability was found from using a customized stem design. However, no patients with abnormal geometry of the upper femur were included in this study."	Data suggest lack of efficacy from customized cementless femoral stem use.
Salemyr 2015 (Score=5.5)	Hip arthroplasty	RCT	Sponsored by ÅkeWiberg Stiftelse, Ulla and GustafUgglas Stiftelse, Sven Norén Foundation, Loo and Hans Ostermans Stiftelse, Stockholm County Council and Karolinska Institutet. The authors declared no conflict of interest.	N=51 patients with primary osteoarthritis.	Mean age: 62 years; 22 males, 29 females.	Patients received allocated treatment with porous titanium cup group (n=25) vs. patients received allocated treatment in control group (n=26).	Follow-up at 12 and 24 months.	Bone mineral density was restored after intervention, difference was -1.5% (p=0.483; 95%CI: 2.8 to-5.9). Higher BMI related to lower demineralization (p=0.007).	In this prospective randomized controlled trial on a new porous titanium cup we found, compared to the control group, no clinically relevant differences regarding periacetabular bone preservation, implant fixation or clinical outcome up to two years postoperatively.	At 2 years post op, data suggest similar efficacy.

McCaskie 1997 (score=5.5)	Hip arthroplasty	RCT	No mention of sponsorship. No COI.	N = 31 THR	No mention of age or sex.	Finger-packing (n=15) vs. cement-gun technique femoral canal before cementing (n=16).	No mention of follow-up.	Maximum pressure in cement insertion mean ± SD: Finger 96.4±15.9; gun 118.3±48.7. Oxygen saturation -4.5±4.9% vs. 0.78±0.97 (p = 0.006).	"Gun technique produced the highest pressure peaks and mean pressure. These results support that gun method promotes better interlock."	Higher pressures associated with gun use, but both better cement and less hypoxemia with gun use.
Berger 1997 (score=5.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 60 THA	No mention of age or sex.	Femoral component inserted with (n=31) vs. without distal centralizing device (PMMA) for primary hybrid total hip arthroplasty (n=29)	No mention of follow-up.	Prostheses of centralizer group valgus mean of 0.2°±1.2°. Range of angles 2.7° for valgus, 2.7° varus. Prostheses of uncentralizer group varus mean of 1.5°± 1.7°. Range of 2.6° of valgus to 5.6° of varus. 21% of centralizers vs. 16% of uncentralizers showed voids. Fewer cement mantle deficiencies with vs. without centralizer (p <0.001).	"Decreased incidence of cement mantle deficiencies and a more neutral prosthetic alignment four with distal centralizing device."	Centralizing device use improved overall cementing quality, but did not reduce voids.
Nivbrant 1999 (score=5.0)	Hip arthroplasty	RCT	Sponsored by the Swedish Medical Research Council MFR K98-17x-07941-12c and Anatomica Sweden and Biomet. No mention of COI.	N = 40 OA	Mean age: 67 years, 16 males, 24 females	Cemented Scientific Hip Prosthesis (SHP) (n=20) vs. Lubinus SP2 prosthesis (n=20).	Pre-operation, 2 years	Three-dimensional wear at 2-year follow-up (mean, 95%CL): SP2: 0.3, 0.1 vs SHP: 0.4, 0.1 (p = 0.05). Results of radiographic evaluation, median (range) for radiolucent lines stem post-op: SP2: 5 (0-16) vs. SHP: 6 (0-27) (p = 0.02).	"The subsidence of the SHP stem is the most pronounced so far recorded with radiostereometry in stems without a completely polished surface. This subsidence and the rotational instability imply a substantial risk of abrasive wear and increased stresses in the cement mantle."	Suggests lubinus prosthesis superior.

Christie 1995 (score=5.0)	Hip arthroplasty	RCT	No mention of sponsorship. No COI.	N = 24 All femoral neck fractures	Mean age: 72.9 years; 5 males, 19 females	Minimal washout of the medullary canal before cement insertion (n-=12) vs. extensive washout by allocation of alternate cases to groups (n=12).	No mention of follow-up.	Grade 3 or 4 maximal embolic responses of 50% in lavage group vs. 91.7% in control, p <0.05. Mean duration embolic response 270.4 vs. 421.9 sec, p <0.05. Mean number large emboli 2.3 vs. 7.1, p <0.05. Mean fall end-tidal CO2 1 vs. 5.5mmHg, p <0.05.	"We consider that thorough lavage should be an essential part of the preparation of the proximal femur before cement insertion."	Thorough lavage appears important.
Hermann 2016 (Score=5.0)	Hip arthroplasty	RCT	Sponsored by the Danish Rheumatism Association. The authors declared no conflict of interest.	N=80 patients with osteoarthritis.	Mean age: 70.4 ± 7.6 years; 28 males, 52 females.	Intervention group with supervised preoperative progressive explosive RT program (n=40) vs. control group with standardized preoperative preparation (n=40).	Follow-up at 10 weeks, 3 months.	Comparing to the control group, the intervention group showed 10 points higher for HOOS-ADL function score (p<0.001, 95%CI: 4.7-15.3), and effect size was 0.8 (95%CI:0.3-1.3).	Progressive explosive-type RT was feasible in the included group of hip OA patients scheduled for THA and resulted in significant improvement in self-reported outcomes and increased leg muscle power.	Usual care bias. Data suggest improved self-reported outcomes including more leg muscle power in progressive explosive RT group.
Digas 2005 (score=5.0)	Hip arthroplasty	RCT	Sponsored by m the Swedish Research Council, Tecres S.p.A. Italy and the Göteborg Medical Society and Smith & Nephew. No mention of COI.	N = 90 95.6% OA	Mean age: 70 years; 19 males, 71 females	Same as above	0-5 years	Between post-op follow-up and 2-year follow-up, bone close to fluoride cement showed no significant changes (p >0.1). Uncemented sockets had reduction in bone mineral density in regions 1-3 (-3 to -17%, p = 0.001-0.04). Decrease post-op year	Use of fluoride cement did not influence the periprosthetic BMD 2 years after the examination. Increased loss of BMD with use of uncemented press-fit cups in the region in which osteolytic lesions are commonly	Addition of fluoride to the cement of no added benefit.

								(p = 0.001-0.01) without certain further changes following year (p >0.2). Cups cemented with Palacos, 14% increase BMD in region 5 (p = 0.02).	found suggests that stress shielding may initiate development of this complication.	
Wykman 1991 (score=5.0)	Hip arthroplasty	RCT	Sponsored by grants from Karolinska Institute's Research Funds, Loo and Hans Osterman Foundation, Ulla and Gustafaf Uggla Foundation, and the Swedish Association against Rheumatism. No mention of COI.	N = 150 76.6%OA, 10% RA	Mean age: 66.1 years; 57 males, 93 females	Cemented [629] (n=75) vs. uncemented (Honnart Patel-Garches) total hip arthroplasty (n=75).	6 months, 1 year, 5 years	At 50 months, durability of prosthetic success 78% Charnley vs. 73% HP-Garches (NS). Probability of prosthesis survival 88% for Charnley vs. 82% (NS). Harris hip score (median) Charnley vs. HP-Garches: pre-op 37.3 vs. 38.1; at 6 months 89.4 vs. 74.3 (p <0.001); most recent evaluation 95.3 vs. 88.7.	"There was no significant difference between the groups at the most recent evaluation. Our findings are not consistent with earlier optimistic expectations on press-fit noncemented total hip arthroplasties."	No clear advantage to cementation.
Digas 2004 (score=5.0)	Hip arthroplasty	RCT	Sponsored by Swedish Research Council, Tecres S.p.A. Italy, Goteborg Medical Society and Smith & Nephew. No mention of COI.	N = 90 95.6% OA	Mean age: 67 years; 21 males, 75 females	Cemex fluoride (n=32) vs. palacos gentamicin cement (n=27) vs. hybrid group (femoral component separately randomized to either cement) (n=37). All	Pre-operation, 2 years	Harris hip score after 2 years 0.24. Pain after 2 years 0.15. Cup translation (mm) medial (+)/lateral (-) mean value: Cemex-F -0.01; Uncemented 0.12; Palacos -0.09 p-value=0.05. Proximal (+)/(-) p-value = 0.79. Anterior (+)/ (-) p-value = 0.72. Cup rotations anterior (+)--posterior (-) tilt p-value = 0.56. Ante- (-	"Appearance of radiolucent lines was almost equal in the two cemented groups. Uncemented cups had less radiolucent lines at 2 years. Fluoride containing cement or uncemented fixation did not improve the early postoperative stability of the socket."	Although more migration of uncemented and less radiolucent lines, no clear advantage of cementing regarding outcomes such as Hip Scores or pain. Fluoride issues addressed in "Miscellaneous" section below.

						Spectron stems. Whole polyethylene Reflection and press-fit Trilogy cups.		)/retroversion (+) p-value 0.66. Increase (+)/decrease (-) of the inclination mean value: Cemex-F -0.09; Uncemented 0.23; Palacos -0.21, p = 0.14.		
Reigstad 1993 (score=5.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 120 OA	Mean age: 64.5 years; 32 males, 87 females	Cemented Landos Titane (n=60) vs. uncemented Zweymüller/ Endler (n=60).	4 months, 1, 2, 3, 4, 5 years	Frequency of ectopic bone formation around 2 types of prostheses varied insignificantly after 5 years. Woman with uncemented protheses developed more bone atrophy (p = 0.03) and cortical hypertrophy (p = 0.04). Cemented vs. uncemented cases that did not develop bone atrophy: after 1 year 19 vs. 25; after 5 years 12 vs. 18. Cortical hypertrophy free cases: after 1 year 58 vs. 37; after 5 years 52 vs. 22 (p <0.05).	"The age and body weight of the patients and the stem size did not affect the bone changes, but woman with uncemented stems developed more bone atrophy than did men."	Two major variables different between groups (type and cement), which limits strength of conclusions.
Brodner 2003 (score=5.0)	Hip arthroplasty	RCT	Sponsored by Centerpulse Orthopedics. No mention of COI.	N = 100 OA or osteonecrosis	Mean age: 60.2 years; 30 males, 70 females	Hip arthroplasty Alloclassic without cement treated with a metal-on-metal articulation (n=50) vs. ceramic-on-	Preop, 3, 6 Weeks, 3, 6 Months, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 Years	Serum cobalt median prep 0.15 vs. 0.15µg/L. At one year, 1 vs. 0.15. At 5-years 0.7 vs. 0.15.	"Systemic cobalt release from Metasul metal-on-metal articulations was demonstrated throughout 5-year study period. Median serum cobalt concentrations found to be slightly above detection limit and	Clinical significance uncertain as there is no clinical correlate.

						polyethylene bearing (n=50).			remained in a constant range. Serum cobalt concentrations did not reflect a so-called run-in wear period of metal-on-metal articulations."	
Kärrholm 1994 (score=4.5)	Hip arthroplasty	RCT	Sponsored by the Swedish Medical Research Council, the Swedish Society of Medicine, the IngaBritt and Arne Lundberg Research Foundation, the Greta and Einar Asker Foundation, the Goteborg Medical Society, the Ulla and Gustaf af Uggla Foundation, the Doctor Felix Neubergh Foundation, and the Nordiska Samfundet fOr Vetenskap utan DjurforsOk. No COI.	N = 60 OA	Mean age: 53.4 years; 31 males, 33 females	Cemented (n=20) vs hydroxyapatite coated (n=23) vs. porous coated. All titanium (Tifit) (n=21).	Pre-operation, 1 year, 2 years	Migration of shoulder (mm) medial-lateral: cemented 0.1 (0.0-0.4); Hydroxyapatite-Coated 0.1(0.0-0.6); Porous-coated 0.2 (0.0-1.8) p-value <0.05. Migration of tip (mm) medial-lateral: cemented 0.2 (0.0-1.2); hydroxyapatite-coated 0.4 (0.0-4.6); porous-coated 0.5 (0.1-5.4). Post-op roentgenograms varus-valgus position (degrees): cemented 0.2 (-1.5-3.0); hydroxyapatite-Coated -0.2 (-1.7-3.6); Porous-coated -0.33 (-2.7-1.7). P-value cemented vs. porous-coated <0.05.	"No definite conclusions can be drawn from the present study with regard to the method of fixation that will lead to optimum long-term results." Even though the differences between the three fixation types were small, the low frequency of subsidence of the hydroxyapatite-coated implants suggests possibly long-term favorability."	Some baseline difference (e.g., genders) of uncertain significance. Use of titanium may have confounded results.

Pabinger 2004 (score=4.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 22 THR	Mean age: 75 years; no mention of sex.	CPS stem cemented conventionally using 3rd generation cementation technique (n=10) vs. TRIOS cemented using transprosthetic drainage system (n=12).	2, 5, 7 years	Radiolucencies TRIOS/CPS: 2 years 75%/40%. Mean subsidence at 5 years (range) TRIOS/CPS: 4 years 2.29(0.1-8)/1.38 (0.4-2.9).	"Cementing titanium stems of this design cannot be recommended."	No benefit of the transprosthetic drainage system for cementation. However, high rates of subsidence with TRIOS stems.
Howie 2005 (score=4.5)	Hip arthroplasty	RCT	Sponsored by the Royal Adelaide Hospital and Corin Baxter Healthcare Pty. Ltd.	N = 24 Not well described, but appear to be OA and AVN	Mean age: 48.2 years; 15 males, 9 females	Resurfacing (McMinn, Corin) (n=11) vs. total hip arthroplasty (Exeter) (n=13).	Pre-operation, 6 months, 1 year, 2 years	At followup median 8.5y, 8/11 (73%) of resurfaced hips revised to total arthroplasty. Failures due to femoral neck fractures, loosening of acetabular components.	"Although there may be an advantage in bone preservation with resurfacing hip replacement, clinical trials are required to demonstrate it has a midterm success that reasonably approaches that of total hip replacement."	Small trial. Sparse methods and data. Study stopped due at 2 yrs due to surgical failures in resurfaced hips.
Wykman 1992 (score=4.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 19 Cemented THA	Mean age: 68.8 years; 7 males, 12 females	Continuous irrigation with Ringer solution during cement curing (n-11) vs. no irrigation (n=8).	No mention of follow-up.	Among those without irrigation, 9/11 (81.8%) exceeded 44ºC during 2.7 min. With irrigation, 2/8 (25%) exceeded 44ºC for 18s and 46s. Median maximum temperatures: irrigation 40.9 vs. no irrigation 48.8ºC, p = 0.007.	"Continuous water irrigation reduced the amount of heat at the bone-cement interface; median maximum temperature was 41 (37-48) ºC."	No long-term outcomes.

Thanner 1995 (score=4.5)	Hip arthroplasty	RCT	Sponsored by the IngaBritt and Arne Lundberg Research Foundation, Doctor F&ix Neubergh Foundation and the Swedish Medical Research Foundation. No mention of COI.	N = 30 THA	Mean age: 71 years; 8 males, 22 females	Fixation of the prosthesis, using Boneloc (n=14) vs. Palacos with gentamicin (n=16).	3, 6 weeks, 6, 12 months	Cups fixed with Palacos displayed small lateral migration; cups fixated with Boneloc migrated medially (6 weeks, 6 and 12 months; p = 0.03). In group fixed with standard cement, mean proximal-distal migration of stem close to 0 throughout observation period. With Boneloc increasing subsidence recorded especially after 6 months (6 months vs. 12 months; p = 0.03, 6 weeks vs. 1 year; p = 0.002).	The cold-curing cement provided an inferior fixation of both the acetabular and femoral components compared to standard cement.	Boneloc cement appeared inferior.
Thomsen 1992 (score=4.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 77 THA	Mean age: 71.2 years; no mention of sex	Comparison of 3 plugs in THA: 1) bone plug made from femoral head (n=22) vs 2) Richards polyethylene plug (n=29) vs 3) Thackray polyethylene plug (n=23) was 38mm	No mention of follow-up.	The quality of cement packing with Thackray polyethylene plug was significantly better compared to other 2 options (p = 0.02, p = 0.03).	"The Thackray polyethylene plug (38 mm, disc-shaped), with its large and flexible diameter, was best able to seal the femoral canal and produced significantly better cement packing compared to both the autologous bone plug and the Richard polyethylene plug."	Unclear if this is an RCT.

Dienstknecht 2013 (Score=4.5)	Hip arthroplasty	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=134 patients with unilateral total hip arthroplasty.	Mean age: 61.3 years; 60 males, 74 females.	Bauer transgluteal lateral approach group with BMI less than 30 (n=42) vs. MicroHip minimal invasive approach group with BMI less than 30 (n=36) vs. Bauer group with BMI equal or greater than 30 (n=41) vs. MicroHip group with BMI equal or greater than 30 (n=15).	Follow-up at 3 months.	Among the four groups, functional outcome was improved by the end of the follow-up, comparing with the functional status before surgery ($p<0.001$).	"[O]obese patients gain similar benefit from MicroHip THA as do non-obese patients."	Data suggest regardless of THA approach, obese patients have later mobilization longer lengths of stay and worse functional outcomes compared to those with normal BMI.
Amanatullah 2011 (Score=4.5)	Hip arthroplasty	RCT	Partially sponsored by Heraeus Medical GmbH in Germany. One or more of the author have received or will receive benefits for personal or professional use.	N= 312 patients indicated for total hip arthroplasty	Mean age: 52.4 years; 190 males, 122 females.	Patients with ceramic-ceramic articulations (n=166) vs. patients with ceramic-polyethylene articulations (n=146).	Follow-up at 2 and 5 years.	The mean Harris Hip score increased from 43±10 before the surgery to 91±27 postoperatively ($p<0.01$)., but no significant difference was found between the two groups ($p>0.05$). Total intraoperative and postoperative implant fracture incidence was significant in ceramic-ceramic group ($p=0.049$).	"[B]oth ceramic-ceramic and ceramic-polyethylene couples had excellent short-term to midterm clinical results. However, it should be noted that ceramic-polyethylene couples did not offer sufficiently low linear wear rates to theoretically prevent osteolysis in longer-term follow-up."	Data suggest ceramic-ceramic group had significantly higher ceramic implant fracture otherwise, comparable outcomes between groups.

Naresh 1997 (score=4.5)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 226 patients with primary or secondary osteoarthritis of the hip	Mean Age: 64.5 years; 118 males, 108 females.	Patients who received noncemented total hip implants (n = 112) vs patients who received cemented total hip implants (n = 114)	Ranged from 2 to 6 years	Difference of 37% heterotopic ossification for cemented group vs 32% for noncemented, however, this was not significant with p = .87	"There was no significant difference in the prevalence of heterotopic ossification between cemented and noncemented total hip replacements in patients with osteoarthrosis."	Data suggest no significant differences between groups.
Visser 2002 (score=4.0)	Hip arthroplasty	RCT	No sponsorship. No mention of COI.	N = 93 THA	No mention of age or sex.	Biosem II plug (n=32) vs. Cemlock plug (n=28) vs. Thackray plug; all Stanmore prostheses (n=33).	No mention of follow-up.	40/93 (43%) plugs migrated >1cm. Difference in migration between 3 plugs significant (p = 0.001). Biosem plug unstable in 78% (25/32); Cemlock in 32% (9/28); and Thackray 18% (6/33). Leakage of cement below plug most frequent in Thackray group (20 hips). Quantity of cement below plug varied between 0.5 and 4cm.	"Comparing the results, the most stable plug in our study was the Thackray plug; however, the difference with the resorbable Cemlock plug was not significant, with failure in 18% of cases. The Biosem plug was not able to resist the pressure during cementing and was abandoned in our clinic."	Polyethylene plug superior to 2 different biodegradable plugs.
Foucher 2011 (score=4.0)	Hip arthroplasty	RCT	Sponsored by Rush Arthritis and Orthropedic Institute. No COI.	N = 32 subjects scheduled for total hip replacements with a single surgeon and a diagnosis of primary unilateral hip osteoarthritis requiring THA.	Mean Age: 51 years; 27 males, 24 females.	Modified Watson-Jones group (n=16) vs Two-incision group (n=16)	Follow up preop, 3 weeks, 3 months, 6 months, and 1 year.	No significant time-by-incision interactions for any gait parameter between groups (p≥0.591)	"In conclusion, our results confirm and extend recent reports that found no compelling evidence that different MIS approaches result in different patterns of functional recovery. Furthermore, even with minimally	BMI differences between groups data suggest comparable efficacy.

									invasive approaches that seek minimal soft tissue damage during surgery, functional recovery is not complete—normal gait is not fully restored by THA."	
Wembridge 2006 (score=4.0)	Hip arthroplasty	RCT	No sponsorship. No mention of COI.	N = 32 THA	No mention of age or sex.	Ultra-high-molecular-weight polyethylene (Hardinge) (n=15) vs. biodegradable (Amberflex Summit Medical) femoral cement restrictor (n=15).	No mention of follow-up.	Mean migration of Hardinge was 6 times lower (0.5 vs. 3.0cm, p <0.002) than that of the biodegradable restrictor.	"Although there are theoretical advantages in avoiding UHMWPE restrictors, the current biodegradable alternative is actually inferior and its use cannot be endorsed."	Ultra-short term follow-up period of 5 days only.
Kroon 2006 (score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 103 Total hip surgery	No mention of age; 29 males, 74 females	Three intramedullary resorbable cement plugs in vitro and in vivo. (1) SEM II plus (n=37) vs. (2) C-plug (n=31) vs. (3) REX plug (n=35).	No mention of follow-up.	In vitro: C-plug unstable 4 of 5 times, SEM II once and minimal cement leakage 4 times. REX plug stable without leakage. In vivo: 17/37 (45.9%) SEM II migrations within 1cm margin. C plug unstable 23/31 (74.2%). REX plug unstable 16/35 (54.3%). Mean migrations corrected for size: C-plug 3.16±0.46 vs. SEM II	"We do not recommend the use of the C-plug in cemented hip arthroplasty. The REX plug is a promising design; however, insertion problems in vivo lead to disappointing results, so the insertion technique must be improved. The SEM II plug performs well in the case of a short stem and has a reproducible insertion technique."	Most significant variables were type of plug (p = 0.02) and size of plug (p = 0.02). Medium-sized plugs were best.

								1.71±0.46 vs. REX 2.74±0.47.		
Stilling 2009 (score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship. No COI.	N = 28 patients with osteoarthritis of the hip.	Mean Age: 57.9 years; 10 males, 15 females	Received a Ti-coated implant (n=13) vs received an HA-coated implant (n=15)	Follow up between 5.0 – 12.6 years	8 of 14 HA cups were revised vs 2 of 12 Ti cups (p=0.045). Distribution of wear in the HA group (SD=2.6;1.97-10.56 mm) vs Ti group (SD=0.9; 2.51-5.36 mm) (p=0.017)	"Our findings suggest inferior survival of medium thickness spray-dried HA-coated cups with individual cases of excessive PE wear and premature cup failure. These findings apply to first-generation modular cups and may not apply to other cup designs and new HA-coating technologies."	Data suggest inferiority of medium thickness HA coated cups at 15 years.
Nivbrant 2001 (score=4.0)	Hip arthroplasty	RCT	Sponsored by the Swedish Medical Research Council (MFR K97-17X-07941-11B), IngaBritt and Arne Lundberg Reserach Foundation, Doctor Félix Neu- bergh Foundation, Swedish Medical Research Foundation, Tecres S.p.A., Italy, Schering Plough, Sweden and Walde- mar Link, Germany. No mention of COI.	N = 44 Primary arthrosis of the hip undergoing THR	Mean age: 67.5 years; 18 males, 28 females	Fixation with Cemex Rx (n=23 hips) vs. Palacos R cement of both components (n=23 hips).	Pre-operation, 2 years, 5 years	Harris hip score Cemex/Palacos: total 5 years 94/97; pain 5 years 44/44. "Measurements of postoperative bone turnover, metal release and implant migration up to 5 years after the operation showed no significant differences."	"The stems migrated similarly inside the cement mantle regardless of the type of cement used."	Suggests low proportion monomer is not superior.

Carlsson 1993 (score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 226 Hip arthro-plasties	Mean age: 68.1 years; 97 males, 129 females	Low (n=112) vs. high viscosity cement (n=114).	Pre-operation, 2 years, 5 years	Low viscosity cement with 9/112 (8.0%) vs. high viscosity 13/114 (11.4%) with definite or probable loosening. Differences in outcomes with younger more likely to have loosening (p = 0.03) and with posterior approach (p = 0.02).	"No difference was found between cement of high and low viscosity with regard to prosthetic fixation."	High dropouts (126/352 = 35.8%) from original RCT. No control for prostheses types. Variable follow-up length. Surgical procedures and prostheses differed and not controlled. Post-hoc excluded non-OA. Gentamicin both in and not in cement and not randomized. Study flaws limit potential conclusions.
Wegrzyn 2015 (score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship. COI: Royalties from a company or supplier: Zimmer, Pipeline, Mako/Stryker. Speakers bureau/paid presentations for a company or supplier: Zimmer. Paid employee for a company or supplier: American Joint Replacement Registry (AJRR)-Part-time Medical Director. Paid consultant for a company or supplier: Pipeline Biomedical – Medical Advisory Board, Zimmer – Consultant. Unpaid consultants for a company or supplier: Ketai Medical Devices. Stock or stock options in a company or supplier: Pipeline Biomedical, Ketal Medical Devices. Board member/committee	N = 113 patients eligible for primary cementless or hybrid THA with sufficient periacetabular bone stock for peripheral rim fixation.	Mean Age: 59.5 years; 52 males, 34 females.	Cementless monoblock acetabular components made of porous tantalum (n=45) vs porous-coated titanium-alloy (n=41)	Averaged 143 months in the TM group and 145 in the control group.	4% of porous tantalum monoblock cups presented with radiolucent lines vs 33% of porous-coated titanium monoblock cups (p<0.001).	"In conclusion, this RCT confirmed that excellent long-term fixation can be expected with a porous tantalum monoblock cup, which demonstrated 100% survivorship at an average 12 year follow-up, and significantly fewer radiolucencies when compared to a more conventional porous-coated titanium monoblock cup."	Data suggest comparable long term efficacy.

			appointments for a society: Pipeline Biomedical – Medical Advisory Board.							
Incavo 1998 (score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 91 81% OA, 9.9% ON, 5.5% trauma	Mean age: 55 years; 54 males, 37 females	Surface coating in profile femoral prostheses: 1) smooth (n=21) vs. 2) porous coated (n=23) vs. 3) hydroxyapatite (HA) coated (n=24). Multi-center. Full weight-bearing allowed immediately post-op.	24, 48 months	Good/excellent results 19/26 (73%) vs. 20/28 (71%) vs. 22/25 (88%). Harris hip scores favored HA coated (85.1 vs. 89.8 vs. 96.0, p = 0.004 HA vs. smooth) as did functional scores. Pain, ROM, activity scores NS; 3 of 4 with painful femoral loosening had smooth stems. Radiolucent lines 14% vs. 0% vs. 8%. Spot welds 28% vs. 65% vs. 54%.	"Clinical differences exist and are attributable to the type of surface coating used for the cementless femoral components in THA."	HA coated had superior Harris Hip Scores and function. More loosening in smooth stems and poorer results for function suggest smooth stems are inferior.
Kärrholm 2002 (score=4.0)	Hip arthroplasty	RCT	Sponsored by IngaBritt and Arne Lundbergs Foundation, Neubergh Research Foundation, Zimmer USA, Göteborgs Läkaresällskap, and Hallands Läns Landstigs Research Foundation. No COI.	N = 65 OA	Mean age: 59 years; 39 males, 26 females	Epoch reduced stiffness stem (n=28) vs. anatomic stem, both porous coated (n=37).	3 months, 6 months, 1 year, 2 years,3 years	Epoch stem loss of bone mineral significantly reduced at 2 years in Gruen regions 1, 2, 6, 7 (p <0.0005 to 0.04). Significantly more endocortical contact on anteroposterior (p <0.0005) and lateral radiograph (p = 0.02) for Epoch stems. Epoch stems fewer	"Contrary to previous studies of other designs with reduced stiffness, the Epoch stem achieved excellent primary fixation. Despite this rigid fixation, the proximal loss of bone-mineral density was less than that associated with the	Several significant baseline differences present. States stratification on gender, however, genders not equal (p = 0.03). This suggests either protocol violations or randomization failure. Two different surgical approaches used.

								sclerotic lines surrounding stem (p ≤ 0.002) at 2 years post-operatively. No difference for Harris hip score evaluated at same hospital.	stem with a stiffer design."	
Seyler 2006 (score=4.0)	Hip arthroplasty	RCT	Sponsored by Stryker Orthopaedics. COI: one or more of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Stryker Orthopaedics).	N = 210 OA or osteonecrosis	Mean age: 45.5 years; 151 males, 45 females	Stratified enrollments for OA and osteonecrosis. Compared alumina-on-alumina (n=158) vs. cobalt-chromium-on-polyethylene surfaces (n=52).	Preoperative, 6 months, 1, 2, 3, 4, 5, 6, 7, 8 years	Seven-year survival; probability 95.5% for osteonecrotic hips; 89.4% OA with alumina-on-alumina vs. 92.3% ON, 92.9% OA for cobalt-chromium-on-polyethylene. Harris hip scores (baseline/6 months/5 years): ON AA (45.8±12.3/93.8±8.5/97.5±4.0) vs. OA AA (49.7±12.3/95.3±8.5/95.4±10.2) vs. ON CCP (42.2±13.9/90.4±11.4/96.5±8.0) vs. OA CCP (48.81±3.3/95.3±6.6/97.3±4.0), p = 0.85 between groups. No differences complications or revisions.	"The results…were comparable. The low revision rate for the alumina-on-alumina bearing is encouraging and offers a promising option for younger, more active patients who have this challenging disease."	Long-term study of 7 years. Unequal sized groups due to modification of study midway. Data suggest comparable outcomes.
Weissinger 2011 (score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship or COI.	N = 80 patients with primary osteoarthritis or avascular necrosis of the femoral head.	Mean Age: 65.8 years; 26 males, 54	Received a metal-on-metal bearing (n=42) vs received a ceramic-on-ceramic bearing (n=38) in their	Follow up at 2 years.	Median Harris Hip score went from 50.3 to 92 in the metal group vs 52.2 to 91.5 in the ceramic group (p=0.75) Medium level of cobalt in the metal group was 1.2 µg/L vs 0.15 µg/L in the	"Our prospective randomized study showed after two years no difference clinically between the two groups of metal-on-metal and ceramic-on-ceramic bearings with total	Sparse methods. Data suggest similar efficacy.

					females.	total hip replacement		ceramic group (p<0.0001)	endoprostheses of the hip. Although medium serum-cobalt level in the metal-on-metal group with 1,2µ/L is a significant higher value, whereas it lies in the ceramic-on-ceramic group below the detectable limit."	
Parvizi 2016 (Score=4.0)	Hip arthroplasty	RCT	Sponsored by Zimmer. No mention of COI.	N=84 patients with hip end stage arthritis.	Age range: 18-75 years; 32 males, 52 females.	Patients received total hip arthroplasty using direct anterior approach (n=44) vs. patients received total hip arthroplasty using direct lateral approach (n=40).	Follow-up at 6 months, 1 and 2 years.	Functional outcome at 6 weeks to 6 months in direct anterior group showed better performance in TUG, LEFS, and gait speed (p=0.0001; p=0.0267). Also, patients in direct anterior group go back to work and able to drive earlier than direct lateral group (p<0.08; p<0.002).	"It seems that the use of select surgical approaches may confer some benefits in early functional recovery but not in other measured parameters."	Data suggest THA using the DA approach is better for earlier functional outcomes.
Dienstknecht 2014 (Score=4.0)	Hip arthroplasty	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=143 patients with primary hip osteoarthritis.	Mean age: 62 years; 63 males, 80 females.	Patients underwent unilateral total hip arthroplasty with mini-incision approach (n=55) vs. patients underwent unilateral total hip arthroplasty	Follow-up at 3 months.	Micro-hip group indicated lower mean incision length 9.3 cm (p<0.001), lower time of surgery 60 minutes (p=0.021), and lower pain VAS (p<0.05).	"THA through the Micro-hip approach achieved faster pain relief."	BMI Baseline differences in standard vs. micro-hip group (30.1 vs. 27.6) which could bias observed results. Data suggest the mini-incision (micro-hip) approach was associated with faster pain relief probably due to shorter incision.

						with standard lateral transgluteal approach (n=88).				
Corten 2011 (Score=4.0)	Hip arthroplasty	RCT	The authors declared no conflict of interest.	N=250 patients underwent hip arthroplasty.	Mean age: 64 years;	Cementless fixation group (n=126) vs. cemented fixation group (n=124).	Follow-up at 17, and 22 years.	Top hip arthroplasty was influenced by patients' age in younger group (p<0.001). Female patients indicated better cementless total hip arthroplasty survivorship on acetabular and femoral sides (p=0.001).	"The efficacy of future RCTs can be enhanced by randomizing patients in specific patient cohorts stratified to age and gender in multicenter RCTs."	Data suggest that at 17 years follow-up, the cementless fixation device had about ½ as many revisions as the cement device.
Lorenzen 2013 (score=3.5)										Data suggest posterior approach, HRA may result in increased post-op ischemia.
Tiusanen 2013 (Score=3.5)										Sparse methods. Data suggest the 28 mm metal on metal bearings group had higher urine chromium and cobalt concentrations.

Buljan 2012 (Score=3.5)										Data suggest patient convenience would tend to favor weekly erythropoietin.
Kobayashi 2016 (Score =3.5)										Sparse methods. Data suggest teriparatide group showed higher lumbar BMD at 2 years but both meds.

Evidence for the Use of Osteotomy

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Osteotomy; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthritis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 132 articles in PubMed, 152 in Scopus, 98 in CINAHL, 29 in Cochrane Library, 8000 in Google Scholar, and 0 from other sources. We considered for inclusion 25 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 29 articles considered for inclusion, 2 randomized trials and 6 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow -up:	Results:	Conclusion:	Comments:
Borsalino 1987 (score=4.5)	Osteotomy	RCT	No mention of sponsorship or COI.	N=32 patients with degenerative osteoarthritis of the hip.	Mean age: 55.5 years; 9 males, 23 females	Treatment group: (n=16) received an osteotomy vs Control Group: (n=16): received control stimulators	40 and 90 days	Bone callus presence on day 40 was 0.8 in the stimulated group and 0.31 in the control ($p < 0.02$). Presence of trabecular bridging in the lateral cortex was 1.06 for treatment and 0.5 for control ($p < 0.02$). Trabecular bridging at the medial cortex was 1.06 for treatment and 0.5 for control ($p < 0.02$). On day 90, Bone callus on the medial cortex was 1.93 for treatment vs 1.37 for control ($p < 0.05$). Density measure of bone callus was 34.8 for treatment vs 22.5 for control ($p <0.05$). Presence of trabecular bridging in the lateral cortex was 2.47 for treatment and 1.44 for control ($p < 0.001$). Trabecular bridging at the medial cortex was 2.4 for treatment and 1.56 for control ($p < 0.001$)	"In this extremely homogeneous patient population, PEMF stimulation favored osteotomy healing."	Data suggest PEMF favored osteotomy healing in old fractures.
Bong 1981 (score=4.0)	Osteotomy	RCT	No mention of sponsorship or COI.	N = 150 Unstable inter-trochanteric fractures	Mean age: 63.7 years; 87 males, 63 females	Skeletal traction with tibial pin (n=50) vs. medial displacement osteotomy (n=50) vs. valgus osteotomy (n=50)	3 months, 6 months	Percentages of cases with poor results: conservative 26.1% vs. medial displacement osteotomy 14.6% vs. valgus osteotomy 20.5%. 1 non-union in conservative group. 1 AVN in valgus osteotomy.27.2% of operative groups had mechanical failure.	"[S]howed no significant difference between those treated with the Dimon and Hughston osteotomy and those treated by the Sarmiento osteotomy. Conservative treatment of skeletal traction for unstable fracture was found to be well tolerated."	Data suggest superior results with surgery.

Evidence for the Use of Acupuncture Post Arthroplasty

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: acupuncture, acupressure, acupuncture therapy, pharmacoacupuncture, auricular acupuncture, arthroplasty; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 11 articles in PubMed, 1001 in Scopus (went through first 100), 3 in CINAHL, 18 in Cochrane Library, 5600 in Google Scholar (went through first 100), and 0 from other sources. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Of the 6 articles considered for inclusion, 4 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Usichenko 2005 (score=8.0)	Acupuncture Post Arthroplasty	RCT	No mention of sponsorship or COI.	N = 61 THA	Mean age: 67.1 years; 24 males, 30 females	Auricular acupuncture (AA group) (n=29) – needles were inserted at four specific acupunture points ipsilateral to surgery site (lung, shenmen, forehead, hip). vs. Sham (Control Group) (n=25) – non-acupuncture points of the helix ipsilateral to the site of surgery were used.	3 days post-operation	Auricular acupuncture 32% less piritramide vs. control 1st 36 post-op hours (37 vs. 54mg, p = 0.004). Total dose 36% lower (0.54 vs. 0.84 mg/kg, p = 0.002). Time to 1st request lower (40 vs. 25 minutes, p = 0.04).	"(Auricular acupuncture) could be used to reduce postoperative analgesic requirement."	No differences in rates of belief of receipt of real acupuncture.
Usichenko 2006 (score=7.5)	Acupuncture Post Arthroplasty	RCT	No mention of sponsorship or COI.	N = 64 THA	Mean age: 67.5 years; 28 males, 19 females	Auricular acupuncture (AA group) (n=30) – needles were inserted at four specific acupunture points ipsilateral to surgery site (lung, shenmen, forehead, hip). vs. Sham (Control group) (n=27) – non-acupuncture points of the helix ipsilateral to the site of surgery were used.	No mention of follow up.	21% less fentanyl (3.9±1.4 vs. 4.9±1.2, p = 0.005) in acupuncture group vs. sham. 6 in acupuncture group required intraoperative atropine vs. 3 (NS).	"Auricular acupuncture reduced fentanyl requirement compared to sham procedure during hip arthroplasty."	Data suggest mild reduction in fentanyl. No other differences. Considering quality evidence, traditional acupuncture not superior to sham for LBP, arthritis. Study requires replication.
Haslam 2001 (score=3.0)	Acupuncture Post Arthroplasty									Small sample, sparse data. Unclear if controls already had same treatment, thus potentially biased to favor acupuncture. Controls wait listed for arthroplasty; likely biases in favor of intervention.

Fargas-Babjak 1989 (score=2.5)										Intervention group instructed to use maximum intensity tolerated, thus true blinding absent. High dropouts. Pain tools had contradictory responses from same patients on same questions suggesting confusion or misinterpretation. No demonstrated improvements in functional outcomes.

Evidence for the Use of Hip Resurfacing

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hip Resurfacing & Metal on Metal Hip Prostheses; Hip Osteoarthritis controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 139 articles in PubMed, 385 in Scopus, 10 in CINAHL, 6 in Cochrane Library, 121 in Google Scholar, and 6 from other sources. We considered for inclusion 10 from PubMed, 18 from Scopus, 3 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 6 from other sources. Of the 41 articles considered for inclusion, 15 randomized trials and 22 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Garbuz 2010 (score=7.5)	Hip Resurfacing	RCT	Sponsored by the institution of one or more of the authors (DSG, MT, NVG, BAM, CPD) has received funding from Zimmer, Inc. No mention of COI.	N = 104 Patients required to be suitable for hip resurfacing	Mean age: 51.8 years; 93 males, 11 females	Hip resurfacing (Durom) (n=48) vs. large-head arthroplasty (Metasul) (n=56). Durom acetabula both groups; 2 years follow-up.	2 months, 1 years, 2 years	WOMAC pain (pre/mean 1 year): Resurface (48.9/91.5) vs. large head THA (52.4/90.0), NS. Serum cobalt levels rose 46-fold with THA vs. 3.9-fold with resurfacing THA (5.09 vs. 0.51µg/L, p <0.001).	"Due to these excessive high metal ion levels, the authors recommend against further use of this particular large-head total hip arthroplasty."	Data suggest comparable efficacy but serum cobalt levels were elevated 1 year post-op in the large head TH group and these levels continued to increase at a later time intervals.
Costa 2012 (Score= 7.0)	Hip Resurfacing	RCT	Sponsored by the Research for Patient Benefit scheme of the National Institute of Health Research, and University of Warwick and University Hospitals Coventry and Warwickshire NHS trust. The authors declared no conflict of interest.	N=126 severe hip joint arthritis patients underwent hip resurfacing surgery.	Mean age: 56.5 years; 73 males, 52 females.	Resurfacing arthroplasty group (n=60) vs. total hip arthroplasty group (n=66).	Follow-up at 6 weeks, 3, 6, and 12 months.	For postoperative 12 months, no significant difference was found for hip function between treatment group and control group measured by Oxford hip score (p=0.242) and Harris hip score (p=0.070). However, the 95% CIs of treatment group effect were wide, measured by Harris hip score 6.04 (95%CI: -0.51 to 12.58) and Oxford hip score 2.23 (95%CI: -1.52 to 5.98), which inferred to potential clinical effect.	"No evidence of a difference in hip function was seen in patients with severe arthritis of the hip, one year after receiving a total hip arthroplasty versus resurfacing arthroplasty."	Data suggest comparable efficacy between group with no differences in post-operative function.
Peterse n 2011 (Score= 7.0)	Hip Resurfacing	RCT	Sponsored by the Society of Danish Physiotherapists, Forskningsinitiativet Arthus Amt, and SAHVA. The authors	N=30 patients with osteoarthritis scheduled for total hip replacement.	Mean age: 60.5 years; 7 males, 15 females	Patients assigned to hip resurfacing system group (n=11) vs. patients assigned to conventional hybrid prosthesis group (n=11).	Follow-up at 3 months.	Mean differences of step length 0.03m (p≤0.001, 95%CI: 0.1 to 0.4) and stand phase duration 0.7% (p=0.003, 95%CI: 0.3 to 1.1) between surgery group and non-surgery group were significant. Lower power produced by muscles around hip were found in the surgery group	"[G]ait impairment persisted with no differences between the conventional prosthesis	Data suggest comparable efficacy.

			declared no conflict of interest.					(11.9 W) than non-surgery group (p≤0.001, 95%CI: 8.6 to 15.2).	and the resurfacing system."	
Lavigne 2010 (score=7 .0)	Hip Resurfacin g	RCT	Sponsored by One or more of the authors (ML) have received funding from Zimmer, Warsaw, IN. No COI.	N = 48 All with OA and <65yrs, included 14 healthy controls	Mean age: 48.5 years; 37 males, 11 females	Hip resurfacing (Durom) (n=24) vs. large-head total hip arthroplasty (CLS stem) (n=24) Durom acetabula both groups; 1 year follow-up.	3, 6, 12 months	Fast walking speed (m/s) (baseline/3/6/12 months): HR (1.58/ 1.62/1.71/1.82) vs. THA (1.50/1.65/1.68/ 1.73) (NS). No difference in walking speed, step length, cadence, postural balance. Functional reach favored HR.	"(Hip Resurfacing) did not provide better clinical function over large-head THA."	Younger, active population. Data suggest comparable efficacy.
Tice 2015 (Score= 6.0)	Hip Resurfacin g	RCT	Sponsored by CORIN, MicroPORT, MATortho, MEDACTA, and Depuy. The authors declared no conflict of interest.	N=120 patients received cemented or cementless femoral component.	Mean age: 49.4 years; 105 males, 15 females.	Patients assigned to cemented component group (n=60) vs. patients assigned to cementless component group (n=60).	Follow-up at 2 years.	At 6 months and 1 year postoperative, cementless group showed higher BMD than that in cemented group (p<0.05). At 2 years postoperative, cementless group showed insignificant higher BMD (p=0.155).	"The results show better preservation of femoral neck BMD with a cementless femoral component after two years of follow-up."	At 2 years BMD is preserved better in the cementless group.
Venditt oli 2010 (Score= 5.0)	Hip Resurfacin g	RCT	Sponsored by Zimmer in Warsaw U.S.A. The authors declared no conflict of interest.	N=209 hips received hip arthroplasty or hip resurfacing.	Mean age: 50.1 years; 72 males, 137 females.	Total hip arthroplasty group (n=100) vs. hip resurfacing group (n=109).	Follow-up at 36 to 72 months , average 56 months .	WOMAC scores differences was found at 12 and 24 months between THA and HR groups (p=0.007). Scores on different time showed different significance: it is significant between 3 and 6 months (p<0.001), significant between 6 and 12 months (p=0.001), but not between 12 and 24 months (p=0.916).	"Higher early aseptic loosening rate was found in HR and long-term survival analysis of both patient cohorts is necessary to determine whether the potential bone preservation	Patients and treaters not blinded although study claims blinding. Data suggest comparable efficacy at 3 -6 years post with similar reoperation rates. However, at 1-2 years post surgery, WOMAC scores in HR group were statistically better but also

									advantage offers by HR will overcome its earlier higher failure rate."	showed a higher aseptic loosening rate.
Zijlstra 2011 (Score= 5.0)	Hip Resurfacing	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=200 hips	Mean age: 71 years; 41 males, 159 females.	Metal-on-polyethylene group (n=98) vs. metal-on-metal group (n=102).	Follow-up at 5.6 years.	After 5 years, Harris hip score and Oxford score indicated no differences between MP group and MM group (p=0.791).	"[C]emented 28mm metal-on-metal total hip arthroplasty shows no clinical superiority over 28mm metal-on-polyethylene arthroplasty."	Data suggest the clinical performance is similar at 5 years post intervention between the 2 groups.
Girard 2006 (score=4.5)	Hip Resurfacing	RCT	No mention of sponsorship. No COI.	N = 104 Unilateral or mild bilateral OA, also had 16 patients with dysplasia or Perthe's disease	Mean age: 47.5 years; 65 males, 39 females	Total hip arthroplasty (CLS Spotorno, Metasul, Allofit, Zimmer)(n=55) vs. hip resurfacing (Durom, Zimmer)(n=49)	No mention of follow-up.	Horizontal center of rotation reconstructed in 60% THA vs. 84% SRA groups to within ±3mm of contralateral side. Mean vertical location not different (p = 0.74). Mean post-op femoral offset increased 5.1mm in TWH vs. decreased 3.3mm SRA groups (p = 0.0001). Leg length increased in THA vs. SRA groups with 60% normalized in THA vs. 86% in SRA (p = 0.002).	"The radiological parameters of acetabular reconstruction were similar in both groups. Restoration of the normal proximal femoral anatomy was more precise with SRA (surface replacement arthroplasty)."	Baseline BMI higher in THA group (p = 0.06). Data suggest comparable immediate post-surgical results, however no intermediate or long term follow-up. Data suggest SRA allows for more precision in restoration of femoral anatomy compared to THA.
Howie 2005	Hip Resurfacing	RCT	Sponsored by the Royal Adelaide Hospital and Corin	N = 24 Not well described,	Mean age: 48.2 years; 15	Resurfacing (n=11) (McMinn, Corin) vs. total	Pre-operation, 6	At followup median 8.5y, 8/11 (73%) of resurfaced hips revised to total arthroplasty. Failures due to femoral	"Although there may be an advantage	Small trial. Sparse methods and data. Study stopped due

(score=4.5)			Baxter Healthcare Pty. Ltd.	but appear to be OA and AVN	males, 9 females	hip arthroplasty (Exeter): (n=13)	months, 1 year, 2 years	neck fractures, loosening of acetabular components.	in bone preservation with resurfacing hip replacement, clinical trials are required to demonstrate it has a midterm success that reasonably approaches that of total hip replacement. "	at 2 yrs due to surgical failures in resurfaced hips.
Venditt oli 2006 (Score= 4.5)	Hip Resurfacin g	RCT	No mention of sponsorship or COI.	N=210 hips with degenerative hip joint disease.	Mean age: 49.8 years; 137 males, 73 females.	Total hip arthroplasty with uncemented titanium tapered stem and acetabular component, and 28 mm metal on metal bearing (n=103) vs. hybrid metal on metal surface replacement arthroplasty (n=107).	Follow-up at 6, 40 months.	WOMAC score and Merle d'Aubigne-postel scale showed no significant difference between THA (p=0.363) and SRA (p=0.942) groups. UCLA activity score showed difference between THA (6.3) and SRA (7.1) groups (p=0.037).	"Both techniques present different types of complications but similar rates of overall occurrence of complications. Surface replacement arthroplasty has a clear benefit over THA in proximal femoral bone preservation,	Data suggest accelerated recovery in SRA group with femoral bone preservation compared to THA.

									but the long term survivorship of the SRA will determine the real value of this advantage."	
Venditt oli 2006a (Score= 4.5)	Hip Resurfacin g	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=210 hips with degenerative hip disease.	Mean age: 49.8 years; 137 males, 73 females.	Resurfacing arthroplasty group (n=107) vs. total hip replacement group (n=103)	No mentio n of follow-up.	Between the groups used component 54.9mm for resurfacing and 54.74 mm for total hip replacement, no significant difference was found (p=0.77) acetabular component showed no difference among the groups of different surgeons (p=0.89). For male, acetabular component size was larger (p<0.0001), and significantly correlated to BMI (p=0.016).	"[W]ith a specific design of acetabular implant and by following a careful surgical technique, removal of bone on the acetabular side is comparable with that of total hip replacement. "	Baseline BMI differences (29.6 vs. 27.2). Data suggest acetabular bone resurfacing is comparable to THA.
Penny 2013 (Score= 4.5)	Hip Resurfacin g	RCT	Sponsored by Danish Ministry of the Interior and Health. The authors declared no conflict of interest.	N=71 patients underwent resurfacing hip arthroplasty.	Mean age: 58 years; 45 males, 26 females	Patients assigned to resurfacing hip arthroplasty group (n=20) vs. Standard total hip arthroplasty (n=34) vs. large head total hip arthroplasty group (n=17).	Follow-up at 2 years.	After 2 to 6 months, range of motion improved to 13 degrees with large articulations comparing with standard hip arthroplasty, but not significant (p=0.5). After 2 years, the total range of motion were within 9 degrees, but not statistically significant (p=0.6).	"Head size had no influence on range of motion. The lack of restriction allowed for large articulations did not improve the clinical and	At 2 years, data suggest comparable efficacy.

									patient–perceived outcomes. The more extensive surgical procedure of RHA did not impair the rehabilitation. ”	
Venditt oli 2013 (Score= 4.0)	Hip Resurfacin g	RCT	Sponsored by Zimmer, Warsaw, Indiana. The authors declared no conflict of interst.	N=219 hips with degenerative hip joint disease.	Mean age: 50.1 years; 147 males, 72 females.	Total hip replacement group (n=100) vs. hip resurfacing group (n=109).	Follow-up at 6.6 to 9.3 years.	UCLA activity score was significant improved in hip resurfacing group at last follow-up (p=0.035). WOMAC (p=0.1) and PMA scores (p=0.3) showed no significant difference in both groups from 24 months to last follow-up.	“[I]n young patients suffering from hip joint degeneration both devices provided similar, excellent clinical outcomes and revision rates after 6.6 to 9.3 years. Although both techniques had similar complication rates, the complications were different in nature.”	6-9 years follow-up. Patients and surgeons not blinded although, Study say they were. Data suggest comparable efficacy.
Rama 2009 (Score= 4.0)	Hip Resurfacin g	RCT	No mention of sponsorship. The	N=200 patients with hip arthritis.	Mean age: 50.1 years; 131	Patients assigned to surface replacement arthroplasty	Follow-up at 1 year.	Heterotopic ossification and WOMAC (p=0.005), Merle D’Aubigne scores (p=0.036) indicated significant negative correlation. Surface	“ Although patient-related	Baseline differences in weight between groups

			authors declared no conflict of interest.		males, 69 females.	(n=103) vs. patients assigned to total hip arthroplasty (n=97).		replacement arthroplasty patients indicated negative outcome both on WOMAC and Merle D'Aubigne scores (p=0.014, p=0.011). Both groups indicated adverse outcome in external rotation and less average flexion (p=0.014, p=0.030).	factors seem to be important in the occurrence of HO after hip arthroplasty, the severity of HO appears to be influenced by the local surgical factors. Severe HO can affect the clinical outcome adversely."	(SRA=80.8kg vs. THA=87.8kg). Data suggest SRA group had a significantly higher rate 0f severe heterotrophic ossification vs. THA (12.6% vs. 2.1%) at 1 year follow-up.
Wang 2012 (Score= 3.5)	Hip Resurfacing									Sparse methods. Completers vs. dropouts not described. Data suggest hip flexion was better in HRA group.

inclusion criteria.

Evidence for the Use of Pre-operative Education

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Preoperative education, Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 28 articles in PubMed, 2319 in Scopus, 1 in CINAHL, 36 in Cochrane Library, 6770 in Google Scholar, and 23 from other sources. We considered for inclusion 3 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 12 from other sources. Of the 17 articles considered for inclusion, 14 randomized trials and 3 systematic studies met the inclusion criteria.

Evidence for the Use of Pre-operative Education

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Giraudet-Le Quintrec 2003 (score=6.5)	Pre-operative education	RCT	No mention of sponsorship or COI.	N = 100 THR	Mean age: 63.5 years; 44 males, 56 females	Intervention group (n=48) - patients attended a ½ day collective multidisciplinary information session 2 to 6 weeks before surgery and received the usual verbal information and standard information leaflet. vs. Control group (n=51) – patients received the usual verbal information and standard information leaflet.	2, 6 weeks pre-operation, 7 days post-operation, 24 months post-operation	Patients receiving education significantly less anxious just before surgery than control (-4.98; 95% CI, -8.62 to –1.34, p = 0.01), in linear regression after adjustment for gender, trait, state anxiety at baseline, depression score, and health assessment questionnaire score. Intervention group had less pain before surgery (p = 0.04), and borderline after surgery (p = 0.07).	"The current study showed the value of developing alternative information approaches for informing patients and answering their questions. Group discussion with the care team seems to be useful."	Suggests education is effective to reduce anxiety and pain especially pre-operatively.
Siggeirsdottir 2005 (score=5.5)	Pre-operative education	RCT	Sponsored by the memorial foundation of Helga Jonsdottir and Sigurlidi Kristjansson, Landspitalinn University Hospital Research Foundation, the Icelandic Geriatrical Council Fund, the Göran Bauer Fund and the Swedish Council for Working	N = 50 patients scheduled to undergo total hip replacement.	Mean age: 67.6 years; 24 males, 26 females	Control group (n=27) – patients received "Conventional" rehabilitation augmented by stay at rehabilitation center. vs. Study group (n=23) – patients received pre-op and post-op education program and home visits from outpatient team.	2 and 6 months	Mean hospital stay SG 6.4 days vs. CG 10 days, p <0.001). During 6-month study period, non-fatal complications were not different (9 in SG vs 12 in CG, p = 0.3). Oxford Hip Scores were better for SG at 2 months (p = 0.03) and the difference remained throughout the study.	"Our preoperative education program, followed by postoperative home-based rehabilitation, appears to be safer and more effective in improving function and QOL after THR than conventional treatment."	Suggests educational program and home visits superior to rehabilitation stay. Hospital stays longer than in US.

			Life and Social Research. No COI.							
Mancuso 2008 (score=5.5)	Pre-operative education	RCT	Sponsored by one or more of the authors (CAM) have received funding from the Department of Orthopedic Surgery, Hospital for Special Surgery, and the Center for Aging Research and Clinical Care, Division of Geriatrics and Gerontology, Joan and Sanford I. Weill Medical College of Cornell University through NIA. No mention of COI.	N = 177 THR N = 143 TKR	Mean age: 70.9 years; 139 males, 181 females	Two RCTs for patients undergoing THA or TKA. Control group (n=90) – patients received standard class. vs. Intervention group (n=87) – patients received the standard class plus additional information focusing on expectations of recovery during 12 months after surgery.	12 months	Main outcome was within-patient change in pre-operative expectation scores (maximum increase, +100; maximum decrease, -100) before and after class. Mean changes in hip scores were 3.3±8 for intervention patients (range, -22±32) and 4.9±8 for control patients (range, -13±29).	"[E]xpectations of patients undergoing THA and patients undergoing TKA can be modified by classes administered before surgery."	More controls were retired at baseline (69% vs. 54%, p = 0.05).
Gocen 2004 (score=5.0)	Pre-operative education	RCT	No mention of sponsorship or COI.	N = 60 THR, all thrust plate prostheses	Mean age: 51.3 years; 21 males, 38 females	Study group (n=29) - patients received pre-op physiotherapy (strengthen limbs and hip ROM for 8 weeks) and educational program. vs. Control group (n=30) – patients did not receive exercises or education program prior to surgery.	8 weeks prior to operation, 3 months, 2 years	First day for activity (exercise vs. controls): walking 2.1± 0.2 vs. 2.2±0.41, p=0.14; climbing stairs 6.2±1.7 vs 7.4±1.0, p = 0.01; bed transfer 2.9±0.6 vs 3.3±0.7, p = 0.02. Improvements in Harris Hip scores not significant at 3 months or 2 years (p >0.05).	"[T]he routine use of preoperative physiotherapy and education programme is not useful in total hip replacement surgery."	Baseline differences present with exercise group younger (p = 0.01) and lower BMI (p = 0.06), Harris Hip scores (p = 0.13) suggesting randomization failure. Authors report study as negative based on Harris Hip score. However, all 5 functional post-op measures favor exercise group.

Wong 1985 (score=5.0)	Pre-operative education	RCT	Sponsored by National Health and Research Development Program, Health and Welfare Canada. No mention of COI.	N = 98 THR	Mean age: 67.7 years, 31 males, 67 females	Experimental group (n=51) – patients received pre-operative teaching that combined educational and behavioral strategies by a research assistants. vs. Control group (n=47) – did not receive pre-operative teaching.	No mention of follow up.	Significant difference between experimental and controls in regularity, willingness, accuracy with which they performed prescribed post-op exercises. Experimental patients significantly more satisfied with approach to pre-op teaching than controls.	"The findings suggest that an approach to preoperative teaching that combines educational and behavioral strategies significantly improves patients' adherence to the prescribed postoperative activities."	Four day study, no long-term follow-up. No outcome data such as length of stay, performance benchmarks or long-term complications.
Daltroy 1998 (score=5.0)	Pre-operative education	RCT	Sponsored by an Arthritis Health Professionals grant from the Arthritis Foundation and in part by NIH grant. No mention of COI.	N = 222 47% THR 53% TKR	Mean age: 64±12 years; 75 males, 147 females	Information (n=54) – patients received slide-tape with post-operative inpatient rehabilitation information. vs. Relaxation (n=54) – patients received Benson's Relaxation Response with bedside audiotape. Vs. Relaxation and Information Group (n=54) Vs. Control group (n=54)	4 days post-operation	Relaxation response did not influence post-operative outcomes, but information reduced length of stay (data not described in detail). Main outcomes were not analyzed or not reported. Instead, sub-analyses were performed. Sub-analyses suggested those in denial and with anxiety may benefit from educational interventions.	"Patients who exhibit most denial and highest anxiety may benefit from educational interventions, but patients directly expressing desire for information may be a poor guide in deciding which patients would benefit, compared with more formal psychological testing for denial and anxiety."	Conclusion does not directly follow the study's primary hypothesis and design. Due to problems with inadequate time to practice relaxation, the primary hypothesis was either not tested (or possibly was negative for differences between the groups).
Vukomanovic 2008	Pre-operative	RCT	No mention of sponsorship or COI.	N = 45 THR	Mean age: 58.2 years; 15	Study group (n=18) – patients received short-term intensive	15 month post-operation	Groups started walking at same time, but study group walked up and	"The short-term preoperative program of	Program components not described. Frequency of

(score=4.5)	education				males, 30 females	preoperative preparation (education and physical therapy). vs. Control group (n=18) – patient did not receive preoperative education and physical therapy		down stairs (3.7±1.66 vs. 5.37±1.46, p = 0.002), used toilet (2.3±0.92 vs. 3.2±1.24, p = 0.02) and chair (2.2±1.01 vs. 3.25±1.21, p = 0.006) significantly earlier than the control group.	education with the elements of physical therapy accelerated early functional recovery of patients (younger than 70) immediately after THA and we recommend it for routine use."	activities not described.
Huang 2017 (score=4.5)	Pre-operative education	Prospective RCT	No COI or sponsorship.	N=108 patients with total hip replacement surgery.	Mean age: 66 years; 63 male, 53 female.	Comparison Group (CG) (n=54) - received no additional care other than standard for THA. Vs. Education empowerment Group (EEG) (n=54) - received five sessions over 12-weeks to develop own self-management program.	2, 6 and 10 weeks after discharge	Patients in EEG had higher tendencies for self-care and less likely to display depressive emotions than comparison group.	"This education empowerment intervention was very effective in enhancing participants' outcomes. Moreover, involving both older adults and their caregivers for the participation this program is recommended for a greater impact."	Data suggest the empowerment education group had less depressive symptoms and demonstrated higher self-care competence.
Butler 1996 (score=4.5)	Pre-operative education	RCT	Sponsored by The Department of Nursing provided a research grant to help cover clerical costs, and the Department of Orthopaedics provided a research grant to cover the cost of test	N = 132 THR	Mean age: 62.6±13 years; 39 males, 41 females	Booklet (n=30) – patients received a total hip replacement educational booklet. vs. No booklet (n=40) – patients did not receive the booklet.	4-6 weeks pre-operation	Length of stays higher for women (12.2 vs. 8.2 days). Less anxiety reported in booklet group. Booklet group engaged in deep breathing, coughing, log rolling and leg exercises more than controls (p <0.001). Booklet group used less PT (32.7 vs. 45.6, p = 0.001).	"Compared to the No-Booklet patients, patients who had received the booklet were less anxious at the time of hospital admission and at discharge, were more likely to have practised physiotherapy	Study included first time as well as other THR patients. 32 or 80 first timers received the booklet and 48 did not, resulting in a potential significant confounding.

			materials. Publication of the booklet was made possible by an Educational Grant from Zimmer of Canada, Ltd. No mention of COI.						exercises prior to hospitalization, and required significantly less occupational therapy and physiotherapy while in hospital."	
Pour 2007 (score=4.5)	Pre-operative rehabilitation	RCT	Sponsored by one or more of the authors received, in any one year, outside funding or grants in excess of $10,000 from Stryker. No COI.	N = 94 THR, uncemented, proximally coated tapered stem (Accolade) and plasma-sprayed acetabular component (Trident)	Mean age: 60.8 years; 48 males, 46 females	Group A (n=25) - standard incision (>10cm) and standard pre-/post-op care (2-3 days PCA analgesia). Vs. Group-B (n=23) - small incision (≤10 cm) and standard pre-/post-op protocols. Vs. Group-C (n=25) - standard incision but pre-op counseling, accelerated rehabilitation, altered pain control regimen (OxyContin 5mg Q 4-6 hours. PRN plus celecoxib 200mg a day. Vs. Group-D (n=21) - small incision, pre-op counseling, accelerated rehabilitation, altered pain control regimen.	6 weeks post-operation	Hospital lengths of stay (standard vs. accelerated rehab): 4.2 days (range 3-8) vs. 3.5 (range 2-5) (p = 0.001). Walking independently or supervised at discharge 60.4% vs. 84.8%, p = 0.009. Walking distance at discharge: 24.3m (range 3.5-91.5) vs. 35m (range 7-91.5), p = 0.008. Equianalgesic requirement [507]: 26.8(2.4-113.7) vs. 41.2 (2.4-120); p = 0.01. No benefits of short incision shown.	"This study highlights the importance of factors such as family education, patient preconditioning, preemptive analgesia, and accelerated preoperative and postoperative rehabilitation in influencing the outcome of total hip arthroplasty."	Due to multiple interventions, the effects of any single intervention are unclear. Suggests combination of education, pre-operative gait training and exercise, assistive walking the day of surgery, and oral narcotics plus celecoxib are more effective. No benefit shown of small incision. Overall equianalgesic opioid dose higher in accelerated rehabilitation.

Gammon 1996 (score=4.0)	Pre-operative education	RCT	No mention of sponsorship or COI.	N = 82 All pre-surgery THA patients	No mention of mean age, range: 44-82 years; 26 males, 56 females	Educational program (n=41) - procedural, sensory and coping information. vs. Usual education (n=41) - usual advice by ward, medical and nursing staff.	No mention of follow-up.	Anxiety scores for information group mean 4.2 vs. 4.4, p <0.001. Sense of control scores 19.9 vs. 11.2, p <0.01. Patient sense of coping 6.6 vs. 4.3, p <0.001.	"[P]reparatory information of various types and in different forms appears to have positive effects on psychological coping outcomes for THR patients, which may have influenced postoperative recovery."	Differences in anxiety (mean 4.2, range 0-11 vs. mean 4.4, range 0-16) stated statistically significant, but biological significance appears questionable. Sense of control appears significant.
Hopman-Rock 2000 (score=4.0)	Pre-operative education	RCT	Sponsored by the Netherlands Health Research and Development Council. No mention of COI.	N = 120 Hip or knee OA	Mean age: 65.3 years; 83 females, 22 males.	Experiment group (n=56) – patients received two hour weekly exercise sessions (1.25 hour education, 45-minute exercises with HEP at least 3 times a week for 6 weeks. vs. Control group (n=49) – patients received non-interventional controls.	Follow-up at baseline 6 months.	IRGL pain scale (baseline/post/followup): exercise (14.0±4.0/13.6±3.6/14.2±4.0) vs. controls (13.7±3.5/14.9±3.8/14.3±4.0), p = 0.045. Pain intolerance also favored exercise (p = 0.011) as did quality of life (p = 0.039).	"[T]his self-management program was reasonably effective in terms of the educational and exercise components."	Non-interventional control group may bias in favor of intervention. Exercises appear unstructured and not well described. Data support exercises, although results did not persist at follow-up.
Ferrara 2008 (score=4.0)	Pre-operative education	RCT	No mention of COI or sponsorship.	N = 23 patients with end-stage osteoarthritis, on	Mean age: 63.43 years; 9 males, 14 females	Study group (n=11) – patients received physiotherapy, group and individual exercises, 5 days per week, physical therapist session for 60 minutes per day. vs.	Follow-up at day prior to surgery and at 15 days, 4 weeks, and 3 months post-surgery	Primary outcomes for physiotherapy and control groups, respectively: WOMAC function score 33.7±13.8, 43.5±9.5 (p=0.63), WOMAC pain score 8.0±3.8, 11.0±3.6	"Pre-operative physiotherapy in patients undergoing hip arthroplasty does not improve impairment and health-related quality of life after	Data suggest lack of efficacy but PT and education may be appropriate for end stage OA.

				waiting list for total hip replacement surgery at the University Hospital 'Agostino Gemelli' in Rome		Control group (n=12) – patients performed exercise only after surgery.		(p=0.70), WOMAC stiffness socre 4.82±1.88, 4.58±1.62 (p=0.80), Hip Harris Score 43.6±15.7, 34.9±15.5 (p=0.24), Barthel Index 84.5±6.7, 75.0±16.2 (p=0.06), Visual Analogue scale 5.5±2.2, 7.3±2.0 (p=0.04), SF-36 PCS 34.4±4.05, 27.3±10.3 (p=0.048), SF-36 MCS 51.1±11.2, 40.9±11.6 (p=1.14)	intervention. Physiotherapy and educational therapy may be useful for end-stage osteoarthritis."	
Parsons 2013 (score=2.0)										Usual care bias data suggest tailored pre-operative assessment plus health management clinic may be of benefit by improving patient satisfaction and thus positively speeding recovery time

Evidence for the Use of Pre- and Post-Operative Rehabilitation Programs

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Pre-operative rehabilitation, post-operative rehabilitation, cardiovascular fitness, flexibility, strengthening, aquatic rehabilitation, exercise program, Arthroplasty; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 68 articles in PubMed, 2664 in Scopus (Went through first 100), 18 in CINAHL, 115 in Cochrane Library, 603 in Google Scholar, and 98 from other sources. We considered for inclusion 13 from PubMed, 1 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 7 from other sources. Of the 26 articles considered for inclusion, 19 randomized trials and 6 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Austin 2017 (score=6.0)	Pre- and Post-operative rehabilitation programs	RCT	No sponsorship. More than one author received financial compensation for work on this research.	N = 108 patients undergoing primary, unilateral total hip arthroplasty, eligible for direct home discharge	Mean age: 61.7 years; 61 males, 47 females.	All received daily inpatient physical and occupational therapy. Formal physical therapy (n=54) - Outpatient physical therapy group, 2 weeks of in-home physical therapy and then 2-3 weekly sessions for 8 weeks. vs. Home exercise (n=54) - Unsupervised home exercise group, 10 weeks of	Follow-up at 1, 6, and 12 months.	Intention-to-treat groups had significant improvement in function measured via the Harris hip score, the Western Ontario and McMaster Universities Osteoarthritis Index, and Short Form-36 Helath Survey ($p<0.0001$ for all outcomes). Improvement in Harris hip score from preoperative baseline to 1 month postoperative: Formal outpatient therapy - 21.5 points (95% CI 16.2-26.9), Home exercise group – 23.3 points (95% CI 18.3-28.4). At post-operative 6 to 12 months follow-up: formal outpatient therapy – 36.0 points (30.9-41.2), home exercise 35.6 points (30.9-40.4). Difference between groups at both 1 month and	"This randomized trial suggests that unsupervised home exercise is both safe and efficacious for a majority of patients undergoing total hip arthroplasty, and formal physical therapy may not be required."	Data suggest similar efficacy between treatment groups, but there was significant noncompliance observed in treatment regimes.

						exercises based on detailed physical therapy manual.		6-12 months were not significant when controlling for confounders (p=0.82)		
Svege 2013 (score=6.0)	Pre- and Post-operative rehabilitation programs	RCT	Sponsored by the Ullevaal University Hospital, Oslo, and the Norwegian Foundation for Health and Rehabilitation, via the Norwegian Rheumatism Association. No COI.	N = 109 with hip pain for at least 3 months, radiographically verified minimum join space via Danielsson's criterion (<4 mm for <70 years patients, <3 mm for >70 patients) and Harris Hip Score between 60-95	Mean age: 57.81 years; 50 males, 59 females.	All patients received three group education sessions. Exercise therapy (n=55) – twelve weeks, two to three times per week, strengthening, flexibility, and functional exercises. vs. Control group (n=54) - 2 month follow-up visit to physiotherapy clinic.	Follow-up at 4, 10, 16, 29 months and 6 years	22 exercise group patients and 31 control group patients underwent total hip replacement within 3.6-6.1 years. Estimated median time to THR: 5.4 (CI 4.5-6.2) for exercise group, 3.5 (CI 2.3-4.6) for control group. Kaplan-Maier analysis at 6 years survival to THR: 0.41 exercise group, 0.25 control group (p=0.034).	"Our findings in this explanatory study suggest that exercise therapy in addition to patient education can reduce the need for THR by 44% in patients with hip OA."	Data suggest benefit from combined exercise therapy in addition to education.
Foley 2003 (score=6.0)	Pre- and Post-operative rehabilitation programs	RCT	Foley completed this research in order to fulfill requirements for the award of	N=105 community living participants with clinical hip or knee OA	Mean age: 70.9 years; 53 males, 52 females.	Hydro group (n=35) - Hydrotherapy, walking and strengthening exercises, three sessions per week for six weeks.	Follow-up at 6 weeks.	WOMAC self reported function score median difference – hydrotherapy group -1.0, gym group -1.0, control – 0.0. Between group difference not significant (p>0.05).	"Functional gains were achieved with both exercise programmes compared with the control group."	Data suggest gym better than hydrotherapy for strength and both exercise groups better than control.

			BSc(Hons) at the Flinders University of South Australia.			vs. Gym group (n=35) - Gym exercise, same frequency as hydrotherapy group. vs. Control group (n=35) – received fortnightly telephone calls to record any changes in condition, drug use, or injuries and were offered exercise treatment after the study period.				
Peak 2005 (score=6.0)	Pre- and Post-operative rehabilitation programs	RCT	No sponsorship or COI.	N = 265 patients all cementless femoral (Accolade) and cups (Trident PSL). All anterolateral approach.	Mean age: 58.3 years; 139 males, 126 females	Unrestriced group (n=152) - No post-operative restrictions other than limit to <90º flexion, 45º external and internal rotation, avoid adduction for first 6 weeks post-op. vs. Restricted group (n=151) - same restrictions plus	6 months	One patient from restricted group experienced dislocation vs. none. No differences in prevalence of limp at 6 months (12.5% restricted group vs. 13.2%, p = 0.80). Greater satisfaction with recovery in unrestricted (89.4% vs. 74.3%, p <0.001.) Data on achievement of functional goals restricted/unrestricted: return to work within 6 weeks 18.8% vs. 50.0% (p <0.001). RTW at mean 9.5 (1.0-32.0) vs. 6.5 (0.7-20.0) weeks, p <0.001; ability to perform	"[A]nterolateral approach is likely to be associated with a low dislocation rate. Removal of several restrictions did not increase the prevalence of dislocation following primary hip arthroplasty… it did promote substantially lower costs and was associated with a higher level of patient satisfaction as patients achieved a faster	Cost estimates do not include lost wages, which likely understate cost savings by possibly at least 4-fold.

						placement of abduction pillow in the operating room and bed, use of elevated toilet seats and elevated chairs, no sleeping on the side, no driving or riding in an automobile.		activities of daily living at 6 months 96.5% of pre-operative value (25-200) vs. 106.4 (25-350) %, p = 0.015. More rehabilitation stays required in restricted group (125 hips vs. 100 hips, p <0.002). Cost savings approximately $655 per patient in unrestricted group. Unrestricted group returned to side-sleeping sooner (p < 0.001), ride in autos more often (p < 0.026), and drive autos more often (p < 0.001).	return to daily functions in the early postoperative period."	
Unver 2004 (score=5.5)	Pre- and Post-operative rehabilitation programs	RCT	No mention of sponsorship or COI.	N = 51 patients. All thrust plate prostheses.	Mean age:49.4 years; 15 males, 36 females	Group 1 (control group) (n=24) – patients received accelerated rehabilitation with partial weight baring. vs. Group 2 [739] (n=27) – received accelerated rehabilitation with full weight bearing.	3 months, 1 year	Group 1 vs. Group 2: 3-month post-operative follow-up 6-minute walk test (m) 182.5±58.2 vs 215.8±52.5 (p = 0.023). Duration of crutch use (weeks) 12.0±1.5 vs. 7.2±1.2 (p <0.001). Harris Hip score 81.4±9.3 vs. 89.3±4.6 (p <0.001). Hospital discharge 15.2±3.5 vs. 11.6±2.7 days (p = 0.001). Walking distance at discharge (which is 2 different times) 164.1±134.8 vs. 290.0±145.2m, p = 0.001.	"These results suggest that patients with [thrust plate prostheses] can tolerate an accelerated rehabilitation program with early weight bearing and will gain the goals of rehabilitation earlier."	Results strongly support early weight bearing and advancement of activities for thrust plate prostheses. Differences at time of hospital discharge understate benefits as early full weight bearing patients were discharged earlier.
Bulthuis 2007 (score=5.0)	Pre- and Post-operative rehabilitation programs	RCT	Sponsored by grants from RVVZ and The Dutch Arthritis	N = 114 patients with RA or OA hospitalized for joint	Mean age: 68.1 years; 21 males, 77 females	Intensive Treatement Group (IET) (n=58) - 3 weeks at a resort; BID to QID exercise sessions.	3, 13, 26 and 52 weeks	Range of motion scale (baseline/13 weeks/52 weeks): intensive (2.8/1.8/2.3) vs. usual (2.7/2.7/2.6) (p <0.01 for 13 weeks). HAQ walking: intensive (2.3/1.2/1.0) vs.	"Intensive short-term exercise training of arthritis patients, immediately after hospital discharge results in improved regain of function."	Subpopulation of larger DAPPER RCT. Heterogeneous mix of patients and multiple cointerventions may limit implications.

			Foundation. No COI.	flares or arthro-plasty		vs. Usual Care Group (UC) (n=40) – patients received either physical therapy by a local physical therapist or temporary admission to a nursing home.		usual (2.2/1.2/1.0) (NS). No differences at any time for RAND-36 physical or mental component scales.		Data suggest minimal intermediate but no long-term improvements as no differences at 52 weeks.
Bulthuis 2008 (score=5.0)	Pre- and Post-operative rehabilitation programs	RCT	Sponsored by grants from RVVZ and The Dutch Arthritis Foundation. No mention of COI.	N = 85 Patients with rheumatic diseases	Mean age: 69 years; 15 males, 70 females	Intensive treatment Group (IET) (n=50) - 3 weeks at resort; BID to QID exercise sessions. vs. Usual care group (UC) (N=35) – patients received physical therapy and/or temporary nursing home placement.	6, 12 months	Twenty-five percent of patients did not complete cost questionnaires. Usual care treated by PT 1.8 times more. No differences in hospitalizations. Mean costs per patient 2,068€ lower for intensive treatment.	"(Intensive exercise training) results in better quality of life at lower costs after 1 year. Thus, IET is the dominant strategy compared with (usual care)."	Sub-sub group analysis of data from Bulthuis 2007 and same weaknesses, except dropout rate greater. Unclear of extent costs apply outside Netherlands.
Rooks 2006 (score=5.0)	Pre- and Post-operative rehabilitation programs	RCT	Sponsored by the New England Baptist Bone and Joint Institute, the New England Baptist Hospital, and NIH grant. Dr. Rooks is recipient of	N = 108 Patients scheduled to undergo hip (n = 63) or knee (n = 45) arthroplasty	Mean age: 62.1 years; 48 males, 60 females	Exercise (n=39) – patients received six-week pre-op program of exercise (water and land-based exercise, cardiovascular, strength and flexibility, 30-60 minute sessions, 3 times a week).	8, 26 weeks	WOMAC scores (baseline/ pre-op/8 weeks) for THA patients improved at pre-op measure (exercise 29.1± 12.9/26.9±11.9/12.8 ±9.0 vs. education 29.8±11.2/ 33.7±10.9/ 12.9±8.0) pre-op p = 0.02. SF-36 scores -0.4 vs. -14.3, at pre-op assessment p = 0.003. Differences not present at 8 weeks. Fewer complications in exercise group (0 vs. 4, p = 0.04).	"A 6-week presurgical exercise program can safely improve preoperative functional status and muscle strength levels in persons undergoing THA. Additionally, exercise participation prior to total joint arthroplasty dramatically reduces	Results more favorable for hip than knee arthroplasty patients. Education controls 3.7 times more likely to be discharged to rehabilitation facility compared with exercise group. High dropout rate. Study suggests preoperative

			an Arthritis Foundation Investigator Award and a grant from the NIH. Dr. Katz's work was supported by grants from the NIH. Drs. Huang and Iversen's work was supported by a grant from the NIH. No mention of COI.			vs. Control (n=39) – patients received two handouts in the mail and three telephone calls.		Exercise group more likely to walk 50 feet on post-op Day 3 (76% vs. 61%). Exercise group more likely discharged to home 65% vs. 44%.	the odds of inpatient rehabilitation."	exercise effective for improving functional status and preventing inpatient rehabilitation.
Wang 2002 (score=5.0)	Pre- and Post-operative rehabilitation programs	RCT	No mention of sponsorship or COI.	N = 28 patients scheduled to undergo hip arthroplasty.	Mean age: 67.1 years; 10 males, 18 females	Exercise group (n=15) – patients underwent 2 1-hour sessions a week for 8 pre-op weeks of hydrotherapy, stationary bike riding, resistive exercises, 2 home sessions, week of strengthening and flexibility. vs.	3, 12, 24 weeks	Mean walk distances (Week 12/Week 24): exercise (503.7/549.7m) vs. controls (450.2/485.1m), p = 0.061. Numbers of steps per minute, stride length, gait velocity all comparable at baseline, but favored exercise group at Weeks 3, 12, 24.	"[P]erioperative customized exercise program(s) are well tolerated in the elderly patient with endstage hip arthritis and are effective in improving the rate of recovery in ambulatory function in the first 6 mo after total hip arthroplasty."	Small sample sizes. Suggests perioperative exercise has short term benefits with differences lasting to 6 month duration of observations.

						Control group (n=13) – patient underwent usual peri-op care. All given post-op exercises during Weeks 3-12, with some to Week 24.				
Gocen 2004 (score=5.0)	Pre- and Post-operative rehabilitation programs	RCT	No mention of sponsorship or COI.	N = 60 THR, all thrust plate prostheses.	Mean age: 51.3 years; 21 males, 38 females	Study group (n=29) - patients received pre-op physiotherapy (strengthen limbs and hip ROM for 8 weeks) and educational program. vs. Control group (n=30) – patients did not receive exercises or education program prior to surgery.	8 weeks prior to operation, 3 months, 2 years	First day for activity (exercise vs. controls): walking 2.1± 0.2 vs. 2.2±0.41, p=0.14; climbing stairs 6.2±1.7 vs 7.4±1.0, p = 0.01; bed transfer 2.9±0.6 vs 3.3±0.7, p = 0.02. Improvements in Harris Hip scores not significant at 3 months or 2 years (p >0.05).	"[T]he routine use of preoperative physiotherapy and education programme is not useful in total hip replacement surgery."	Baseline differences present with exercise group younger (p = 0.01) and lower BMI (p = 0.06), Harris Hip scores (p = 0.13) suggesting randomization failure. Authors report study as negative based on Harris Hip score. However, all 5 functional post-op measures favor exercise group.
Vukomanovic 2008 (score=4.5)	Pre- and Post-operative rehabilitation programs	RCT	No mention of sponsorship or COI.	N = 45 patient scheduled to undergo total hip replacement surgery.	Mean age: 58.2 years; 15 males, 30 females	Study group (n=18) – patients received short-term intensive preoperative preparation (education and physical therapy). vs. Control group (n=18) – patient	15 months post-operation.	Groups started walking at same time, but study group walked up and down stairs (3.7±1.66 vs. 5.37±1.46, p = 0.002), used toilet (2.3±0.92 vs. 3.2±1.24, p = 0.02) and chair (2.2±1.01 vs. 3.25±1.21, p = 0.006) significantly earlier than the control group.	"The short-term preoperative program of education with the elements of physical therapy accelerated early functional recovery of patients (younger than 70) immediately after THA and we recommend it for routine use."	Program components not described. Frequency of activities not described.

						did not receive preoperative education and physical therapy				
Kishida 2001 (score=4.5)	Pre- and Post-operative rehabilitation programs	RCT	No mention of sponsorship. No COI.	N = 33 all cementless arthroplasties	Mean age: 51.5 years; 10 males, 23 females	Group A (n=17) – immediate Full weight-bearing vs. Group B (n=16) – late full-weight bearing (delayed 6 weeks post-operatively).	6 weeks, 3 months, 6 months, 5 years	Rehabilitation to walk with cane 5.8 vs. 44.8 days (p = 0.0001). Hospital stay 30.1 vs. 46.7 days (p = 0.006). No differences in radiolucent lines.	"Full weight-bearing immediately after cementless THA shortened the rehabilitation process and the hospital stay without radiographic migration of the components or clinical complications."	Results support immediate weight bearing. The length of hospital stay data (Osaka, Japan) are quite long compared with U.S.
Pour 2007 (score=4.5)	Pre- and Post-operative rehabilitation programs	RCT	Sponsored by one or more of the authors received, in any one year, outside funding or grants in excess of $10,000 from Stryker. No COI.	N = 94 THR, uncemented, proximally coated tapered stem (Accolade) and plasma-sprayed acetabular component (Trident)	Mean age: 60.8 years; 48 males, 46 females	Group A (n=25) - standard incision (>10cm) and standard pre-/post-op care (2-3 days PCA analgesia). Vs. Group-B (n=23) - small incision (≤10 cm) and standard pre-/post-op protocols. Vs. Group-C (n=25) - standard incision but pre-op counseling, accelerated rehabilitation, altered pain	6 weeks post-operation	Hospital lengths of stay (standard vs. accelerated rehab): 4.2 days (range 3-8) vs. 3.5 (range 2-5) (p = 0.001). Walking independently or supervised at discharge 60.4% vs. 84.8%, p = 0.009. Walking distance at discharge: 24.3m (range 3.5-91.5) vs. 35m (range 7-91.5), p = 0.008. Equianalgesic requirement [507]: 26.8(2.4-113.7) vs. 41.2 (2.4-120); p = 0.01. No benefits of short incision shown.	"This study highlights the importance of factors such as family education, patient preconditioning, preemptive analgesia, and accelerated preoperative and postoperative rehabilitation in influencing the outcome of total hip arthroplasty."	Due to multiple interventions, the effects of any single intervention are unclear. Suggests combination of education, pre-operative gait training and exercise, assistive walking the day of surgery, and oral narcotics plus celecoxib are more effective. No benefit shown of small incision. Overall equianalgesic opioid dose higher in accelerated rehabilitation.

						control regimen (OxyContin 5mg Q 4-6 hours. PRN plus celecoxib 200mg a day. Vs. Group-D (n=21) - small incision, pre-op counseling, accelerated rehabilitation, altered pain control regimen.				
Galea 2008 (score=4.5)	Pre- and Post-operative rehabilitation programs	RCT	Sponsored by Arthritis Australia and the National Arthritis and Musculoskeletal Health Initiative. No mention of COI.	N = 23 patients with unilateral THR.	Mean age: 67.6 years; 7 males, 16 females	Center-Based Group (n=11) – patients received supervised center-based exercise (twice a week for 45 minutes with 7 exercises). vs. Home Based Group (n=12) – patients received home-based exercise for 8 weeks. Exercises included figure of 8, sit to stand, active simple leg stance, climbing steps, hip abduction, heel raise, side stepping.	8 weeks	Walking speed (baseline/post): Center-based (100.0±25.2/116.7±18.1) vs. home-based (102.2±14.1/117.4±16.7) (NS). Multiple other measures also improved (e.g., steps/min, step length) but most were not different between groups.	"No group differences were found in the majority of the outcome measures. This finding is important because it shows that THR patients can achieve significant improvements through a targeted strengthening program delivered at a center or at home."	Small sample size. Multiple interventions. Data suggest rehabilitation with a home program may be equally efficacious in this group with mean age of ~68 years.

Ferrara 2008 (score=4.0)	Pre- and Post-operative rehabilitation programs	RCT	No mention of COI or sponsorship.	N = 23 patients with end-stage osteoarthritis, on waiting list for total hip replacement surgery at the University Hospital 'Agostino Gemelli' in Rome	Mean age: 63.43 years; 9 males, 14 females	Study group (n=11) – patients received physiotherapy, group and individual exercises, 5 days per week, physical therapist session for 60 minutes per day. vs. Control group (n=12) – patients performed exercise only after surgery.	Follow-up at day prior to surgery and at 15 days, 4 weeks, and 3 months post-surgery	Primary outcomes for physiotherapy and control groups, respectively: WOMAC function score 33.7±13.8, 43.5±9.5 (p=0.63), WOMAC pain score 8.0±3.8, 11.0±3.6 (p=0.70), WOMAC stiffness socre 4.82±1.88, 4.58±1.62 (p=0.80), Hip Harris Score 43.6±15.7, 34.9±15.5 (p=0.24), Barthel Index 84.5±6.7, 75.0±16.2 (p=0.06), Visual Analogue scale 5.5±2.2, 7.3±2.0 (p=0.04), SF-36 PCS 34.4±4.05, 27.3±10.3 (p=0.048), SF-36 MCS 51.1±11.2, 40.9±11.6 (p=1.14)	"Pre-operative physiotherapy in patients undergoing hip arthroplasty does not improve impairment and health-related quality of life after intervention. Physiotherapy and educational therapy may be useful for end-stage osteoarthritis."	Lack of efficacy. Data suggest pre-operative PT in end stage OA patients was not beneficial. Sample may be underpowered to demonstrate any benefit.
Maire 2003 (score=4.0)	Pre- and Post-operative rehabilitation programs	RCT	No mention of sponsorship or COI.	N = 14 All post-THR	Mean age: 77 years; 2 males, 12 females	Training group (n=7) – patients received exercise training for muscular strength, range of motion, aquatics, and walking for 2 hrs/day, and exercise-training program with an arm ergometer. vs. Controls (n=7) - patients received exercise training for muscular	1 month, 2 months	Six-minute walk test results at 2 months: training 404.5 vs. controls 259.0m, p <0.01. VO2 (baseline/post-op/2 months): training (7.5/9.0/13.0) vs. controls (6.9/5.6/9.8).	"These results stress the importance of physical training in a rehabilitation program after total hip joint arthroplasty and this should be considered for improving the current practices in rehabilitation."	Very small sample size; 6-week treatment protocol suggests upper extremity exercise may help, however bias may be different degrees of rehab contact. Also, drop in post-op results before training for controls concerning for confounding.

						strength, range of motion, aquatics, and walking for 2 hrs/day.				
Wylde 2014 (score=3.5)										Pilot feasibility RCT. High dropout rate in a small sample.
Berge 2004 (score=3.0)										Data suggest pre and post-operative pain management programs may be of limited benefit, but appear not to cause delay in surgery.
Okoro 2013 (score=3.0)										Sparse methods including limited baseline data and randomization process.

Evidence for the Use of Post-Operative Exercise and/or Rehabilitation Programs

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Post-operative, Exercise, Rehabilitation, weight bearing, walking, Abduction pillow, Elevated toilet seats, elevated Chairs, side sleeping, driving, adaptive equipment, activity limitation, long-handled reacher, shoe horn, sock aid, Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 95 articles in PubMed, 2665 in Scopus (Went through first 100), 11 in CINAHL, 68 in Cochrane Library, 5560 in Google Scholar (Went through first 100), and 16 from other sources. We considered for inclusion 13 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 19 articles considered for inclusion, 8 randomized trials and 3 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Peak 2005 (Score=6.0)	Post-opeartive exercise and/or rehabilitation program	RCT	Authors declared no sponsorship or COI.	N = 265 All cementless femoral (Accolade) and cups (Trident PSL). All anterolateral approach.	Mean age: 58.3 years; 139 males, 126 females.	No post-operative restrictions other than limit to <90º flexion, 45º external and internal rotation, avoid adduction for first 6 weeks post-op (n=151) vs. same restrictions plus placement of abduction pillow in the operating room and bed, use of elevated toilet seats and elevated chairs, no sleeping on the side, no driving or riding in an automobile (n=152).	Follow-up at 6 months.	One patient from restricted group experienced dislocation vs. none. No differences in prevalence of limp at 6 months (12.5% restricted group vs. 13.2%, p = 0.80). Greater satisfaction with recovery in unrestricted (89.4% vs. 74.3%, p <0.001.) Data on achievement of functional goals restricted/unrestricted: return to work within 6 weeks 18.8% vs. 50.0% (p <0.001). RTW at mean 9.5 (1.0-32.0) vs. 6.5 (0.7-20.0) weeks, p <0.001; ability to perform activities of daily living at 6 months 96.5% of pre-operative value (25-200) vs. 106.4 (25-350) %, p = 0.015. More rehabilitation stays required in restricted group (125 hips vs. 100 hips, p <0.002). Cost savings approximately $655 per patient in unrestricted group. Unrestricted group returned to side-sleeping sooner (p < 0.001), ride in autos more often (p < 0.026), and drive autos more often (p < 0.001).	"[A]nterolateral approach is likely to be associated with a low dislocation rate. Removal of several restrictions did not increase the prevalence of dislocation following primary hip arthroplasty… it did promote substantially lower costs and was associated with a higher level of patient satisfaction as patients achieved a faster return to daily functions in the early postoperative period."	Cost estimates do not include lost wages, which likely understate cost savings by possibly at least 4-fold.
Unver 2004 (Score=5.5)	Post-opeartive exercise and/or rehabilitation program	RCT	No mention of sponsorship or COI.	N = 51 All thrust plate prostheses	Mean age: 49.4 years; 15 males, 36 females.	Rehab programs with early partial weight bearing (Group 1: n=24) vs. early full weight bearing (Group 2: n=27). Programmatic differences include weight bearing at 6-8	Follow-up at 3 months.	Group 1 vs. Group 2: 3-month post-operative follow-up 6-minute walk test (m) 182.5±58.2 vs 215.8±52.5 (p = 0.023). Duration of crutch use (weeks) 12.0±1.5 vs. 7.2±1.2 (p <0.001). Harris Hip score 81.4±9.3 vs. 89.3±4.6 (p <0.001). Hospital discharge 15.2±3.5 vs. 11.6±2.7 days (p =	"These results suggest that patients with [thrust plate prostheses] can tolerate an accelerated rehabilitation program with early weight bearing and	Results strongly support early weight bearing and advancement of activities for thrust plate prostheses. Differences at time of hospital discharge understate benefits

						weeks post-op Day 2; active isotonic exercises at 3-4 vs. 2-3 weeks; endurance training at 8-10 vs. 6-8 weeks.		0.001). Walking distance at discharge (which is 2 different times) 164.1±134.8 vs. 290.0±145.2m, p = 0.001.	will gain the goals of rehabilitation earlier."	as early full weight bearing patients were discharged earlier.
Bulthuis 2007 (Score=5.0)	Post-opeartive exercise and/or rehabilitation program	RCT	Sponsored by the Dutch Arthritis Foundation and RVVZ. The authors declared no conflict of interest.	N = 114 RA or OA hospitalized for joint flares or arthroplasty	Mean age: 68.2 years; 21 males, 77 females.	Intensive treatment (3 weeks at a resort; BID to QID exercise sessions) (n=58) vs. usual care (e.g., physical therapy, temporary nursing home placement)(n=40)	Follow-up at 3, 13, 26, and 52 weeks.	Range of motion scale (baseline/13 weeks/52 weeks): intensive (2.8/1.8/2.3) vs. usual (2.7/2.7/2.6) (p <0.01 for 13 weeks). HAQ walking: intensive (2.3/1.2/1.0) vs. usual (2.2/1.2/1.0) (NS). No differences at any time for RAND-36 physical or mental component scales.	"Intensive short-term exercise training of arthritis patients, immediately after hospital discharge results in improved regain of function."	Subpopulation of larger DAPPER RCT. Heterogeneous mix of patients and multiple cointerventions may limit implications. Data suggest minimal intermediate but no long-term improvements as no differences at 52 weeks.
Bulthuis 2008 (score=5.0)	Post-opeartive exercise and/or rehabilitation program	RCT	Sponsored by the Dutch Arthritis Foundation and RVVZ. No mention of conflict of interest.	N = 85 Patients with rheumatic diseases	Mean age: 69 years;17 males, 68 females.	Intensive treatment (3 weeks at resort; BID to QID exercise sessions) vs. usual care (e.g., physical therapy, temporary nursing home placement)	Follow-up at 6 months and 1 year.	Twenty-five percent of patients did not complete cost questionnaires. Usual care treated by PT 1.8 times more. No differences in hospitalizations. Mean costs per patient 2,068€ lower for intensive treatment.	"(Intensive exercise training) results in better quality of life at lower costs after 1 year. Thus, IET is the dominant strategy compared with (usual care)."	Sub-sub group analysis of data from Balthuis 2007 and same weaknesses, except dropout rate greater. Unclear of extent costs apply outside Netherlands.
Pour 2007 (Score=4.5)	Post-opeartive exercise and/or rehabilitation program	RCT	Sponsored by Stryker. One or more authors have received benefits for	N = 94 THR, uncemented, proximally coated tapered stem (Accolade) and	Mean age: 60.8 years; 48 males, 46 females.	Group A standard incision (>10cm) and standard pre-/post-op care (2-3 days PCA analgesia). Group-B small incision (≤10 cm) and standard pre-/post-op protocols. Group-C standard incision	Follow-up at 6 weeks.	Hospital lengths of stay (standard vs. accelerated rehab): 4.2 days (range 3-8) vs. 3.5 (range 2-5) (p = 0.001). Walking independently or supervised at discharge 60.4% vs. 84.8%, p = 0.009. Walking distance at discharge: 24.3m (range 3.5-91.5) vs. 35m (range 7-91.5), p = 0.008. Equianalgesic requirement [507]: 26.8(2.4-113.7) vs. 41.2 (2.4-	"This study highlights the importance of factors such as family education, patient preconditioning, preemptive analgesia, and accelerated preoperative and postoperative	Due to multiple interventions, the effects of any single intervention are unclear. Suggests combination of education, pre-operative gait training and exercise, assistive walking the

			personal or professional use.	plasma-sprayed acetabular component (Trident)		but pre-op counseling, accelerated rehabilitation, altered pain control regimen (OxyContin 5mg Q 4-6 hours. PRN plus celecoxib 200mg a day. Group-D small incision, pre-op counseling, accelerated rehabilitation, altered pain control regimen.		120); p = 0.01. No benefits of short incision shown.	rehabilitation in influencing the outcome of total hip arthroplasty."	day of surgery, and oral narcotics plus celecoxib are more effective. No benefit shown of small incision. Overall equianalgesic opioid dose higher in accelerated rehabilitation.
Galea 2008 (Score=4.5)	Post-opeartive exercise and/or rehabilitation program	RCT	Sponsored by Musculoskeletal Health Initiative, Natioanl arthritis, and Arthritis Australia. The authors declared no conflict of interest.	N = 23 Unilateral THR	Mean age: 67.6 years; 7 males, 16 females.	Supervised center-based exercise (twice a week for 45 minutes with 7 exercises) vs. home-based exercise for 8 weeks. Exercises included figure of 8, sit to stand, active simple leg stance, climbing steps, hip abduction, heel raise, side stepping.	No mention of follow-up.	Walking speed (baseline/post): Center-based (100.0±25.2/116.7±18.1) vs. home-based (102.2±14.1/117.4±16.7) (NS). Multiple other measures also improved (e.g., steps/min, step length) but most were not different between groups.	"No group differences were found in the majority of the outcome measures. This finding is important because it shows that THR patients can achieve significant improvements through a targeted strengthening program delivered at a center or at home."	Small sample size. Multiple interventions. Data suggest rehabilitation with a home program may be equally efficacious in this group with mean age of ~68 years.
Maire 2003 (Score=4.0)	Post-opeartive exercise and/or rehabilitation program	RCT	No mention of sponsorship or COI.	N = 14 All post-THR	Mean age: 77 years;2 males, 12 females.	Training group for 6 weeks (n=7) vs. controls (n=7). Training 1 week after surgery, 3-30 minute sessions a week. Only training group had ergometer exercises.	No mention of follow-up.	Six-minute walk test results at 2 months: training 404.5 vs. controls 259.0m, p <0.01. VO2 (baseline/post-op/2 months): training (7.5/9.0/13.0) vs. controls (6.9/5.6/9.8).	"These results stress the importance of physical training in a rehabilitation program after total hip joint arthroplasty and this should be considered for	Very small sample size; 6-week treatment protocol suggests upper extremity exercise may help, however bias may be different degrees of rehab

						Both groups had exercises (walking, aquatics, ROM) 2 hours a day.			improving the current practices in rehabilitation."	contact. Also, drop in post-op results before training for controls concerning for confounding.
Kishida 2001 (Score=II)	Post-opeartive exercise and/or rehabilitation program	Prospective cohort	No mention of sponsorship. The authors declared no conflict of interest.	N = 33 All cementless arthroplasties	Mean age: 51.5 years; 23 females, 10 males.	Immediate full weight bearing group on second day postoperative (n=17) vs. Late full weight bearing group on 6th week postoperative (n=16).	Follow-up at 5.1 to 5.4 years.	Rehabilitation to walk with cane 5.8 vs. 44.8 days (p = 0.0001). Hospital stay 30.1 vs. 46.7 days (p = 0.006). No differences in radiolucent lines.	"Full weight-bearing immediately after cementless THA shortened the rehabilitation process and the hospital stay without radiographic migration of the components or clinical complications."	Results support immediate weight bearing. The length of hospital stay data (Osaka, Japan) are quite long compared with U.S.

Evidence for the Use of Late Post-Operative Exercises

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Late post-operative exercise; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 4 articles in PubMed, 4 in Scopus, 3 in CINAHL, 0 in Cochrane Library, 653 in Google Scholar, and 19 from other sources. We considered for inclusion 1 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 19 from other sources. Of the 21 articles considered for inclusion, 19 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Trudelle-Jackson 2004 (score=7.5)	Late post-operative exercises	RCT	Sponsored part by the Texas Physical Therapy Education and Research Foundation, Austin, TX. No COI.	N = 34. 4 to 12 months post-operative THA patients	Mean age: 59.5±11.2 years; 13 males, 15 females	Strength and postural stability exercises (n=18) vs. Isometric and active range of motion exercises (n=16)	8 weeks, 4 months, 12 months	Median HQ-12 scores (pre/post intervention): strengthening (21.0/16.0) vs. control (19.0/17.5). Postural stability (pre/post % of unaffected side): strengthening (66.1%/90.4%) vs. control (76.3%/77.0%), p <0.05. Muscle strength also improved in all groups tested in strengthening group (p <0.05).	"An exercise program emphasizing weight bearing and postural stability significantly improved muscle strength, postural stability, and self-perceived function in patients 4 to 12 months after THA."	Suggests therapy emphasizing function including strengthening and postural stability is efficacious in patients who may require additional rehabilitation several months after surgery.
Sherrington 2004 (score=6.5)	Late post-operative exercises	RCT	Sponsored by the Health Research Foundation Sydney South West, Arthritis Foundation of Australia, and National Health and Medical Research Council	N = 120. All had had hip fracture from a fall average 6 months earlier	Mean age: 79±9 years; 25 males, 95 females	Weight-bearing home exercise (n=40) – sit to stand, lateral step-up, forward step-up-and-over, forward foot taps, stepping grid. vs. Non-weight-bearing home exercise (n=40) – hip abduction, flexion, hip and knee flexion and extension, range of knee extension, ankle dorsiflexion and plantarflexion.	4 months	Balance improved in weight- bearing group (pre/4 months): weight bearing (7.0±5.4/11.0± 6.3 steps) vs. non-weight-bearing (7.7±7.1/9.4±6.7) vs. controls (8.3±6.5/9.0±7.3), p <0.001. Functional reach also better in weight-bearing group (17.5±6.8/ 24.8±8.8cm) vs. non-weight-bearing (18.4±9.1/19.9±8.1) vs. controls (17.8±8.7/ 19.4±10.0), p <0.05). No differences in strength (p = 0.92). Timed sit to stand improved more in	"A weight-bearing home exercise program can improve balance and functional ability to a greater extent than a non-weight-bearing program or no intervention among older people who have completed usual care after a fall-related hip fracture."	Results suggest weight bearing exercises are superior to non-weight bearing exercises. Prior treatment of patients not well described, but study suggests significant morbidity before entering trial after fracture an average 6 months earlier.

			Partnership in Injury Grant. No COI.			vs. Control groups (n=40) – Follow-ups at 1 week, 1 and 4 months.		weight-bearing group (p <0.05).		
Monaghan 2017 (Score=6.5)	Late post-operative exercises	RCT	Sponsored by research training fellowship for healthcare professional's award 2012-2014. The authors declared no conflict of interest.	N=63 Patients experienced total hip replacement.	Mean age: 68 years; 43 males, 20 females.	Functional exercise and usual care intervention (n=32) – attended physiotherapy-supervised functional exercise classes twice weekly for 12-18 weeks following THR. vs. Usual care only intervention (n=31).	Follow-up at 12 to 18 weeks.	After 18 weeks intervention, WOMAC function component score was lower significantly in functional exercise group (10.7±9.5 to 5.4±6.6) than control group (9.7±5.09 to 8.8±8.9); while no difference was found in WOMAC stiffness and pain scores between the two groups.	" [P]atients who undertake a physiotherapy-led functional exercise programme between 12 and 18weeks after THR may gain significant functional improvement compared with patients receiving usual care."	Used care bias. Data suggest functional improvement at weeks 12 and 18 post THA in PT led exercise programs.
Mangione 2005 (score=6.0)	Late post-operative exercises	RCT	Sponsored by a Foundation for Physical Therapy Research Grant. No mention of COI.	N = 41 7-50 weeks after hip fracture, with ORIF, partial or total arthroplasty.	Mean age: 78.69±6.8 years; 9 males, 24 females	Aerobic (n=13) – target 65-75% heart rate max. for 20 minutes. vs. Resistance training (n=17)– hip extensors, abductors, knee extensors, plantar flexors, 3 sets of 8 repetitions. vs.	12 weeks	6-minute walk distance (pre/post): aerobic (232.4±122.0/321.1±101.7) vs. resistance (197.1±104.2/278.9±114.6) vs. control (180.6±104.3/266.2±82.4). Maximum lower extremity force: aerobic (55.6±17.4kg/67.1±22.3) vs. resistance (48.5±12.6/59.6±18.2) vs. control (64.1±24.6/67.7±22.2).	"High-intensity exercise performed in the home is feasible for people with hip fracture. Larger sample sizes may be necessary to determine whether the exercise regimen is effective in reducing impairments and improving function."	Small sample size. High dropout rate for resistance training group.

						Wait-list controls (n=11) - Exercise sessions 30-40 minutes, 2 "overload" sessions a week first 2 months, then 1 a week for 1 more month.				
Barker 2013 (Score=6.0)	Late post-operative exercises	RCT	Sponsored by NIHR RFPB grant. No mention of COI.	N=80 male patients underwent hip resurfacing arthroplasty.	Median age: 56 years; 80 males, 0 female.	Treatment Group (n=40) - Tailored postoperative physiotherapy. vs. Control Group (n=40) - Standard physiotherapy.	Follow-up at 16 and 52 weeks.	By 52 weeks, Intervention group's Oxford Hip Score [780] was 45.1±5.3, higher than control group 39.6±8.8, the difference of 5.5-point was significant (p=0.001).	"A tailored physiotherapy programme improved self-reported functional outcomes and hip range of motion in patients undergoing hip resurfacing."	Standard care bias. Data suggest similar efficacy with a slight trend towards greater improvement in accelerated rehab program at one year. Self-reported functional outcomes and hip ROM were better in the tailored PT group.
Rahman n 2009 (Score=6.0)	Late post-operative exercises	RCT	Sponsored by the Wesley Research Institute grant. The authors declared no conflict of interest.	N=65 patients underwent hip or knee replacement surgery.	Mean age: 69.6±8.2 years; 30 males, 35 females.	Aquatic physiotherapy group (n=24) – completed 1 of the 2 aquatic treatment programs daily. vs. Water exercise group (n=21) vs. Ward control (n=20)	Follow-up at 6 months.	For the three primary outcomes, hip abductor strength was significantly greater (mean difference: 3.9 kg) in hydrotherapy group at 14th day (p=0.001); 10-minutes' walk time and WOMAC indicated clinical difference by 37% and 25% respectively, not statistical difference.	"A specific inpatient aquatic physiotherapy program has a positive effect on early recovery of hip strength after joint replacement surgery."	Data suggest benefit in hip abductor strength for post THA and TKA patients from aquatic therapy.
Liebs 2012 (score=5.5)	Late post-operative exercises	2 RCTs	Sponsored by the Society for Support of Research in	N=465 undergoing primary THA	Mean age: 68.7 years; 156 males,	Hip Arthroplasty: Early Aquatic Therapy: (n=138) received aquatic therapy after 6th	Follow-up at 3, 6, 12, 24 months	Post hip arthroplasty showed effect size for primary outcome ranged from .01 (3 months,p=0.8) to 0.19 (6	"Early start of aquatic therapy had contrary effects	Data do not support early aquatic therapy post THA but there was a trend for improved outcomes for TKA.

			and Fighting of Rheumatic Diseases Bad Bramstedt, the Society for Support of Rehabilitation Research in Schleswig-Holstein, the State Insurance Agency of the Free and Hanseatic City of Hamburg, and the German Arthrosis Society. No COI.	(n=280) or TKA (n=185)	309 females	postoperative day for 30 min sessions 3 times/week vs Late Aquatic Therapy: (n=142) received aquatic therapy on the 14th postoperative day for 30 min sessions 3 times/week Vs. Knee Arthroplasty: Early Aquatic Therapy: (n=87) received aquatic therapy after 6th postoperative day for 30 min sessions 3 times/week vs Late Aquatic Therapy: (n=98) received aquatic therapy on the 14th postoperative day for 30 min sessions 3 times/week		months, p=0.52). Post knee arthroplasty showed better mean outcomes for early aquatic therapy group at 3, 6, 12, and 24 months. WOMAC stiffness score for late aquatic therapy group at 12 months was better (effect size=.03). Effect sizes for primary outcome WOMAC physical function ranged from .22 at 6 months (p=0.45) to .39 at 24 months (p=.12).	after TKA when compared with THA and it influenced clinical outcomes after TKA. Although the treatment differences did not achieve statistically significance, the effect size for early aquatic therapy after TKA had the same magnitude as the effect size of nonsteroidal anti-inflammatory drugs in the treatment of osteoarthritis of the knee. However, the results of this study do not support the use of early aquatic therapy after THA. The timing of physiotherapeutic interventions has to be clearly defined when conducting studies to evaluate the effect of physiotherapeutic interventions after TKA and THA."	
Villadsen 2013	Late post-operative exercises	RCT	Sponsored by the Region of	N=165 patients who had	Mean age: 67±8 years; 73	Intervention group (n=84) - Exercise intervention and	Follow-up at 3 months.	After six weeks postoperatively, exercise intervention group	" Eight weeks of supervised neuromuscular	Data suggest that at 3 months NM exercise plus TJA did not show

(Score=5.5)			Southern Denmark, TrygFonden,and the Danish Rheumatism Association. The authors declared no conflict of interest.	schedule knee or hip arthroplasty.	males, 92 females.	educational package for 8 weeks. vs. Control Group (n=81) – patients received Educational package.		indicated significant improvement in activities of daily living (ADL) than educational control group (p=0.0488; 5.6, 95% CI: 0.03-10.3 vs. 5.4, 95%CI: 0.1-10.8). However, no difference in ADL was found after 3 months postoperatively.	exercise prior to total joint arthroplasty (TJA) of the hip or knee did not confer additional benefits 3 months postoperatively compared with TJA alone. However, the intervention group experienced a statistically significant short-term benefit in ADL and pain, suggesting an earlier onset of postoperative recovery."	superiority of TJA clone although there was a statistically significant short term ADL benefit and pain.
Hauer 2002 (score=5.0)	Late post-operative exercises	RCT	Sponsored by a grant from the Ministerium fur Wissenschaft, Forschung und Kunst Baden-Wuerttemberg and the University of Heidelberg.	N = 28 Admitted for injurious falls or hip fracture or arthroplasty, 6-8 weeks after rehabili-tation	Mean age: 81.3 years; 0 males, 28 females	Twelve-week trial of progressive lower extremity resistance training, progressive functional and balance training (n=12) vs. "Placebo motor activity" (calisthenics, games, memory tasks). Intensity at 70-90% maximum workload, 3 times a week, 12 weeks.(n=12)	6, 8 weeks, 3 months	Walking velocity (pre/post/3 months): exercise (0.54±0.21/0.73±0.21/0.72±0.28m/s) vs. controls (0.50±0.18/0.44±0.20/0.49±0.15m/s). Total activity: exercise (9.9±4.8/20.2±3.5/11.0±6.5) vs. controls (6.5±2.3/7.9±3.5/6.5±3.2).	"[P]rogressive resistance training and progressive functional training are safe and effective methods to increase strength and functional performance during rehabilitation in patients after hip surgery and a history of injurious falls."	Heterogeneity of patients may preclude robust conclusions. Age over 75, all female. Most results did not persist, suggesting lack of adherence to behavioral changes.

Husby 2010 (Score=4.5)	Late post-operative exercises	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=24 patients underwent total hip arthroplasty.	Mean age: 57 years; 9 males, 15 females.	Strength training and conventional rehabilitation group (v=12) vs. Conventional rehabilitation only group (n=12).	Follow-up at 6 and 12 months.	After 6 months, intervention group indicated significant improvement by 29% in work efficacy than control group (p=0.034). After 12 months, intervention group improved 30% in work efficacy than control (p=0.047).	"[H]igher work efficiency after 6 and 12 mos and improved rate of force development after 12 mos in total hip arthroplasty patients who performed early maximal strength training combined with conventional rehabilitation after total hip arthroplasty surgery compared with total hip arthroplasty patients receiving conventional rehabilitation only."	Standard care bias. Data suggest easily post-operative maximal strength training increases work efficiency 6-12 post THA (36% vs. 74%).
Unlu 2007 (score=4.0)	Late post-operative exercises	RCT	No mention of sponsorship or COI.	N = 26 1-2 years after hip arthroplasty	Mean age: 51.7 years; 8 males, 18 females	Group 1 - home exercise program (n=9) vs. Group 2 – PT supervised hospital based program (n=8) vs. Group 3 – control (n=9)	6 weeks	Improvements in gait speed (pre/post): group 1 (67.8±23/74.4±24) vs group 2 (48.5±4/56.7±5) vs. group 3 (58.0±12/59.8±14). Maximum isometric abduction torque group 1 (30±12/38±11 ft-lbs.) vs. group 2 (18±10/30±9.8) vs group 3 (18±10/19±8).	"[B]oth home and supervised exercise programmes are effective one year after total hip arthroplasty. Home exercise programmes with close follow-up could be recommended."	Small sample sizes. Suggests improvements in either home exercise or supervised training groups. No clear functional advantage of supervised program.
Umpierres 2014 (Score=4.0)	Late post-operative exercises	RCT	The authors declared no	N=106 hip osteoarthritis	Mean age: 61.4±15.0 years; 49	THAP group (n=52) – received only the assistance provided by the	Follow-up at 15 days after surgery.	Intervention THAPCP group indicated greater improvement in muscle strength force than no	"Our study emphasizes that the action	Assessment made only 15 days following surgery. Data suggest a benefit from the

			sponsorship or COI.	patients underwent hip arthroplasty.	males, 57 females.	multidisciplinary hip group. vs. THAPCP group (n=54) – received the same assistance by the multidisciplinary hip group with the additional presence of a physiotherapy professional.		intervention THAP group (p<0.001) THAPCP group also indicated significant improvement in clinical motor performance which measured by Merle D'Aubigne and Postel scale (p=0.007).	of a physiotherapist is of great importance for the successful rehabilitation of the patient after THA surgery."	THAPCP group but longer follow-up is required to validate results.
Nakanowatari 2016 (Score=4.0)	Late post-operative exercises	RCT	No mention of sponsorship or COI.	N=27 patients with perceived and functional leg length discrepancy.	Mean age: 63.1 years; 1 male, 26 females.	SEA Group (n=10) – patients received specific exercise approach; included post-isometeric muscle relaxation and side shift and hitch exercises for scoliosis. vs. Modifiable heel lift group (n=8) – patients were given an insole-type heel life to correct the functional LLD. vs. Control group (n=9) – received normal	Follow-up at 3 weeks.	After 3 weeks of surgery, functional LLD was smaller in two intervention groups than the control group (p<0.05). Patient-perceived LLD indicated differences among three groups (p=0.01).	"SEA and MHL use, during early post-operative recovery, can produce relevant changes in functional LLD after THA."	Usual care bias. Short follow up time (3 weeks). No blinding nor placebo group. Small sample.

						rehabilitation in the hospital.				
Wolf 2013 (Score=4.0)	Late post-operative exercises	RCT	Sponsored by Zimmer Inc. No COI.	N=39 patients underwent uncemented hip arthroplasty.	Mean age: 54±9 years; 20 males, 19 females.	Full weight bearing group (n=19) – bear full weight after surgery and enrolled in physiotherapeutic program with home exercises. vs. Partial weight bearing group (n=20) – bear partial weight after surgery. Received a short-written home-exercise program.	Follow-up at 5 years.	Body mineral density (BMD) decreased 3% at femoral neck, 3% at total hip, 2% at trochanter, after 5 years of the surgery. No decrease of BMD was found at heels after 2 years of the surgery.	"The postoperative weight-bearing regimen had no effect on changes in body composition or bone mineral density. Five years after total hip arthroplasty there was a decrease in bone mineral content and bone mineral density, but no changes in lean mass or fat mass."	Small sample. Data suggest no difference in body composition and bone mineral density at 1 year but at 5 years, bone mineral density decreased by approximately 3%.
Rooks 2006 (Score=3.5)										High dropout rate. Standard care bias.
Mcnally 1997 (Score=3.5)										Data suggest active movement increase hemodynamic flow preventing thrombosis.
Jogi 2015 (Score=3.0)										Baseline differences between THA and TKA groups. Data suggest exercise plus balance group had better balance than typical exercise group.
Gilbey 2003 (Score=3.0)										Limited methods. Short follow-up period of only 8 weeks. Data suggest a larger study for a longer

										duration may suggest the benefit of exercise on early functional recovery post THA.
Kishida 2001 (Score=II)	Cementless hip arthroplasty/ weight-bearing/ gain walking/ rehabilitation	Prospective cohort	No mention of sponsorship. The authors declared no conflict of interest.	N=33 patients with uncemented total hip arthroplasty.	Mean age: 51.5 years; 10 males, 23 females.	Group A (n=17) – immediate Full weight-bearing vs. Group B (n=16) – late full-weight bearing (delayed 6 weeks post-operatively).	Follow-up at 5.1 to 5.4 years.	No significant differences of Merle d'Aubigne hip score between two groups were found: immediate full weight bearing group (9.6 to 17.7) and late full weight bearing group (8.8 to 17.2). Duration days of hospitalization for immediate group was average 30.1 days, and 46.7 days for late group.	"Full weight-bearing immediately after cementless THA shortened the rehabilitation process and the hospital stay without radiographic migration of the components or clinical complications."	Data support immediate weight bearing post cementless THA for faster recovery and decreased hospitalization days.

*Evidence for specific work, avocational activities, or sports post-operatively***.**

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: vocational, avocational, physical activity, sports; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 47 articles in PubMed, 88 in Scopus, 4 in CINAHL, 2 in Cochrane Library, 216 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 1 systematic studies met the inclusion criteria.

Osteonecrosis

Evidence for the Use of Bone Scans

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: bone scan; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 75 articles in PubMed, 301 in Scopus, 14 in CINAHL, 7 in Cochrane Library, 10600 in Google Scholar, and 1 from other sources. We considered for inclusion 12 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 6 from Google Scholar, and 1 from other sources. Of the 21 articles considered for inclusion, 7 randomized trials and 14 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Diederichs 2017 (Score= 8.5)	Bone scan	diagnostic	Sponsored by the Deutsche Forschungsgemeinschaft. No COI.	N=14 patients with 56 bone segments.	Mean age: 65.4 ± 11.3 years; 6 males, 8 females.	Avascular bone necrosis	SPECT/CT group: received single photon emission computed tomography scanning (n= 56 bone segments) vs. MRI-TIRM group: received MRI with turbo inversion recovery magnitude (n= 56 bone segments) vs. T1-FS group: received contrast enhanced T1 fat sat and mapping (n=56 bone segments).	To diagnose viable or nonviable bone tissue, SPECT/CT indicated highest 90% sensitivity and 94% specificity; TIRM indicated 87% sensitivity and 88% specificity; and T1-FS indicated 90% sensitivity and 88% specificity, while T1-mapping indicated lowest 82% sensitivity and specificity.	"Both bone SPECT/CT and MRI allow a reliable differentiation between viable and nonviable bone tissue in patients after girdlestone arthroplasty."	Data suggest both SPECT/CT and MRI are reliable methods for detecting viable versus non-viable bone post girdlestone arthroplasty.
Ryu 2002 (Score= 7.5)	Bone scintigraphy	diagnostic	No mention of sponsorship or COI.	N=24 patients with normal femoral heads on radiography.	Mean age: 39.5 ± 9.6 years; 14 males, 10 females.	Femoral head osteonecrosis	Bone SPECT group: received ^{99m}Tc-methylene diphosphonate SPECT after renal transplantation (n=24) vs. MRI group: received 1.5-T scanners MRI after renal transplantation (n=24).	To diagnose osteonecrosis, two scanning tools showed significant difference. SPECT indicated 100% sensitivity, and MRI indicated 66% sensitivity ($p<0.005$).	"^{99m}Tc-methylene diphosphonate SPECT is more sensitive than MRI for the detection of femoral head osteonecrosis in renal transplant recipients."	Renal transplant patients. Data suggest SPECT is more sensitive than MRI in early osteonecrosis detection of the femoral head.

Siddiqui 1993 (Score= 7.0)	Bone scan	diagnostic	No mention of sponsorship or COI.	N=104 patients received renal transplantation.	Mean age: 36 years; 58 males, 46 females.	Avascular necrosis	MRI group: received 1.5 Tesla superconducting magnet within 1 week of renal transplantation (n=103) vs. bone scan group: received Apex sp/6 Elscint, Siemens Dual-head Rotacamera, or Raytheon Spectrum bone scintigraphy within 1 week of renal transplantation (n=103).	115 hips indicated normal results in both MRI and bone scan; 6 hips indicated abnormal in both MRI and bone scan. However, 10 hips indicated normal in bone scan but abnormal in MRI; 13 hips indicated normal in MRI but abnormal in bone scan.	"Where the imaging findings were identical to those in the asymptomatic patients as well as those in whom the imaging abnormality regressed, we suggest that the subclinical imaging abnormalities represent mild AVN, which is reversible in some cases."	Small sample of renal transplant patients. Data suggest both MRI and SPECT bone scans are useful but detection of subclinical AVN may require the use of both tests.
Lee 2006 (Score= 6.5)	Bone scintigraphy	Prospective diagnostic	Sponsored by the Samsung grant SBRI C-A6-4191 in Korea. No mention of COI.	N=237 patients experienced renal transplantation with 473 femoral heads.	Mean age: 40±12 years; 127 males, 110 females.	Femoral head avascular osteonecrosis	Grade 1 group: received mildly increased bone scintigraphy 1 year after renal transplantation (n=237) vs. grade 2 group: received definitely increased bone scintigraphy 1 year after renal transplantation (n=237).	To diagnose avascular osteonecrosis, grade 1 bone scintigraphy indicated 91.3 % sensitivity and 74% specificity. Grade 1 bone scintigraphy indicated 56.5% sensitivity and 99.5% specificity. Typical photon defect indicated low 47.8% sensitivity and high 99.1% specificity.	"The incidence of femoral head AVN was low among a prospective cohort of renal transplantation recipients at the time of 1 year after engraftment. Planar bone scintigraphy is sufficient to diagnose AVN in symptomatic patients at risk for femoral head AVN using grade I and II activities as positive criteria."	Data suggest femoral head ON in renal transplants 1 year post transplant was low and bone scans may be useful for detecting at risk patients for developing ON.
Mitchell 1987 (Score= 5.5)	MRI, radiographic imaging	Comparative diagnostic	No mention of sponsorship or COI.	N=39 patients with avascular osteonecrosis	No mention of age. 23 males, 16 females.	Femoral head avascular osteonecrosis	MR group: received T1 weighted SE and T2 weighted MR imaging (n=56 hips) vs. bone scan group: received radionuclide 20 mCi technetium 99m methylene diphosphonate injection scans (n=56 hips).	MR imaging identified 96% abnormalities in femoral head and 94% focal defects. 84% femoral head abnormalities showed flattened in MRI but identified by radiographic bone scans.	"The peripheral double line sign on long TR/TE images may add specificity to the diagnosis of AVN by MR imaging."	Data suggest MRI has characteristic signal pattern which accurately detect femoral head ON.

Mont 2008 (Score= 5.0)	Bone scan	Diagnostic	No mention of sponsorship or COI.	N=48 patients with suspected osteonecrosis in hip, knee, shoulder, or ankle.	Mean age: 39 years; 15 males, 33 females.	Osteonecrosis	Bone scan group: received 20-30 mCi ^{99m} technetium methylenediphosphonate injection bone scanning (n=48) vs. MRI group: received T1 weighted spin-echo and T2 weighted spin-echo MR imaging (n=48)	To diagnose osteonecrosis, MRI identified all lesions, while bone scan indicated 55.8% sensitivity, and MRI indicated 38% in consistency with bone scans. For positive lesions, bone scans indicated 19% positive at Stage I, 56% positive at Stage II, and 80% positive at Stage III. Hip and knee lesions showed higher sensitivity than shoulder and ankle lesions.	"Our results demonstrated the low sensitivity of bone scintigraphy for diagnosing symptomatic osteonecrosis."	Data suggest a lower bone scan sensitivity than MRI and it is particularly least sensitive at early stages of osteonecrosis making it less than ideal for diagnosis compared to MRI.
Mitchell 1986 (Score= 5.0)	Bone scan	Diagnostic	No mention of sponsorship or COI.	N= 435 normal or abnormal hips.	No mention of age and sex.	Avascular necrosis	MRI group: received T1-weighted and T2-weighted MR imaging (n=188) vs. RN group: received technetium-99 methylene diphosphonate radiopharmaceutical scanning (n=141) vs. CT group: received CT/T 8800 and CT/T 9800 scanning (n=106).	For receiver operating characteristic (ROC) scores, MR (mean ROC=0.959±0.0059) and RN (mean ROC=0.914±0.040) groups indicated significant difference ($p<0.0089$), but MR and CT (mean ROC=0.945±0.012) groups indicated no significant difference ($p<0.19$), and CT and RN groups indicated no significant difference ($p<0.15$).	"This is evidence that MR is the most sensitive imaging technique for the early diagnosis of avascular necrosis."	Data suggest MRI is most sensitive for detection of ON of the hip in early stages followed by CT and then bone scans.

Evidence for the Use of Computerized Tomography (CT) Scan

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Computed Tomography, X-Ray Computed, Computerized Tomography, CT scan, CAT Scan, Angiography; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 63 articles in PubMed, 33 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 1,350 in Google Scholar, and 0 from other sources. We considered for inclusion 6 from PubMed, 4 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 12 articles considered for inclusion, 4 randomized trials and 8 systematic studies met the inclusion criteria.

Comments:

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Yuan 2015 (score=7.5)	Computerized Tomography	RCT	Sponsored by The National Natural Science Foundation of China and International Cooperation Project of Shanghai Science and Technology Committee. No mention of COI.	N = 114 patients diagnosed with femoral neck fracture.	Mean age: 58.6 years; 53 male, 61 female.	Osteonecrosis of the femoral head.	Osteonecrosis diagnosis of patients determined using SPECT-CT scans after admission (N=114 patients) vs osteonecrosis diagnosis of the same patients using radiographs and MRI's after admission and over the next two years (N=114 patients).	With a cutoff of 0.55, the sensitivity was 97% and the specificity was 79% with a positive predictive value of 95% and negative of 19%.	"SPECT-CT proved to be reliable and valid for Predicting ONFH after femoral neck fracture."	Data suggest SPECT-CT is both reliable and valid for predicting ONFH post femoral neck fracture.

Barile 2013 (score=7.5)	Computerized Tomography	RCT	No sponsorship or COI.	N = 144 hips of 72 patients with reported AVN on MRI.	Mean age: 60; 28 male, 44 female.	Femoral head avascular necrosis	AVN diagnosis according to MRIs of patients (N=144 hips) vs AVN diagnosis according to CT scans of the same patients (N=144 hips)	35/43 (81%) MRI-proven AVN cases in 22/28 (79%) patients.	"Multidetector CT has high accuracy for detection of AVN; however, this is Frequently missed as an incidental finding (89% missed in the present study). Assessment for signs of femoral AVN should be part of routine search pattern in interpretation of pelvic CT."	Data suggest that although multidetector CT is very accurate for ON detection, there is a high miss rate.
Gayana 2016 (score=5.5)	Computerized Tomography	RCT	No sponsorship or COI.	N = 51 patients with high clinical suspicion of FHAVN and referred for MRI.	Mean age: 32.5 years; 39 male, 12 female.	Avascular Necrosis	AVN diagnosis of patients using MRI on a 3.0 MRI unit (N=102 hips) vs AVN diagnosis of the same	MRI had 96.5% sensitivity, 100% specificity, and 98.03 accuracy. PET/CT had 100%	"F−18 fluoride PET/CT showed good agreement with MRI in the initial diagnosis of FHAVN and can be better	Data suggest good agreement between PET/CT and MRI for diagnosis of early ON

							patients using PET/CT 1 hr after intravenous injection of 370 MBq of F-18 fluoride (N=102 hips)	sensitivity, specificity, and accuracy.	than MRI in detecting early disease."	
Sartoris 1988 (score=3.5)										Data suggest CT plus multiplanar reformation and 3-D image reconstruction superior to plain radiographs for evaluating adult hip disease.
Stevens 2003 (score=N/A)		Comparative Clinical Study								Study performed to evaluate bone morphogenetic protein. Blinded readings of radiological studies not performed, only blinded to treatment. On rater read all images. Data suggest MRI may be inferior for this purpose.

Evidence or use of Helical CT

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Helical CT Scans OR spiral computed tomography; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 3 articles in PubMed, 42 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 913 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: magnetic resonance imaging, mri, mri scan; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 159 articles in PubMed, 346 in Scopus, 83 in CINAHL, 19 in Cochrane Library, 5050 in Google Scholar (Went through first 100), and 0 from other sources. We considered for inclusion 24 from PubMed, 1 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 0 from other sources. Of the 29 articles considered for inclusion, 15 randomized trials and 14 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Miller 1987 (score= 8.0)	Magnetic Resonance Imaging	RCT	No mention of sponsorship or COI.	N =29 hips of patients with clinical and roentgenographic evidence of AVN.	Mean age: 37.7 years; 24 male, 5 female.	Osteonecrosis of the femoral head.	AVN diagnosis according to MRI of the same patients where an MRI on a 1.5 Tesla Technicare super-conducting MRI system was performed (N=29 hips) vs AVN diagnosis according to SPECT imaging of any of the roentgenogram patients where a 20-mCi dose of technetium methylene diphosphonate was injected and SPECT imaging was done (N=24 hips)	MRI had a sensitivity of 100% and specificity of 100%. SPECT had a sensitivity of 58% and a specificity of 78%.	"MRI is highly sensitive in diagnosing osteonecrosis of the femoral head in early and late stages. Although the specificity of MRI in this series was loo%, the patient population did not include a high incidence of processes that can appear similar to osteonecrosis on MRI. A more accurate determination of MRI's specificity would require inclusion of a large number of these processes in the study population. MRI also provides excellent	Data suggest SPECT less specific and less sensitive than MRI in detection of femoral head osteonecrosis.

									anatomic detail of the fem oral head."	
Yeh 2009 (score= 7.5)	Magnetic Resonance Imaging	RCT	Sponsored by Kaohsiung Veterans General Hospital. No mention of COI.	N = 28 hips of 25 patients suffering from early stage avascular necrosis of the femoral head on standard radiographs.	Mean age: 44.8 years; 20 male, 5 female.	Osteonecrosis of the femoral head	AVN diagnosis of patients hips using MR imaging using a 1.5 T magnet (N=28) vs AVN diagnosis of the same patients hips using spiral CT scans on a single-row detector CT scanner (N=28)	MRI done by musculoskeletal radiologist sensitivity was 92.9% and specificity was 28.6%. MRI done by a general radiologist sensitivity was 67.3% and specificity of 42.9%.	"The accuracy of routine MR imaging in the evaluation of subchondral fracture is not satisfactory. False positive diagnosis is not uncommon. Interpretation of routine MR imaging readout should be guarded."	Data suggest MRI not as good as CT for detecting subchondral fractures in ON.
Zibis 2007 (score= 7.0)	Magnetic Resonance Imaging	RCT	No mention of sponsorship or COI.	N = 115 hips of 72 patients who were evaluated and classified according to the ARCO classification criteria with the use of plain radiographs and additional application of MRI.	No mention of age and gender.	Osteonecrosis of the femoral head	AVN diagnosis of patient's hips using MRI with a 1.0 MR scanner (N=115 hips) vs AVN diagnosis of the same patients hips using plain radiographs (N=115 hips)	MRI Sensitivity and specificity was 88% and 90.5% for stage II, 79.2% and 82% for stage III and 76% and 100% for stage IV.	"The ARCO classification could miss important information in stages II and III, where treatment aims at preservation of the hip joint integrity. The results of the present study suggest that MRI should be incorporated in the classification of osteonecrosis (stages	Discordance of ON classification between MRI and radiography. Data suggest MRI better for detection of stages II or III ON.

									II and III), to add accuracy and prognostic value."	
Stevens 2002 (score= 6.0)	Magnetic Resonance Imaging	RCT	No mention of sponsorship or COI.	N = 45 patients hips with stage I and stage II osteonecrosis of the femoral head.	Mean age: 47.8 years; 32 male, 13 female.	Osteonecrosis of the femoral head	AVN diagnosis of patients hips using CT scans with a helical scanner (n=45 hips) vs AVN diagnosis of the same patients hips using radiography (n=45 hips) vs AVN diagnosis of the same patients hips using MR imaging on a 1.5-T system (n=45 hips)	Sensitivity and specificity compared to CT was 71% and 97% for radiography and 38% and 100% for MR imaging.	"CT reveals more subchondral fractures in osteonecrosis of the femoral head than unenhanced radiograph or MR imaging. The high-signal-intensity line seen on T2-weighted MR images appears to represent fluid accumulating in the subchondral fracture, which may indicate a breach in the overlying articular cartilage."	Data suggest CT better than both radiography and MRI in the detection of subchondral fractures in osteonecrosis of the femoral head.
Robinson 1989 (score= 6.0)	Magnetic Resonance Imaging	RCT	No sponsorship or COI.	N = 96 hips of 48 patients who were at high risk for avascular necrosis.	Mean age: 46 years; 34 male, 14 female.	Osteonecrosis of the femoral head	Phase I included evaluation of 96 hips done clinically (n=96) vs MRI (n=96) vs radiography (n=96). Phase II evaluated 23 hips that were classified stage 0,	Abnormal patterns on MRI in 100% of stage 2 and stage 3 classified hips. Abnormal patterns on MRI in 64% of stage 1 classified hips. Abnormal	"Although false-negative and false-positive results were observed with magnetic resonance imaging, the over-all results of this study	Data suggest MRI useful for diagnosis of early ON of femoral head.

							stage 1 or stage 2 in phase 1. These were then evaluated using MRI, conventional radiography, histopathological evaluation of a core-bipsy specimen, and Ficats functional evaluation of bone.	patterns on MRI in 17% of stage-0 classified hips.	suggest that magnetic resonance imaging may be useful for the early diagnosis of avascular necrosis."	
Totty 1984 (score= 5.0)	Magnetic Resonance Imaging	RCT	No mention of sponsorship or COI.	N = 58 patients who had MRIs of the head and body.	Mean age: 52.5 years; 35 male, 23 female.	Osteonecrosis of the femoral head	Not predisposed to hip disease group (Group 1, n=38) vs known femoral head ischemic necrosis or historic predisposition for ischemic necrousis of hip, buttock or thigh pain (Group 2, n=20)	Abnormal patterns on MRI in 15 of 20 patients in group 2. Comparison of 14 hips showed 13 of 14 hips abnormal on both radiographs and MR images. Overall agreement between MRI and radiography was 93%.	"This series of cases shows that MRI can clearly identify ischemic necrosis of femoral head, sometimes when either radiographs or scintigrams give false-negative results."	Data suggest MRI better at imaging normal and ischemic femoral heads than either radiographs or scintographs.
Glickstein 1988 (score= 5.0)	Magnetic Resonance Imaging	RCT	No mention of sponsorship or COI.	N = 61 hips of 45 patients with evidence of AVN or other hip disease.	No mention of age or gender.	Osteonecrosis of the femoral head	AVN diagnosis of patients hips using MR imaging on a 1.5-T superconducting imaging system (N=61 hips) vs the AVN diagnosis of the same patients hips with known cases of Non-AVN hip	MR imaging specificity between 71% and 100% and sensitivity of between 94% and 100%.	"MR imaging can assist the radiologist in discriminating between AVN and other hip disease. The structural and signal features in AVN of the	Data suggest MRI likely beneficial in distinguishing between ON and other diseases of the hip.

							disease (N=26) and biopsy proven AVN (N=35).		hip allow a specific diagnosis of this condition to be made."	
Hu 2014 (score= 5.0)	Magnetic Resonance Imaging	Prognostic	No mention of sponsorship or COI.	N = 30 femoral head specimens of 23 patients who had undertaken hip arthroplasty due to ONFH.	Mean age: 36.5 years; 16 male, 7 female.	Osteonecrosis of the femoral head	Evaluation of 30 femoral heads using 16-slice spiral CT scans (n=30) vs 1.5 T MRI (n=30)	On the CT scans, 22/30 showed subchondral fractures vs 10/30 on MR images. Mean lesion volume for CT scan was 22.03 vs 22.11 for MRI (p=0.677)	"For patients with ONFH in Association Research Circulation Osseous stage III or above, CT and MRI can accurately display the characterization of lesion."	Small sample. Data suggest high degree of correlation between CT and MRI but MRI is most sensitive for detection of osteonecrosis of the femoral head.
Thickman 1986 (score= 4.5)	Magnetic Resonance Imaging	RCT	Sponsored by the General Electric Company. No mention of COI.	N = 90 hips of 45 patients examined for suspected avascular necrosis of the femoral head.	No mention of mean age, ages 19-61 years; 24 male, 21 female.	Osteonecrosis of the femoral head	Of the 90 hips, 52 had biopsy proved AVN. Subsets of these were then examined with MRI (n=52) vs computerized tomography (n=41) vs radionuclide scintigraphy(n=39) vs routine tomography (n=27) vs plain films (n=42)	Radionuclide imaging sensitivity and specificity were 86% and 79%. MRI sensitivity and specificity were 98% and 71%.	"Preliminary results suggest that MR can monitor treatment of the affected hip, and may even be able to predict patient response to therapy. Although further work is necessary to determine the role of MR in the evaluation of the patient presenting	Data suggest MRI has high sensitivity for detecting ON of femoral head.

									with hip pain, MR is a sensitive method in detecting AVN and in monitoring its course in patients suspected of having the disease."	

Evidence for the Use of X-rays/Radiographs

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: X-rays or Radiographs; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 259 articles in PubMed, 526 in Scopus, 283 in CINAHL, 19 in Cochrane Library, 9710 in Google Scholar, and 1 from other sources. We considered for inclusion 6 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 7 articles considered for inclusion, 1 randomized trial and 5 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/ Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Zibis, 2007 (score= 7.0)	X-rays/ radiographs	Diagnostic	No mention of sponsorship for COI.	N = 72 patients (115 hips) with femoral head osteonecrosis.	No mention of age or sex.	Femoral head osteonecrosis.	MRI (n=72) – performed using a 1.0 T MR scanner. Vs. Plain radiographs (n=72) – included anteroposterior and lateral views.	17 hips were classified as stage I, 25 as stage II, 48 as stage III, and 25 as stage IV. The SEN, SP, PPV and NPV of plain radiographs were for stage II 88%, 90.5%, 78.6% and 95%; for stage III 79.2% 82%, 80.8% and 87.2%; for stage IV 76%, 100%, 100% and 90.9%, respectively. The agreement between plain radiographs and MRI was 80.6% for staging the disease,	"In conclusion, the ARCO classification could miss important information in stages II and III, where treatment aims at preservation of the hip joint integrity. The results of the present study suggest that MRI should be incorporated in the classification of osteonecrosis (stages II and III), to add accuracy and prognostic value."	Data suggest high correlation between MRI and radiography for stage I femoral head necrosis, but radiography alone should not be used for stages II, III, or IV.

								71.2% for recording the location of the osteonecrotic lesion, 67.1% for evaluating the size of the lesion, 79.2% for the presence of collapse of the articular surface and 56.3% for the degree of collapse.		
Stevens 2003 (N/A)		Comparative Clinical Study								Study performed to evaluate bone morphogenetic protein. Blinded readings of radiological studies not performed, only blinded to treatment. On rater read all images. Data suggest MRI may be

										inferior for this purpose.

Evidence for targeting coronary artery disease risk factors
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: coronary artery disease, risk factors, smoking, hypertension; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 263 in Scopus, 1 in CINAHL, 0 in Cochrane Library, 1730 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Non-weight Bearing Activities

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: non-weight bearing activity; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 articles in PubMed, 497 in Scopus, 0 in CINAHL, 2 in Cochrane Library, 599 in Google Scholar, and 11 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 11 from other sources. Of the 12 articles considered for inclusion, 3 randomized trials and 8 systematic studies met the inclusion criteria.

Comments:

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Koo, 1995 (score =4.5)	Avoidance of dysbaric exposures	RCT	No sponsorship or COI.	N = 33 with 37 hips Most Stage I osteonecrosis	Mean age: 47 years; 31 males, 2 females	Core decompression (partial weight bearing) (n=18) vs. conservative treatment (non-weight bearing with crutches until pain resolved and analgesics) (n=19)	24, 36, 45 months	At second assessment, 9/10 (90%) symptomatic hips in coring group had pain relief vs. 25% conservatively-treated (p = 0.04). At minimum 24 months, 14/18 (78%) core-decompressed hips vs. 15/19 (79%) non-operated hips developed femoral head collapse, p = 0.79.	"Core decompression may be effective tin symptomatic relief, but is of no greater value than conservative management in preventing collapse in early osteonecrosis of the femoral head."	Weight bearing status differed between the 2 groups. Data suggest core procedure resulted in early symptom reduction, but not more effective than conservative treatment of stage I osteonecrosis.
Neumayr, 2006 (score =4.5)	Avoidance of dysbaric exposures	RCT	Sponsored by grants from National Institutes of	N = 46 patients with 46 hips Stages I, II, or III osteo-necrosis; all	Mean age: 25.6 years; 19 males, 19 females	Core decompression plus physical therapy (n=17) vs	3 months, 3 years; 80 months	At mean 3 years, survival 82% of decompression vs. 86% PT (NS). Mean	"[P]hysical therapy alone appeared to be as effective as hip core decompression	Less advanced disease PT group (stage III 33% vs. 59%) and non-study hips more

			Health. No COI.	sickle cell anemia		physical therapy alone (limited weight bearing, stretching, adductor and other muscle strengthening) (n=21)		improvement in Harris Hip score 18.1 for coring vs. 15.7 PT (NS). No differences in hip survival across stages I-III (92, 82, 82%).	followed by physical therapy in improving hip function and postponing the need for additional surgical intervention at a mean of three years after treatment."	disparate at baseline (19% vs. 47%) suggest randomization failure, thus conclusions difficult to draw. Generalizability from sickle cell anemia to working populations or others unclear.
Stulberg, 1991 (score =4.5)	Avoidance of Dysbaric Exposures	RCT	No mention of sponsorship or COI.	N=36 patients with 55 affected hips. Mainly Stages I, II or III osteonecrosis (2 with stage IV)	Mean age: 38.6 years; no mention of sex.	Coring procedure (partial weight bearing) (n=29) vs. conservative treatment (nonweight bearing for 6 plus weeks) (n=26)	3, 6, 12 months, with yearly follow-up after	Coring procedure superior to conservative treatment for stratified analyses of each Stage (I-III). No further intervention in [Core (%)/Conservative (%)]: Stage I [7(70%)/1(20%)], Stage II [5(71.4)/0(0)], Stage III	"Core decompression produced better results than conservative treatment in the early stages of (osteonecrosis). "	Mean age 39; mean follow-up 27 months. Higher intraosseous pressures in decompression group (52 vs. 44mmHg) may bias against coring. Data suggest core decompression superior to conservative treatment for Stages I, II and III.

								[8(100%)/1(10%)].		

Evidence for the Use of Hyperbaric Oxygen

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, Hyperbaric Oxygen, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 8 articles in PubMed, 183 in Scopus, 15 in CINAHL, 7 in Cochrane Library, 456 in Google Scholar, and 1 from other sources. We considered for inclusion 1 from PubMed, 3 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 5 articles considered for inclusion, 1 randomized trial and 4 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Camporesi 2010 (score=5.5)	Hyperbaric Oxygen	RCT	No sponsorship or COI.	N= 20 patients with unilateral femoral head necrosis	Mean age: 48.9 years; 12 males, 8 females	HBO Group: (n=10) received 2.5 ATA of hyperbaric oxygen for 82 minutes, comprising a period of 60 minutes for a total of 30 treatments vs HBA Group: (n=9) received 2.5 ATA of hyperbaric air for a total of 30 treatments	12 months, 7 years	HBO group showed better improvement after 20 sessions (p=.002) and 30 sessions (p<.001). Improvement in flexion was observed after 10 sessions (p=.335), 20 sessions (p=.356), 30 sessions (p=.195). Extension, adductions, abduction showed improvement after 10 sessions (p<.001), 20 sessions (p<.001), and 30 sessions (p<.001) comparing HBO and HBA groups.	"Hyperbaric oxygen therapy appears to be a viable treatment modality in patients with Ficat II FHN."	Small sample. Data suggest significant improvement in pain in HBO group with treatment gains maintained at 7 years.

Evidence for the Use of Bisphosphonates

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Bisphosphonates, Diphosphonates, Alendronate, Etridonate, Didronel, Ibandronate, Boniva, Risedronate, Actonel, Atelvia, Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 40 articles in PubMed, 5619 in Scopus (Went through first 100), 203 in CINAHL, 40 in Cochrane Library, 2890 in Google Scholar (Went through first 100), and 28 from other sources. We considered for inclusion 8 from PubMed, 0 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 2 from other sources. Of the 12 articles considered for inclusion, 7 randomized trials and 4 systematic studies met the inclusion criteria.

Comments:

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Chen, 2012 (Score= 7.5)	Bisphosphonates	RCT	Sponsored by Merck Sharp & Dohme (IA) Corporation, Taiwan Branch, and by grants from the National Science Council, the National Health Research Institutes, and the Department of Industrial Technology, Economic, Taiwan, Republic of China.	N = 64 patients will non-traumatic osteonecrosis.	Mean age: 46.3 years; 41 males, 11 females.	Alendronate (n=26) – patients received 70 mg of oral alendronate (Fosamax 70-mg tablets; MSD) each week for 104 weeks. Vs. Placebo (n=26) – patients received the placebo the placebo each week for 104 weeks.	Two years.	At the end of our study, 4 of 32 hips in the alendronate treatment group (12.5% [95% CI = 1.1–25.0%]) underwent THA. In comparison, 5 of 33 hips in the placebo group (15.2% [95% CI = 3.0–28.2%]) underwent THA (P=0.837). At the end of the study, 21 of the 32 hips in the alendronate group and 20 of the 33 hips in the placebo group had progressed (P=0.636). The total score for the short form 36 health survey	"[W]e performed a randomized, double-blind, placebo-controlled study of alendronate for the treatment of osteonecrosis of the femoral head. There was no significant pharmacologic function of alendronate in terms of the need for THA, the progression of disease, or the quality of life."	Data suggest lack of efficacy.

			No mention of COI.					in the alendronate group was -6.9±19.3 (p<0.05) and in the placebo group was -2.2±15.4.		
Lai, 2005 (score= 5.0)	Bisphosphonates	RCT	No sponsorship. One or more authors report receiving payment or benefits form MSD.	N = 40 patients (54 hips) with Stage II or III non-traumatic osteonecrosis	Mean age: 42.5 years; 30 males, 10 females.	Alendronate (n=20) – patients took 70 mg of Fosamax orally for 25 weeks. vs.Control (n=20) – patients received no treatment or placebo for 25 weeks.	Two years.	Progression 1+ stage alendronate 4/29 (13.8%) vs. control 20/25 (80.0%), p <0.001. Numbers collapsing: 0 vs. 19, p <0.001. At least 1 surgery for alendronate 3/29 (10.3%) patients vs. 17/25 (68.0%). Final mean Harris Hip scores 74.4±7.8 vs. 49.2±9.2.	"Alendronate appeared to prevent early collapse of the femoral head in the hips with Steinberg stage-II or IIIC nontraumatic osteonecrosis."	Not placebo controlled. Results suggest treatment prevents collapse of femoral head.
Wang, 2008 (score= 5.0)	Bisphosphonates	RCT	Sponsored by Chang Gung Research Fund, National Science Council	N = 52 patients (66 hips) with Osteonecrosis of the femoral head.	Mean age: 37.2 years; 33 males, 15 females.	Group A (n=25) – patients received the extracorporeal shockwave therapy (ESWT). Vs. Group B	1, 3, 6, and 12 months, and then once a year.	The pain score in Group A before treatment and after treatment was 5.03±2.75,	"ESWT and alendronate produced comparable result as compared with ESWT without alendronate in early ONFH. It	Data suggest lack of efficacy of alendronate added to ESWT, as there were no significant differences

			and National Health Research Institute. No mention of COI.			(n=23) – patients received ESWT and alendronate treatment (Fosamax 70 mg) weekly for a year.		0.69±1.19, p<0.001 and in Group B was 5.97±2.30, 0.6±1.06, p<0.001, respectively. The Harris hip score in Group A before treatment and after treatment was 79.2±12.9, 95.3±8.0, p<0.001 and in Group B was 75.1±6.1, 94.3±4.5, p<0.001, respectively.	appears that ESWT is effective with or without the concurrent use of alendronate. The joint effects of alendronate over ESWT in early ONFH are not realized in short-term."	between groups.
Venesmaa 2001 (score= 5.0)	Bisphosphonates	RCT	No mention of sponsorship or COI.	N = 13 HA-coated uncemented THA	Mean age: 62.6 years; 6 males, 7 females	Alendronate 10mg plus calcium carbonate 500mg (n=8) vs. calcium 500mg only (n=5) for 6 months	6 months	Periprosthetic bone mass in all Gruen zones (post-op/3 months/6 months): calcium (1.58±0.12/1.43±0.22/1.43±0.19), p = 0.022 vs. alendronate plus CaCO3 (1.60±0.25/1.55±0.27/1.56	"[A]lendronate seems to be a potent drug to inhibit the periprosthetic bone loss that occurs after primary uncemented THA…the follow-up time was too short and the study population too small to make	Small sample sizes. Data suggest alendronate may be effective, but study underpowered.

								±0.25), NS. Between group differences p <0.05.	firm conclusions…"	
Wilkinson 2001 (score= 5.0)	Bisphosphonates	RCT	Sponsored by grant from the Wishbone Trust (British Orthopaedic Association), The Royal College of Surgeons of England, and the John Charley Trust. No mention of COI.	N = 47 THA	Mean age: 58.5 years; 21 males, 26 females	Single-dose infusion pamidronate 90mg (n=23) vs. placebo (n=24)	1, 6, 12, 26 weeks	Pamidronate significantly reduced bone loss compared with placebo (p< 0.01). Pamidronate associated with suppressing multiple biochemical markers of bone turnover (p <0.05).	"Pamidronate significantly reduces the acute bone loss of proximal femur and pelvis over the first 6 months after total hip arthroplasty. The most protective effect of pamidronate was seen in the medial periprosthetic bone of the femur, the site is where femoral bone typically is most severe."	Single dose study. No long term follow-up. No significant differences in clinical outcomes.
Kang, 2012 (Score= 3.5)										Pilot Study. Data suggest some added benefit with the addition of alendronate to multiple drilling.
Lee, 2015										Open label study. Data suggest lack of

(score= 3.5)										efficacy as zoledronate did not prevent femoral head collapse or need for THA.

Evidence for Use of NSAIDs for treatment of osteonecrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: NSAIDs; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 262 in Scopus, 0 in CINAHL, 11 in Cochrane Library, 1170 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane

Evidence for use of Anti-confulsants for osteonecrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: **Anticonvulsants**; **Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head,** controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 0 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 26 in Google Scholar, and 4 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 4 from other sources. Zero articles met the inclusion criteria.

Evidence for use of gabapentin and pregabalin for osteonecrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Pregabalin; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 3 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 136 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gabapentin; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 0 articles in PubMed, 0 in Scopus, 8 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for use of glococorticosteroids for treatment of osteonecrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: glucocorticosteroids OR glucocorticoids; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 25 articles in PubMed, 3 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 2960 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Core Decompression

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Core Decompression, core decompression surgery; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 123 articles in PubMed, 136 in Scopus, 43 in CINAHL, 1 in Cochrane Library, 1270 in Google Scholar, and 6 from other sources. We considered for inclusion 7 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 6 from other sources. Of the 15 articles considered for inclusion, 12 randomized trials and 1 systematic study met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Ma 2014 (score =7.0)	Core Decompression	RCT	No COI. No mention of sponsorship.	N = 45 patients (53 hips) with Ficat stage I to III avascular necrosis of femoral head	Mean age: 35 ± 9.8 years; Provided gender results for only 39 participants included in the analysis - 28 male, 11 female.	Core decompression with autologous bone graft (control group) (n = 18) vs Core decompression with autologous bone graft and bone marrow aspiration and buffy coat implantation (BBC) (n = 21). Core decompression consisted of 1.5-cm incisions on the fascia and lateral aspect of the thigh, followed by a Kirschner wire driver into mid-line of trochanter. For BBC the bone marrow	Follow-up at 3 and 24 months	Slight increase in visual annual scale (VAS) pain scores in control group from baseline (35.21 ± 3.41mm) to 3 months (38.75 ± 3.27mm) but decreased at 24 months (26.46 ± 2.60mm, p=0.007). BBC group had decreased VAS pain scores from baseline (35.58 ± 4.21mm) to 3 months (24.62 ± 3.50mm, p<0.0.001) and to 24 months (16.92 ± 3.66mm p<0.001). BBC group also displayed significant improvement in joint symptoms via the Lequesne index and WOMAC scores: mean Lequesne index at basal	"Implantation of the autologous BBC grafting combined with core decompression is effective to prevent further progression for the early stages of ANFH."	Data suggest at 24 months, the autologous BBC grafting plus core decompression group had significantly less pain, fewer clinical joint symptoms and statistically fewer hips which further deteriorated.

						was centrifuged at 1500 revolutions per minute for 10 minutes		level = 9.58 ± 0.99 to 5.83 ± 0.93 (p <0.001) after 24 months, average scores of WOMAC: 27.77 ± 4.23 at baseline and 14.81 ± 2.99 (p <0.001) at 24 months		
Tabatabaee 2015 (score =6.5)	Core Decompression	RCT	No mention of sponsorship. COI: One or more of the authors have received or will receive benefits for personal or professional use.	N=28 hips with early ONFH	Mean age: 28.9 years; 19 males, 9 females	Group A: received core decompression with injection with concentrated autologous bone marrow containing MNCs in to the femoral head (n=14) vs Group B: (n=14) received core decompression only	Pre-operative, 16, 12, 18, 24 months	Mean VAS score for Group A was reduced from 35.9±4.5 to 16±2.5 compared to Group B from 38.6±4.6 to 32±4.4 (p<0.001). WOMAC scores for Group A improved form 32±3.8 to 9.7±1.7 at 24 months (p<0.001). For group B, WOMAC scores improved from 35.9±2.7 to 27.2±3.7. MRI showed improvement in group A (p=0.046) compared to worsening in group B (p<0.001).	"[I]mplanting concentrated autologous bone marrow containing MNC in ONFH added to core decompression surgery could be effective in the early stages of ONFH."	24 month follow-up suggesting core decompression with autologous bone marrow stem cell injections improved pain and osteonecrosis via MRI.

Pepke 2016 (score =4.5)	Core decompression	RCT	No mention of sponsorship. No COI.	N=24 patients with non-traumatic FHN.	Mean age: 44.5 years; 22 males, 3 females.	Control (n=14) – patients received CD performed under local anesthesia Vs BMAC (n=11) – patients received CD. 10 mL of the BMAC was instilled into the necrotic zone of the patients.	Follow up at 1 and 2 years.	The VAS score at pre-OP, post-OP, 1 year post-OP, and 2 year post-OP in the control group were 5.5, 2.9 ($p<0.05$), 3.4 ($p<0.05$), and 3.1 ($p<0.05$), respectively; in the BMAC group were 4.7, 3.7 ($p<0.05$), 2.4 ($p<0.05$), and 2.2 ($p<0.05$), respectively. The HHS group scores score at pre-OP, post-OP, 1 year post-OP, and 2 year post-OP in the control group were 62, 76 ($p<0.05$), 82 ($p<0.05$), and 77 ($p<0.05$), respectively; in the BMAC group were 61, 75 ($p<0.05$), 88 ($p<0.05$), and 83 ($p<0.05$), respectively.	”Femoral head necrosis with a spherical head and irreversible necrosis of the bone (ARCO II) profits from core decompression……This trial of 25 hips could not detect a benefit from the additional injection of bone marrow concentrate with regard to bone regeneration and clinical outcome in the short term.”	Data suggests no obvious benefit of the addition of BMAC for treating femoral head osteonecrosis detected at 2 years. Small sample.
Stulberg 1991 (score =4.5)	Core decompression	RCT	No mention of sponsorship and COI.	N = 36 patients with 55 affected hips Mainly Stages I,	Mean age: 38.6 years; gender not specified.	Core decompression (n=19) - Coring procedure (partial weight	Follow up at 25 months, 26 months, 30 months	Coring procedure superior to conservative treatment for stratified analyses of each Stage (I-III). No	“Core decompression produced better results than conservative treatment in the	Mean age 39; mean follow-up 27 months. Higher intraosseous pressures in decompression

				II or III osteonecrosis (2 with stage IV)		bearing) vs. conservative treatment (n=17) - nonweight bearing for 6 plus weeks.	for stages I, II, and III, respectively.	further intervention in [Core (%)/Conservative (%)]: Stage I [7(70%)/1(20%)], Stage II [5(71.4)/0(0)], Stage III [8(100%)/1(10%)].	early stages of (osteonecrosis)."	group (52 vs. 44mmHg) may bias against coring. Data suggest core decompression superior to conservative treatment for Stages I, II and III.
Koo, 1995 (score =4.5)	Core decompression	RCT	No mention of sponsorship or COI.	N = 33 with 37 hips Most Stage I osteonecrosis	Mean age: 47.6 years; 31 males, 2 females.	Core decompression (n=18) - (partial weight bearing. vs. conservative treatment (n=19) - nonweight bearing with crutches until pain resolved and analgesics.	Follow up at baseline and 24 months.	At second assessment, 9/10 (90%) symptomatic hips in coring group had pain relief vs. 25% conservatively-treated (p = 0.04). At minimum 24 months, 14/18 (78%) core-decompressed hips vs. 15/19 (79%) non-operated hips developed femoral head collapse, p = 0.79.	"Core decompression may be effective tin symptomatic relief, but is of no greater value than conservative management in preventing collapse in early osteonecrosis of the femoral head."	Weight bearing status differed between the 2 groups. Data suggest core procedure resulted in early symptom reduction, but not more effective than conservative treatment of stage I osteonecrosis.
Neumayr, 2006 (score =4.5)	Core decompression	RCT	Sponsored by the National Institutes of Health	N = 46 patients with 46 hips Stages I, II, or III osteonecrosis; all sickle	Mean age: 25.63 years; 19 males, 19 females.	Arm A (n=17) –patients received core decompression and physical therapy. Vs Arm B (n=21) – patients received	Follow up at 3 years.	At mean 3 years, survival 82% of decompression vs. 86% PT (NS). Mean improvement in Harris Hip score 18.1 for coring vs. 15.7 PT (NS). No	"[P]hysical therapy alone appeared to be as effective as hip core decompression followed by physical therapy in improving hip function and	Less advanced disease PT group (stage III 33% vs. 59%) and non-study hips more disparate at baseline (19% vs. 47%)

			Grants. No COI.	cell anemia		physical therapy alone limited (weight bearing, stretching, adductor and other muscle strengthening).		differences in hip survival across stages I-III (92, 82, 82%).	postponing the need for additional surgical intervention at a mean of three years after treatment."	suggest randomization failure, thus conclusions difficult to draw. Generalizability from sickle cell anemia to working populations or others unclear.
Cao 2017 (score =4.0)	Core decompression	RCT	Sponsored by the Natural Science Foundation of China and the Major Project and Disease of the Shanghai Health System from the Shanghai Municipal Commission of Health and	N=27 patients with ARCO Stages I to IIIB bilateral osteonecrosis.	Mean age: 31 years; 16 males, 5 females.	CD Group (n=21 hips) – patients received core decompression augmented with autologous bone grafting in one hip. vs. FVFG group (n=21 hips) – patients received concurrent contralateral free vascularized fibular grafting.	Follow up at 6, 12, 28, 24, 30, and 36 months after treatment.	The core decompression group had lower scores at 6 months (67 ± 6 versus 76 ± 5; mean difference, -9; 95% CI, -12 to -6; p<0.001), 12 months (71 ± 6 versus 81 ± 3; mean difference, -10; 95% CI, -13 to -7; p < 0.001), 18 months (72 ± 4 versus 84 ± 4; mean difference, -13; 95% CI, -15 to -7; p<0.001), 24 months (70 ± 5 versus 84 ± 9; mean difference, -14; 95% CI, -17 to -11; p<0.001), 30 months (69 ± 5 versus 83 ± 3;	"Hips that underwent a vascularized fibular grafting procedure fared better than hips receiving core decompression as measured by improved vascularity and less progression of osteonecrosis as measured by ARCO staging. The mean HHS of the fibular-grafted hips was better than that of the decompression-treated hips during the entire postoperative period, but the differences were modest early on, and for the early postoperative period the differences were	3 year follow up. Some patients had different ARCO scores pre-intervention in their hips. Data suggests hips with fibular grafting improved vascularity and ARCO scores compared to core decompression .

			Family Planning. No COI.					mean difference, -14; 95% CI, -17 to -11; p<0.001), and 36 months (68 ± 5 versus 82 ± 3; mean difference, -14; 95% CI, -17 to -11; p < 0.001).	unlikely to have been clinically important; by 18 months after surgery, the differences probably were clinically important. The mid-term outcomes associated with vascularized fibular grafting seen in our patients are associated with improvements in femoral head vascularity and the potential for bone revitalization."	
Chen, 2016 (score =4.0)	Core decompression	RCT	No mention of sponsorship. No COI.	N=71 patients with osteonecrosis of the femoral head.	Mean age: 39.5 years; 44 males, 27 females.	Group A (n=42) – patients received core decompression surgery Vs. Group B (n=29) – patients received core decompression surgery combined with superselective arterial infusion (SAI)	Follow up at 1 and 6 months.	The preoperative Harris hip score in the Ficat II-III groups for group A was 36.38±3.50 and for group B was 32.98±4.36; 1 month after surgery the score was 53.73±4.13 (p<0.01) for group A and 60.43±1.89 (p<0.01) for group B; 6 month after surgery the score was 45.93±5.47 (p<0.01) in group A and 54.05±2.99	"The post-CD SAI could be more effective in relieving the avascular necrosis of femoral head."	Data suggest benefit of core decompression combined with super selective arterial infusion as necrotic tissue visualized on MRI was reduced at 6 months.

								(p<0.01) in group B.		

Evidence for the Use of Arthroplasty Surgery

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: hip arthroplasty, hip replacement; Hip osteonecrosis, avascular necrosis, femur head necrosis, osteonecroses, bone necrosis, aseptic necrosis of bone, Kienboeck disease, necrosis of the femoral head, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 340 articles in PubMed, 2657 in Scopus, 310 in CINAHL, 10 in Cochrane Library, 3270 in Google Scholar, and 1 from other sources. We considered for inclusion 6 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 16 articles considered for inclusion, 11 randomized trials and 1 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Friedl 2009 (Score= 6.5)	Cementless total Hip arthroplasty	RCT	Sponsored by DePuy Orthopaedics and Orthovita. One or more pf the authors have received or will receive benefits for personal or professional use.	N = 50 patients experienced cementless total hip arthroplasty.	Mean age: 61 years; 22 males, 27 females.	Zoledronic acid group: received 4 mg zoledronic acid intravenous infusion 1 day after hip arthroplasty surgery (n=25) vs. placebo group: received 4 mg placebo intravenous infusion 1 day after hip arthroplasty surgery (n=24).	Follow-up at 7 weeks, 6 months, 1, and 2.8 years.	The median Harris hip score in Zoledronic Acid group changed from 23 (baseline) to 100 (2 years follow-up); and the median Harris hip score in control group changed from 31 (baseline) to 96 (2 years follow-up). The differences between mean scores of the two groups was significant ($p<0.001$).	"A single infusion of zoledronic acid shows promise in improving initial fixation of a cementless implant, which may improve the clinical outcome of total hip arthroplasty in patients with osteonecrosis of the femoral head."	Data suggest a single infusion of Zoledronic acid may help prevent migration or loosening of the fixation of a cementless implant.
Kim 2005 (score= 6.5)	Femoral Components	Randomized Crossover Trial	No sponsorship or COI.	N = 52 All osteo-necrosis, all bilateral arthroplasties	Mean age: 44.2 years; 48 males, 4 females	Zirconia femoral head vs. cobalt-chromium head	Pre-operative, 3, 6, 12 months, yearly post-operatively	Mean polyethylene wear rate was 0.08 mm/year with zirconia vs. 0.17 mm/year with cobalt-chromium ($p = 0.004$).	"The mean amount and rate of polyethylene wear were significantly lower in the hips with a zirconia head than they were in the hips with a cobalt-	Volumetric wear data support the zirconia implant vs. cobalt-chromium, but only revisions were 2 zirconia stems. Loosening

								Mean volumetric polyethylene wear was 350.8 mm^3 with zirconia heads vs. 744.7 mm^3 with cobalt-chromium (p = 0.004). Two zirconia stems revised due to loosening vs. no other stems/cups revised. Roughness Ra values of 2 explanted zirconia heads 15.87 and 17.35nm vs. unimplanted zirconia heads of 5.31 and 5.48nm.	chromium head, presumably because the zirconia heads had a smoother articulating surface."	observed to have occurred in those who were not active vs. others doing farm work or playing tennis (despite advice to avoid high impact).
Kim 2002 (score= 6.5)	Surgical Approaches	RCT and crossover for simultaneous	No sponsorship or COI.	N = 156 50 bilateral simultaneous; 106 unilateral	Mean age: 51.0 years; 148 males, 58 females	Cemented (Elite Plus, Simplex-P cement) vs. uncemented (Profile) hip arthroplasty. All cups Duraloc cementless.	1 year	Number of fat globules per high-power field from right atrium total/mean (% affected): cementless stem: 220/2.2. Cementless stem: 331/3.1	Bilateral simultaneous and unilateral total hip arthroplasty and cemented and cementless stems showed similar fat and bone-marrow-cell embolization.	Majority had osteonecrosis. Korean study; authors question generalizability to U.S. Crossover trial for simultaneous arthroplasties is study strength.

								(NS). 49% unilateral vs. 54% bilateral with fat globules in right atrial blood samples (NS). No hemodynamic differences (p = 0.14).		Suggests simultaneous arthroplasties are reasonably safe.
Kim 2003 (score= 6.5)	Cement	RCT	No sponsorship or COI.	N = 98 Osteonecrosis of the femoral head; simul-taneous bilateral THA and unilateral THA	Mean age: 47.3 years; 80 males, 18 females	Simultaneous bilateral total hip arthroplasty with cemented stem in 1 hip and cementless stem in other vs. unilateral total hip arthroplasty with cementless stem	Pre-operative, 6 weeks, 3, 6, 12 months, yearly post-operatively (average 9.3 years)	Linear wear cemented 1.15±0.6 vs. cementless 0.69±0.57mm. Volumetric wear 438.77±228.08 vs. 262.98±218.17mm^3. Wear per year 0.22±0.12 vs. 0.14±0.12mm (p = 0.23). Radiolucent lines <1mm in 14% vs. 5%.	"Although there was no aseptic loosening of the components, a high rate of linear wear of the polyethylene liner and a high rate of osteolysis in these high-risk young patients remain challenging problems."	Appears to be subset of Kim 2002 population. Suggests long term outcomes may be poorer than other studies, possibly young age and/or other osteonecrosis-related factors.
Xie 2016 (Score= 6.0)	Cementless total Hip arthroplasty	RCT	Sponsored by the China Health Ministry Program. The authors declared no COI.	N=210 patients with femoral head osteoarthritis or osteonecrosis.	Mean age: 60.79 years; 67 males, 143 females.	IV group: received 1.5 g intravenous use of tranexamic acid (n=70) vs. local group: received 3 g	Follow-up at 30 days.	Four primary outcomes included. Total blood loss (TBL) indicated significant differences among the three groups,	"Combined administration of intravenous and local TXA in primary unilateral THA can effectively decrease total blood loss and elicit higher	Data suggest combination TXA ragmen better than IV or local TXA alone in reducing blood loss in cementless THA.

						local use of tranexamic acid (n=70) vs. combined group: received 1 g intravenous use of tranexamic acid and 2 g local use of tranexamic acid (n=70).		combined group (776.75 ± 188.95 ml) showed lower level than other two groups (p=0.001). Maximum Haemoglobin drop also indicated significant group difference: combined group (2.98 ± 0.78 g/dL) showed lower level than other two (p<0.001). No pulmonary embolism (PE) data was collected during follow-up. Incidence of deep venous thrombosis (DVT) indicated no significant difference among groups (p=0.774).	postoperative haemoglobin levels without the risk of higher complication rates."	
Brodner 2003	Miscellaneous	RCT	Sponsored by grants	N = 100 OA or	Mean age: 60.2	Hip arthroplasty	Pre-operati	Serum cobalt median prep	"Systemic cobalt release from	Clinical significance

(score= 5.0)			or outside funding from Centerpulse Orthopedics. No COI.	osteonecrosis	years; 19 males, 31 females	Alloclassic without cement treated with a metal-on-metal articulation vs. ceramic-on-polyethylene bearing	vely, 3, 6 weeks, 3, 6 months, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 years	0.15 vs. 0.15µg/L. At one year, 1 vs. 0.15. At 5-years 0.7 vs. 0.15.	Metasul metal-on-metal articulations was demonstrated throughout 5-year study period. Median serum cobalt concentrations found to be slightly above detection limit and remained in a constant range. Serum cobalt concentrations did not reflect a so-called run-in wear period of metal-on-metal articulations."	uncertain as there is no clinical correlate.
Howie 2005 (score= 4.5)	Metal-on-Metal Hip Resurfacing	RCT	Sponsored by Roynl Adelaide Hospital and Corin Baxter 1-lcalthcnre Pty. Ltd. No mention of COI.	N = 24 Not well described, but appear to be OA and AVN	Mean age: 48.2 years; 15 males, 9 females	Resurfacing (McMinn, Corin) vs. total hip arthroplasty (Exeter)	3, 6 months, 1 year, 2 years	At followup median 8.5y, 8/11 (73%) of resurfaced hips revised to total arthroplasty. Failures due to femoral neck fractures, loosening of acetabular components.	"Although there may be an advantage in bone preservation with resurfacing hip replacement, clinical trials are required to demonstrate it has a midterm success that reasonably approaches that of total hip replacement."	Small trial. Sparse methods and data. Study stopped due at 2 yrs due to surgical failures in resurfaced hips.
Incavo 1998	Femoral	RCT	No mention of	N = 91 81% OA, 9.9% ON,	Mean age: 55 years; 54	Surface coating in profile	6 months, 1	Good/excellent results 19/26 (73%)	"Clinical differences exist and are	HA coated had superior Harris Hip Scores and

(score= 4.0)	Compo nents		sponsorshi p or COI.	5.5% trauma	males, 37 females	femoral prostheses: 1) smooth; 2) porous coated vs. 3) hydroxyapat ite (HA) coated. Multi-center. Full weight-bearing allowed immediately post-op.	year, 24 , 48 months	vs. 20/28 (71%) vs. 22/25 (88%). Harris hip scores favored HA coated (85.1 vs. 89.8 vs. 96.0, p = 0.004 HA vs. smooth) as did functional scores. Pain, ROM, activity scores NS; 3 of 4 with painful femoral loosening had smooth stems. Radiolucent lines 14% vs. 0% vs. 8%. Spot welds 28% vs. 65% vs. 54%.	attributable to the type of surface coating used for the cementless femoral components in THA."	function. More loosening in smooth stems and poorer results for function suggest smooth stems are inferior.
Seyler, 2006 (score= 4.0)	Avoida nce of dysbari c exposur es	RCT	Sponsored by Stryker Orthopaedi cs. COI: one or more of the authors have received or will receive benefits for personal or professiona l use.	N = 210 OA or osteonecr osis	Mean age: 48.7 years; 151 males, 45 females	Stratified enrollments for OA and osteonecrosi s. Compared alumina-on-alumina (n=158) vs. cobalt-chromium-on-polyethylene	Pre-operati ve, 6 months , 1, 2, 3, 4, 5, 6, 7, 8 years	Seven-year survival probability 95.5% for osteonecrotic hips; 89.4% for OA with alumina-on-alumina vs. 92.3% for ON and 92.9% for OA with cobalt-	"The results…were comparable. The low revision rate for the alumina-on-alumina bearing is encouraging and offers a promising option for younger, more active patients who	Long-term study of 7 years. Unequal sized groups due to modification of study midway. Data suggest comparable outcomes.

						surfaces (n=52)		chromium-on-polyethylene. Harris hip scores (baseline/ 6 months/5 years): ON AA (45.8±12.3/93 .8±8.5/97.5±4. 0) vs. OA AA (49.7± 12.3/95.3±8.5 /95.4±10.2) vs. ON CCP (42.2±13.9/ 90.4±11.4/96. 5±8.0) vs. OA CCP (48.81±3.3/ 95.3±6.6/97.3 ±4.0), p = 0.85 between groups. No differences in complications or revisions.	have this challenging disease."	

HIP Fractures

Evidence for the use of Bone Scans

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: bone scans; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, subtrochanteric fractures, femoral neck fracture, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 81 articles in PubMed, 565 in Scopus, 5 in CINAHL, 16 in Cochrane Library, 9350 in Google Scholar, and 4 from other sources. We considered for inclusion 2 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 4 from other sources. Of the 10 articles considered for inclusion, 7 diagnostic studies and 3 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Kiuru 2002 (score= 7.0)	Bone scans/MRI	Diagnostic	Sponsored by the Radiological Society of Finland and the Sports Research Foundation of Finland. No mention of COI.	N = 50 conscripts at the Central Military Hospital in Helsinki, Finland with stress related pain in the pelvis or in the lower extremities.	Mean age: 20.1 years; 42 males, 8 females.	Hip fracture	The same 50 patients received two phase bone scintigraphy and MR imaging on a 1.0 T unit after undergoing radiographs.	Sensitivity of radiography vs bone scintigraphy was 56%, specificity 94%, accuracy 67%, positive predictive value (PPV) 95%, and negative predictive value (NPV) 48%. Sensitivity for MR imaging vs bone scintigraphy was 100%, specificity 86%, accuracy 95%, PPV 93% and NPV 100%.	"In conclusion, clinical diagnosis of bone stress injuries is unreliable. MR imaging is more sensitive than two-phase bone scintigraphy, and MR imaging should be used as the gold standard in the assessment of stress injuries of bone. Radiography reveals mainly the late phases of bone stress injuries, such as stress fracture and callus."	Data suggest MRI is more sensitive than two-phase bone scintigraphy and can detect bone injuries earlier.
Shin 1996 (score= 6.0)	Bone scans	Diagnostic	Sponsored by the Clinical Investigations Department, Naval Medical Center in San Diego	N = 22 hips from 19 patients with unilateral or bilateral hip pain with negative plain	Mean age: 19.6 years; 19 males, 0 females.	Hip Fracture	22 hips of 19 patients received plain radiographs, radionuclide bone scans in planar and SPECT	Radionuclide imaging had 15 true-positives and 7 false positives. Sensitivity of	"Magnetic resonance imaging is a sensitive and specific diagnostic tool that aids in the differential diagnosis of hip pain	Data suggest MRI has comparable sensitivity to bone scan but better specificity.

			California. No COI.	radiographs and positive radionuclide bone scans.			modes using single-head gamma camera, and MRI scans on a 1.5 T magnet.	radionuclide bone scans was 100%. Magnetic resonance imaging (MRI) had 15 true positives and 7 true-negative results. Sensitivity, specificity and accuracy for MRI were 100%.	in endurance athletes at increased risk for femoral neck stress fractures. The role of MRI as a primary diagnostic imaging modality in athletes with hip pain is evolving. We have found that MRI is superior to radionuclide imaging in differentiating causes of hip pain in the endurance athlete."	
Fairclough 1987 (score= 4.5)	Bone scans/Radiography	Diagnostic	No mention of sponsorship or COI.	N = 43 elderly patients with suspected femoral neck fracture and negative bone scans.	Mean age: 77 years; No mention of gender.	Hip Fracture	43 patients with negative bone scans had an isotope scan. 30 patients had normal scans and 13 had specific bone scan abnormalities later shown to be fractures.	Bone scans resulted in zero false-positives and no false-negatives after three months.	"This study shows that isotope bone-scanning is highly reliable in the identification of "occult" fractures of the hip and may allow the surgeon to operate before displacement occurs, thus improving the prognosis.	Data suggest that if there is a strong index of suspicion that an elderly patient has a hip fracture (even though it is radiographically negative), a bone scan should be performed.

Kim 2017 (score= 4.5)	Bone scans	Diagnostic	No mention of sponsorship. No COI.	N = 44 patients who underwent surgical fixation for femoral neck fractures	Mean age: 66.9 years; 11 males, 33 females.	Osteonecrosis of the Femoral Head	44 patients had bone SPECT done within 2 weeks postoperatively and whole body planar bone scintigraphy. Plain radiographs were done at 6 weeks, 3, 6, 9, 12, and 24 months.	OFH detection time on simple radiographs was 19.1 months. Sensitivity and specificity of early SPECT to predict development of OFH was 100% and 49%. Late bone SPECT had 100% sensitivity and 100% specificity.	"Normal femoral head uptake on early bone SPECT within second postoperative week effectively predicts normal healing without osteonecrosis in the patients who were received the internal fixation of femur neck fractures. A decreased uptake in the femoral head on early bone SPECT indicates an increased risk of osteonecrosis, although some patients showing decreased uptake recover and show normal uptake in a late bone SPECT. The occurrence of OFH after femoral	Data suggest SPECT can predict OFH risk after femoral neck fracture at least 3 months post-surgery but prior to that time frame SPECT shows low specificity.

									neck fracture can be reliably predicted by bone SPECT at 3 months after surgery."	
Yoon 2013 (score= 4.0)	Bone scans	Diagnostic	No sponsors hip or COI.	N = 54 patients who received internal fixation using cannulated screws for non-displaced femoral neck fracture who underwent bones scans ad follow up for three or more years.	Mean age: 42.2 years; 26 males, 28 females.	Hip Fracture	54 patients had bone scans with two weeks post operatively, 47 had another 1-6 months post op, 13 had a third 12-18 months post op, and 8 had a fourth bone scan 18-24 months post op.	Average femoral head ratio (FHR) was 0.99 for the bone scans within 2 weeks, 1.69 for the 1-6 months group, 1.29 for the 12-18 month group, and 1.05 for the 18-24 month group.	"Early postoperative bone scan results should not be over interpreted when predicting osteonecrosis of the femoral head. It must be considered that there are unique patterns of isotope uptake with the passage of time, such as cold uptake in the early stage, hot uptake in a couple of months postoperatively and iso-uptake in the late stage."	Data suggest early bone scan results are not necessarily predictive of osteonecrosis of the femoral head after undisplaced femoral neck fractures.
Rizzo 1993 (score= 4.0)	Bone scans	Diagnostic	No sponsors hip or COI.	N = 62 patients with suspected hip fracture but negative radiogra	Mean age: 73 years; 23 males, 39 females.	Hip Fracture	62 patients were examined with magnetic resonance imaging (MRI) with T1-	23 patients had both negative MRI's and bone scans. Sensitivity of MRI	"Magnetic resonance imaging was as accurate as bone-scanning in the assessment of occult	Data suggest MRI is as accurate as bone scan in detecting occult hip fractures and may

				phic findings/			weighted cornal sections within 24 hours of admission and bone scans within 72 hours of admission.	was greater than the sensitivity of bone scans.	fractures of the hip. The magnetic resonance imaging took less than fifteen minutes to perform, and it was tolerated well by the patient. Magnetic resonance imaging provides an early diagnosis of occult fractures about the hip and may decrease the length of the stay in the hospital by expediting definitive treatment. ”	assist in providing an early diagnosis.
Calder 1994 (score= 3.5)	Bone scans	Diagnostic								Small sample (10 patients) SPECT may be more accurate in assessing vascularity of the femoral head.

Evidence for the use of Computerized Tomography (CT)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: X-Ray Computed Tomography, Computerized Tomography,

CT scan, CAT Scan; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, subtrochanteric fractures, femoral neck fracture, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 536 articles in PubMed (Went through first 100 of best match and all most recent), 358 in Scopus (Went through first 100), 48 in CINAHL, 22 in Cochrane Library, 23800 in Google Scholar (Went through first 100), and 5 from other sources. We considered for inclusion 15 from PubMed, 0 from Scopus, 4 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 5 from other sources. Of the 26 articles considered for inclusion, 26 diagnostic

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
O'Toole 2013 (Score=7.0)	X-Ray/CT	Diagnostic	The authors declared no sponsorship or COI.	N=86 patients with femoral shaft fracture with or without femoral neck fractures.	No mention of age and sex.	Femoral neck fracture	Computed tomography: axial-view 3-, 40- to 60-mm section multidetector pelvis CT vs. plain radiography: AP-view pelvis plain radiography and femoral shaft plain radiography. All patients were included.	The three imaging technique indicated 94% high specificity, 95% 1 minus negative post-test high probability, 65% poor sensitivity, and 58% positive post-test poor probability.	Plain radiography and computed tomography have rates of missed femoral neck fractures that are similar and substantial, with a sensitivity of only 56%–64%. Our data emphasize the importance of intraoperative and postoperative imaging in detecting nondisplaced femoral neck fractures in association with femoral shaft fractures.	Data suggest both imaging techniques of CT and plain radiography have similar rates of missed femoral neck fracture (sensitivity 56%-64%) associated with femoral shaft fracture Data suggest importance of post and intraoperative imaging in detecting non-displaced femoral neck fracture.
Stevens 2003 (score=6.0)	X-ray/CT/MRI	Diagnostic	No mention of sponsorship or COI.	N= 45 patients with stage I and stage II osteonecrosis of the femoral head	Mean age: 47.8 years; 32 males, 13 females.	Hip fracture	All patients had a surgical core decompression of the hip – alone or with rhBMP-2 on an absorbable collagen sponge (rhBMP/ACS) implanted in the decompression site. They were then evaluated with radiography	MR imaging has a sensitivity of 38% and a specificity of 100% while unenhanced radiography has a sensitivity of 71% and a specificity of 97%, when compared to CT.	"CT reveals more subchondral fractures in osteonecrosis of the femoral head than unenhanced radiography or MR imaging. The high-signal-intensity line seen on T2-weighted MR images appears to represent fluid	Data suggest CT better than MRI and both better than radiography in detecting subchondral fractures in femoral head osteonecrosis.

							and MR imaging. 2 weeks after surgery, CT and MR were performed. 6 and 12 months after surgery, radiography, CT, and MR were performed. (n=45)		accumulating in the subchondral fracture, which may indicate a breach in the overlying articular cartilage."	
Reddy 2015 (Score=6.0)	CT	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=25 patients experienced hip fracture who took pelvis CT.	Mean age: 77 years; 7 males, 19 females.	Hip fracture	True positive group: patients were detected by DECT-VNC to have bone marrow edema (n=18) vs. False positive group: patients had false signs of bone marrow (n=3) vs. True negative group: patients showed no bone marrow edema (n=2) vs. False negative group: patients received fracture diagnosis but had negative sign of bone marrow edema via DECT-VNC (n=2)	Dual-energy computed tomography virtual non-calcium (DECT-VNC) indicated high sensitivity (90%), and low specificity (40%). For outcome predict, DECT-VNC showed 86% positive and 50% negative value.	"However, the results of our study, with a mean patient age of 77 years, demonstrate that DECT-VNC can be successfully applied in clinical practice for the assessment of bone marrow edema in this elderly group of patients."	Small sample size. Data suggest DECT-VNC is very sensitive but lacks adequate specificity for detecting hip fractures in individuals with normal radiographs.

Duane 2008 (Score=5.5)	CT/X-ray	Diagnostic	No mention of sponsorship or COI.	N=1388 patients sustained blunt trauma.	Mean age: 38.8 years; no mention of sex.	Pelvic fracture	Clinical examination (CE) vs. Plain films (PXR) vs. CT of the pelvis. All patients were included.	168 out of 1388 patients were diagnosed with pelvic fracture by CT scans; the incidence of fracture was 12.1%. Clinical examination indicated 96.43% sensitivity, 99.03% negative predictive value, 50.25% specificity, and 21.07% positive predictive value. CT was considered as the gold standard.	"In conclusion, clinically significant pelvic fractures are diagnosed better by CE than PXR compared with CT, eliminating the need for routine pelvic radiographs. The majority of patients with blunt trauma undergo CT making additional plain films unnecessary and therefore a wasted expense."	Data suggest CE>CT>plain radiographs in diagnosing pelvic fractures.
Harley 1982 (Score=5.5)	X-Ray/CT	Diagnostic	No mention of sponsorship or COI.	N=26 patients with suspicion of posterior femoral head dislocation or acetabular fracture.	Age range: 17 to 66 years; 21 males, 5 females.	Acetabular fracture	Computed tomography: 5mm slice thickness with GE 8800 with scan time 9.6 seconds vs. plain radiography. All patients were included.	For detecting sacroiliac joint abnormalities by CT and plain radiography, the preponderance of false-negative errors was statistically significant (p=0.05 vs. p=0.01). CT accurately identified all the sacrum fractures, but plain radiography incorrectly interpreted or missed some cases, but the differences between the two instruments was not statistically significant.	"Sensitivity of both examinations for abnormalities of the sacroiliac joint was relatively poor, but examinations were highly specific. Determination of the stable fracture fragment(s) was readily accomplished by CT scanning in all 26 patients; in five patients incorrect determinations were made with conventional radiographs alone."	Small sample. Data suggest suspicion of either femoral head dislocation or an acetabular injury should be followed up with CT.

Sadozai 2016 (Score=5.5)	CT/MRI	Diagnostic / retrospective	No mention of sponsorship. The authors declared no COI.	N=78 hips to be scanned by CT.	No mention of age or sex.	Occult femoral neck fracture	Computed tomography (CT): utilized Siemens Somatom Sensation 64 CT scanners vs. subsequent magnetic resonance imaging (MRI). All hips were included.	In this study, CT scans indicated 86% sensitivity, 98% specificity, 96% positive predictive value, 92% negative predictive value, and 92% accuracy.	"We therefore recommend that MRI should be offered when a fracture is suspected. CT scans should be reserved for when MRI is not available, but a negative scan should be confirmed with subsequent MRI."	Data suggest not all OHFs are detected with CT (86% sensitivity and 98% specificity), and MRI should be performed when OHF is suspected with negative CT results.
Isida 2015 (Score=5.5)	CT/X-ray	Diagnostic/ prospective consecutive case series	No mention of sponsorship. The authors declared no COI.	N=110 patients with proximal femur fracture in trochanter.	Mean age: 85 years; 22 males, 88 females.	Trochanteric fracture	A/P pelvis plain X-rays vs. Computed tomography. All patients were included.	CT scans detected 93% lesser trochanter fractures, 94% greater trochanter fracture, and 51% lateral wall ruptures; while X-rays detected 81%, 75% and 35% of the three fractures respectively. Thus, the X-ray indicated 48% sensitivity and 29% negative predictive value. CT indicated 95% sensitivity and 79% negative predictive value.	"The current results of this study suggest that comminution contributes to instability and that this finding is not taken into account in the AO classification, which is not well suited for this type of fracture and raises the question of how to best evaluate and treat these fractures."	Data suggest standard X-rays underestimate the complexity of trochanteric fractures and show poor reproducibility.
Ito 2018 (score=5.5)	CT	Diagnostic	Sponsored by Asahi-Kasei Phrama, Astellas Pharma, Chugai Pharmaceutical, Daiichi-Sankyo, MSD, and Ono Pharmaceutical. COI, one or more	N = 102 female Japanese patients from the Zone study diagnosed with primary osteoporosis based on the Diagnostic	Mean age: 73.4 years; 0 males, 102 females.	Bone Mineral Density	Once yearly intravenous infusion of Zoledronic acid 5 mg group (N = 49) vs placebo group (N = 53) for two years.	Cortical thickness of the femoral neck at baseline vs percent change at 24 months was 1.64 vs 4.09 for the Zoledronic acid group ($p<0.01$) while it was 1.58 vs 0.52 for the placebo group ($p>0.05$).	"The results demonstrated that once-yearly intravenous infusion of zoledronic acid improved volumetric bone	Data suggest yearly infusions of zoledronic acid may reduce hip fracture risk in Japanese women.

			of the authors have received or will receive benefits for personal or professional use.	Criteria for Primary Osteoporosis by the Japanese Society for Bone and Mineral Research				Similar results of improvement in the zoledronic acid group were seen in the cortical CSA and total CSA at the interochanteric region and shaft, total vBMD at all sites, cortical vBMD at the neck and shaft, SM and CSMI at the shaft and BR at the intertrochanteric region and neck.	mineral density (vBMD), cortical bone geometry parameters, and CT-derived biomechanical parameters at the femoral neck, intertrochanteric region, and shaft; particularly at the intertrochanteric region, significant improvements in cortical bone geometry parameters and CT-derived biomechanical parameters, compared with those in the placebo group, were detectable early, at 12 months. The present data suggest that zoledronic acid has a possibility to reduce the risk of hip fractures in Japanese patients with osteoporosis."	
Meier 2014 (Score=5.5)	MRI/ CT	Diagnostic	The authors declared no sponsorship or COI.	N=27 patients with avascular necrosis.	Mean age: 49.2 years; 13 males, 14 females.	Subchondral femoral head fracture	Magnetic resonance imaging (MRI) for bone marrow oedema (BME):	The avascular femoral head location did not correlate with the CT / MRI images (p>0.05). Avascular necrosis size	"[B]one marrow oedema adjacent to the demarcated necrotic segment with facultative	Data suggest bone marrow edema visualized on MRI represents stage

							1.5-T system with phased-array body coil vs. hip computed tomography (CT): 64 row multidetector system with 512x512 matrix and 300 mm view field. All patients were included.	significantly correlated with subchondral fractures MRI images (p<0.001; k=0.718), but with CT images indicated no correlation (p=0.318; k=0.11). Subchondral fractures extent and femoral head were graded higher on CT images than MRI images (p=0.001).	extension into the femoral neck observed in patients with AVN of the femoral head represents a secondary sign of a subchondral fracture and, thus, indicates ARCO stage 3 disease, even if the fracture line is not visible on MR images."	3 disease in femoral head AVN and is a sign of subchondral fracture.
Collin 2016 (Score=5.0)	MRI / CT	Diagnostic	The authors declared no sponsorship or COI.	N=44 patients experienced low energy trauma.	Mean age: 84 years; 14 males, 30 females.	Hip fracture	Computed tomography (CT) with 16 detectors row scanner and medium B60s sharp reconstruction kernel (120 kVp / 70 mA) vs. Magnetic resonance imaging (MRI) with 1.5 Tesla symphony whole body scanner. All patients were included.	18 fractures and 26 negative cases were reported via CT diagnosis, observer agreement was good (SE=0.08, CI: 0.72 to 1.00, k=0.87). 20 fractures and 24 negative cases were reported via MRI scans, and the observer agreement was good (k=1.00). MRI changed the two reviewers CT diagnoses in 32% and 34% respectively.	"[M]RI was deemed a more reliable modality to interpret than CT in hip fracture diagnosis. For clinical decision-making, MRI seems to have a higher accuracy than CT. Even though CT has a high clinical utility in evaluating occult hip fracture, a negative CT finding cannot completely rule out a hip fracture in patients where clinical findings of hip fracture persevere."	Data suggest MRI better than CT for imaging occult or suspected hip fracture.

Lubovsky 2005 (Score=5.0)	MRI / CT	Diagnostic	No mention of sponsorship or COI.	N=13 patients	Mean age: 73 years; 2 males, 11 females.	Occult hip fracture	Group A: patients took both CT and MRI (n=6) vs. Group B: patients took MRI only (n=7).	Four patients in Group A (67%) received inaccurate misdiagnosis via CT images. On the contrary, all the patients in Group B (100%) received accurate and precise diagnosis via MRI scans.	"MRI was found to be a more accurate modality than CTscan for obtaining early diagnosis of occult hip fractures. These results point out the advantage of immediate MRI imaging in patients with occult hip fracture enabling a more effective treatment, a shorter hospitalisation period entailing decreased medical costs."	Small sample. Data suggest MRI more accurate than CT for identification of occult hip fractures.
Thomas 2016 (Score=5.0)	CT	Diagnostic / retrospective	No mention of sponsorship or COI.	N=1443 patients with hip pain (N=199 meet inclusion criteria).	Median age: 85 years; 63 males, 136 females.	Hip fracture	CT group: patients who met the inclusion criteria received first-line investigation with CT scans (n=199) vs. MRI group: included patients received second-line investigation with MRI (n=4).	Multidetector CT indicated 100% sensitivity and 100% specificity for occult hip fracture. 67.3% patients got CT scans in 24 hours of their initial pelvic radiographs, comparing with 30% patients got MRI.	"From our experiences, over a 30-month period at a busy university tertiary hospital, MDCTwith slice thickness of 0.625 mm, can be recommend as an appropriate first-line investigation for occult NOF fractures."	Data suggest multidetector CT is both sensitive and specific for detecting occult hip fracture.
Davis 2013 (Score=5.0)	CT/X-ray	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=15 patients with OTA 62-A1 (isolated unilateral posterior wall)	No mention of age or sex.	Acetabular fracture	Plain radiography (high quality anteroposterior, oblique) vs. axial computed tomography. All	Poor agreement of interobserver reliability arose among subjects (k=0.12). The correct percentage of assessment of wall	"Orthopedic traumatologists expert in acetabular fracture care cannot adequately	Small sample. Data suggest hip stability cannot be reliably determined using only plain

				acetabular fracture.			patients were included.	fracture size range and hip dislocation history was only 53% for initial review and 52% for second review. Sensitivity was 100% for initial review and 57% for the second. Specificity was 13% for initial and 47% for second review.	determine hip stability status for fractures involving 20%–50% of the posterior wall using plain radiographs, computed tomography, and the patient's hip dislocation status."	radiographs and CT. If diagnosis is uncertain ORIF may be the best treatment option.
Cabarrus 2008 (Score=4.5)	MRI / CT	Diagnostic	No mention of sponsorship or COI.	N=145 patients who were suspected to have pelvic insufficiency fracture.	Mean age: 65.9 ± 17.7 years; 41 males, 104 females.	Insufficiency fracture	MRI with TR/TE 600 milliseconds minimum, STIT of 3000/68 15o milliseconds inversion time, and 4 mm slice thickness (n=145) vs. CT with 8, 16 and 64 MDCT scanners, and 1.25-7 mm slice thickness (n=64).	MRI indicated 98% sensitivity (95%CI=94-100), while CT indicated 53% sensitivity (95%CI=39-64). For diagnosis of fracture, MRI better depicted 36.4% fractures, while CT better depicted 29.5%, and both MRI and CT better depicted 34.1%.	"This study showed that MRI was substantially better than CT in detecting insufficiency fractures. In addition, two or more insufficiency fractures were frequently present, typical fracture combinations were found, and insufficiency fractures were frequently associated with malignant disease.	Data suggest MRI better than CT for imaging pelvic insufficiency fractures such that if there is suspicion that fracture is present MRI should be performed if other imaging tests are negative.
Haubro 2015 (Score=4.5)	MRI / CT	Diagnostic	The authors declared no sponsorship or COI.	N=67 Danish patients with hip pain caused by fall.	Mean age: 80.5 years; 27 males, 40 females.	Occult proximal femur fracture	CT with GE 1 slice and GE 4 slice VCT scanners (0.625 mm 0.984 pitch, 0.625 mm image interval) vs. MRI with Phillips 1T	For senior consulting radiologist diagnostic accuracy, CT scanning indicated 87% sensitivity (95%CI=0.60-0.98), missed 13 fractures, and 100% specificity. MRI only missed 2 fractures and	"MRI was observed to have a higher diagnostic accuracy than CT in detecting occult fractures of the hip. Interobserver analysis showed high kappa values	Data suggest MRI better than CT for imaging occult hip fracture.

							Panorama, 1.5T Acieva, and 3T Acieva. All patients were included.	indicated high sensitivity (≈100%) and specificity (≈100%).	corresponding substantial agreement in both CT and MRI."	
Gill 2013 (Score=4.0)	MRI /CT	Diagnostic	No mention of sponsorship or COI.	N=92 patients with suspicion of hip fracture.	Mean age: 82 years; 33 males, 59 females.	Occult hip fracture	CT scans with multi-slice helical Siemens scanners (x1 62 slice & x4 quad slice) (n=61) vs. MRI with T1 weighted spine echo coronal and Short Tau Inversion Recovery axial scan (Philips 1.5T or 3T) (n=31).	37% patients were identified with occult hip fracture. 38% patients who underwent CT were diagnosed with hip fracture, while 36% who underwent MRI got hip fracture diagnosis.	"Our findings show that modern multislice CT may be comparable with MRI for detecting occult fracture."	Data suggest comparable efficacy between CT and MRI in finding radiograph negative occult hip fracture.
Resnik 1991 (Score=4.0)	CT/ X-ray	Diagnostic/ consecutive case series	No mention of sponsorship or COI.	N=50 patients with posterior portion of pelvis injuries.	Mean age: 36 years; 36 males, 14 females.	Pelvic fracture	CT: iliac crests-acetabular roofs for 10 mm intervals and then pubic rami for 3 to 4 mm intervals vs. Anteroposterior plain radiography of pelvis. All patients were included.	CT detected 80% of hip joint fragments, 10% sacroiliac diastasis, 16% of sacral fractures, 21% iliac fractures, 7% acetabular fractures, 3% superior pubic ramus, and 9% inferior pubic ischium. On the other hand, plain films indicated 9% misdiagnosis frequency of acute pelvic dislocations and fractures.	"We conclude that the efficacy of plain radiographs in detecting pelvic fractures in patients with acute pelvic trauma is sufficient to identify virtually all clinically important fractures and dislocations."	Data suggest plain radiographs detect most clinically significant pelvic fractures.

Moed 1993 (Score=4.0)	CT	Diagnostic	No mention of sponsorship or COI.	N=10 patients with femoral head fracture.	No mention of age or sex.	Hip fracture	Standard hip radiography: to evaluate parallel fracture plane; vs. pelvic oblique hip radiography: to detect fracture displacement or joint congruency extent; vs. Computed axial tomography (CT): to detect femoral head fracture plane. All patients were included in three scans.	Anteroposterior radiograph indicated the location and displacement of fracture accurately, but plain radiograph was not effective. Oblique radiograph helped joint congruency evaluation. Angled pelvic radiograph before operation accurately confirmed the observation of fracture displacement during the operation.	"Most importantly, Similar radiographs, reproducible from one examination to the next, could readily be obtained after operation, providing excellent information concerning the adequacy and maintenance of fracture reduction and the progression of fracture healing."	Data suggest the CT-directed pelvic oblique radiograph appears to be best in detecting femoral head fracture.
Chen 2012 (Score=4.0)	CT	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=825 patients with femoral neck fractures.	Mean age: 62 years; 386 males, 439 females.	Incomplete femoral neck fracture	Computed tomography scan image vs. X-ray image. All femoral neck fractures were included in both scans.	CT scans caught all femoral neck fractures accurately, thus CT was better to detect complete fractures of femoral neck, comparing with X-ray ($p<0.001$, chi-square= 17.177). All the patients with femoral neck fractures experienced surgeries, and all recovered well without occurrence of avascular necrosis.	"[o]ur study shows that incomplete femoral neck fractures identified on X-ray films are actually complete fractures on CT scan. Incomplete femoral neck fractures may be much less frequent than we expect."	Small sample size. Data suggest incomplete fractures imaged on radiographs are classified as complete fractures via CT.
Nishiyama 2014 (Score=4.0)	CT	Diagnostic	Sponsored by the Natural Science and Engineering Research Council of Canada, the Canadian Institutes of	N=35 Japanese female patients with femoral neck or trochanteric fractures.	Mean age: 81.2 years; 0 male, 35 females.	Hip fracture	Fracture group: female patients had femoral neck or trochanteric fractures (n=35) vs. control group: age matched	Participants with femoral neck fracture and patients with trochanteric fracture showed no significant differences in stiffness, failure load, or	"FE analysis of QCT images to estimate bone strength of the proximal femur is a promising technique to	Data suggest SVM models in combination with FE analysis can accurately identify those with and those

			Health Research, and Vanier Canada Graduate Scholarships. One author has received or will receive benefits for personal or professional use.				female who are fracture free (n=35).	volumetric bone mineral density (p>0.18). Support vector machine (SVM) model classification indicated 93.9% sensitivity and 89.2% specificity.	classify women with and without hip fractures when combined with SVM models."	without hip fracture.
Chung 2016 (Score=3.5)										Small sample. Data suggest 3-D CT is a poor imaging tool for diagnosing occult intertrochanteric fractures.
Gill 2013 (Score=3.0)										Retrospective case series. Data suggest as much as 10% of occult hip fracture likely are missed on initial radiographs.
Magu 2014 (Score=3.0)										Data suggest CT can accurately measure the fragment of the precise size of a head fragment of the proximal femur.
Sharma 2013 (Score=3.0)										Data may suggest spiral CT with multiplanar and 3-D reformations may have treatment benefit in pelvic and hip fracture.

Kumar 2014 (Score=3.0)										Data suggest at 6 weeks postoperative internal fixation, PET/CT appears to predict future status of the femoral head.
Kim 2013 (Score=3.0)										Retrospective consecutive case series. Small sample. Data suggest MRI-CT is beneficial in evaluating isolated fractures of the greater trochanter.

Evidence for the use of Helical CT for Evaluating Hip Fracture with suspected Osteonecrosis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Helical CT Scans, Helical computed tomography, Tomography, Spiral Computed ; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, subtrochanteric fractures, femoral neck fracture, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 10 articles in PubMed, 27 in Scopus, 12 in CINAHL, 1 in Cochrane Library, 2380 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Magnetic Resonance Imaging (MRI)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Magnetic Resonance Imaging (MRI); Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, subtrochanteric fractures, femoral neck fracture, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 220 articles in PubMed, 180

in Scopus, 48 in CINAHL, 42 in Cochrane Library, 18,400 in Google Scholar, and 0 from other sources. We considered for inclusion 10 from PubMed, 1 from Scopus, 6 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 18 articles considered for inclusion, 15 diagnostic studies and 1 systematic studies met the inclusion criteria.

Evidence for the Use of Magnetic Resonance Imaging (MRI)

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Kiuru 2002 (score=7.0)	Bone Scan/MRI	Diagnostic	Sponsored by the Radiological Society of Finland and the Sports Research Foundation of Finland. No mention of COI.	N = 50 conscripts at the Central Military Hospital in Helsinki, Finland with stress related pain in the pelvis or in the lower extremities.	Mean age: 20.1 years; 42 males, 8 females.	Hip fracture	The same 50 patients received two phase bone scintigraphy and MR imaging on a 1.0 T unit after undergoing radiographs.	Sensitivity of radiography vs bone scintigraphy was 56%, specificity 94%, accuracy 67%, positive predictive value (PPV) 95%, and negative predictive value (NPV) 48%. Sensitivity for MR imaging vs bone scintigraphy was 100%, specificity 86%, accuracy 95%, PPV 93% and NPV 100%.	"In conclusion, clinical diagnosis of bone stress injuries is unreliable. MR imaging is more sensitive than two-phase bone scintigraphy, and MR imaging should be used as the gold standard in the assessment of stress injuries of bone. Radiography reveals mainly the late phases of bone stress injuries, such as stress fracture and callus."	Data suggest MRI is more sensitive than two-phase bone scintigraphy and can detect bone injuries earlier.
Stevens 2003 (score=6.0)	X-ray/CT/MRI	Diagnostic	No mention of sponsorship or COI.	N= 45 patients with stage I and stage II osteonecrosis of the femoral head	Mean age: 47.8 years; 32 males, 13 females.	Hip fracture	All patients had a surgical core decompression of the hip – alone or with rhBMP-2 on an	MR imaging has a sensitivity of 38% and a specificity of 100% while	"CT reveals more subchondral fractures in osteonecrosis of the femoral head than unenhanced	Data suggest CT better than MRI and both better than radiography in detecting subchondral

							absorbable collagen sponge (rhBMP/ACS) implanted in the decompression site. They were then evaluated with radiography and MR imaging. 2 weeks after surgery, CT and MR were performed. 6 and 12 months after surgery, radiography, CT, and MR were performed. (n=45)	unenhanced radiography has a sensitivity of 71% and a specificity of 97%, when compared to CT.	radiography or MR imaging. The high-signal-intensity line seen on T2-weighted MR images appears to represent fluid accumulating in the subchondral fracture, which may indicate a breach in the overlying articular cartilage."	fractures in femoral head osteonecrosis.
Shin 1996 (score=6.0)	Bone Scan/MRI	Diagnostic	Sponsored by the Clinical Investigations Department, Naval Medical Center in San Diego California. No COI.	N = 22 hips from 19 patients with unilateral or bilateral hip pain with negative plain radiographs and positive radionuclide bone scans.	Mean age: 19.6 years; 19 males, 0 females.	Hip Fracture	22 hips of 19 patients received plain radiographs, radionuclide bone scans in planar and SPECT modes using single-head gamma camera, and MRI scans on a 1.5 T magnet.	Radionuclide imaging had 15 true-positives and 7 false positives. Sensitivity of radionuclide bone scans was 100%. Magnetic resonance imaging (MRI) had 15 true positives and 7 true-negative results. Sensitivity, specificity and accuracy for MRI were 100%.	"Magnetic resonance imaging is a sensitive and specific diagnostic tool that aids in the differential diagnosis of hip pain in endurance athletes at increased risk for femoral neck stress fractures. The role of MRI as a primary diagnostic imaging modality in athletes with hip pain is evolving. We have found that MRI is superior to radionuclide imaging in	Data suggest MRI has comparable sensitivity to bone scan but better specificity.

									differentiating causes of hip pain in the endurance athlete."	
Sadozai 2016 (Score=5.5)	CT/MRI	Diagnostic / retrospective	No mention of sponsorship. The authors declared no COI.	N=78 hips to be scanned by CT.	No mention of age or sex.	Occult femoral neck fracture	Computed tomography (CT): utilized Siemens Somatom Sensation 64 CT scanners vs. subsequent magnetic resonance imaging (MRI). All hips were included.	In this study, CT scans indicated 86% sensitivity, 98% specificity, 96% positive predictive value, 92% negative predictive value, and 92% accuracy.	"We therefore recommend that MRI should be offered when a fracture is suspected. CT scans should be reserved for when MRI is not available, but a negative scan should be confirmed with subsequent MRI."	Data suggest not all OHFs are detected with CT (86% sensitivity and 98% specificity), and MRI should be performed when OHF is suspected with negative CT results.
Kawasaki 2001 (score=5.5)	MRI	Diagnostic	No mention of sponsorship or COI.	N = 31 patients who had undergone internal fixation for femoral neck fractures.	Mean age: 61 years; 11 males, 20 females.	Hip Fracture	The 31 patient's fractures were classified by Garden classification using MRI and then using plain radiograph during follow up. They were then divided in to 5 groups based on the band image on MRI: The normal group (N=19), lateral type (B1, N=1) surface type (B2, N=4), intermediate type (B3, N=3) and extended type (B4, N=4)	The sensitivity, specificity, and accuracy of MRI vs plain radiography for osteonecrosis of the femoral head was 50%, 83%, and 74% at 2 months and 100%, 83%, and 87% at 6 months.	"The current results revealed that the period when osteonecrosis of the femoral head can be predicted is 6 months after surgery. Thus, the patient who shows band images by MRI at 6 months must be followed up carefully. The patients in the B3 and B4 Groups of the MRI classification have a high incidence of collapse of the femoral head."	Data suggest diagnosis of femoral head osteonecrosis via MRI is best at 6 months post-surgery.

Iwata 2012 (score=4.5)	MRI	Diagnostic	No sponsorship or COI.	N = 26 patients with symptoms suggestive of a fracture of the femoral neck who had normal radiographs.	Mean age: 79.3 years; 4 males, 22 females.	Hip Fracture	MRI T_1-weighted coronal sections were used for N = 26 patients, MRI T_2-weighted coronal sections were used for N = 25 of the same patients, and normal radiographs were done for N = 26 of the same patients.	Sensitivity of MRI T_1-weighted coronal sections was 100% and sensitivity of MRI T_2-weighted coronal sections was 84%.	"If there is a clinical suspicion of a hip fracture with normal radiographs, T1-weighted coronal MRI is the best sequence of images for identifying a fracture."	Data supports use of T_1-weighted coronal MRI if clinical suspicion of a hip fracture persists despite normal radiographs.
Frihagen 2005 (score=4.5)	MRI	Diagnostic	No sponsorship or COI.	N = 100 patients examined by MRI due continued clinical suspicion of hip fracture after negative or suspect radiographic findings.	Mean age: 80 years; 33 males, 67 females.	Hip Fracture	All 100 patients were assessed using magnetic resonance imaging as well as conventional radiographs, diagnosis were compared.	Of the 52 patients with negative radiographs, 34 (65%) were diagnosed with complete fracture with MRI. Of the 41 patients with suspected fracture on radiographs, 35 (85%) were diagnosed with complete fracture with MRI.	"MRI is a useful tool for demonstration of occult hip fractures. In the absence of a hip fracture, another explanation for the patient's pain and disability will often be given."	Prospective consecutive case series. Data suggest MRI can assist in the identification of radiograph negative occult hip fractures with a high index of suspicion for fracture, helping in making better treatment decisions.
Rizzo 1993 (score=4.0)	MRI	Diagnostic	No sponsorship or COI.	N = 62 patients where hip fracture was clinically suspected after negative radiographic findings.	Mean age: 73 years; 23 males, 39 females.	Hip Fracture	All 62 patients had an MRI of the hip within 24 hours of admission using either a 0.6 or 1.5 tesla superconducting magnet. The same 62 patients also had a technetium-99m bone scan within 72 hours of admission.	MRI found 37 fractures while bone scan found 36. The sensitivity of the MRI performed within 24 hours was greater than that of the bone scan	"Magnetic resonance imaging was as accurate as bone-scanning in the assessment of occult fractures of the hip. The magnetic resonance imaging took less	Data suggest MRI as good as bone scan for imaging occult hip fractures and provides early diagnostic information crucial to treatment decisions.

								performed with 72 hours.	than fifteen minutes to perform. And it was tolerated well by the patient. Magnetic resonance imaging provides an early diagnosis of occult fractures about the hip and may decrease the length of the stay in the hospital by expediting definitive treatment."	
Pejic 2017 (score=4.0)	MRI	Diagnostic	Sponsored by ALF grants from the Region Skane, Sweden. No COI.	N = 616 patients at a hospital who had an MRI scan of the hip after trauma.	Mean age: 82.5 years; 455 males, 161 females.	Hip Fracture	All 616 patients had x-rays performed as well an MRI done on average 40 hours later.	True occult hip fracture rate was 1.6%. 228 of the 616 MRI scans showed hip fracture. 30% of MRIs performed lead to surgery. At 6 months post-surgery, 90 of 228 patients had adverse advents. MRI group had lower hip complication rate than historical cohort (P=0.0007)	"The diagnosis set by MRI, with a high share of pelvic fractures or no fracture, reflects the difficulty in differential diagnosis in this group of patients. The rate of occult hip fractures was low and patient with pelvic fractures already known from X-ray did not have additional hip fractures. Thus, a reduction of MRIs can be feasible. Contrary, we	Retrospective case series. Data show MRI rates increased over the ten year study period and often there was no fracture found suggesting the difficulty in making the diagnosis.

									found a tendency to use the MRI more often. The group with MRI diagnosed hip fractures does not suffer more complications then the regular hip patients despite their delay to surgery being longer."	
Kaushik 2009 (score=4.0)	MRI	Diagnostic	No mention of sponsorship or COI.	N = 30 patients with post-traumatic intracapsular fractures who fulfil the standard criteria for internal fixation.	Mean age: 47.5 years; 15 males, 15 females.	Hip Fracture	All 30 patients received standard radiographs of the hip as well as a dynamic MRI using a sigma 1.0 T superconducting system.	Sensitivity, specificity, and accuracy of MRI was 86.9%, 87.5% and 87%.	"Thus dynamic MRI appears to be a sensitive modality for assessing the vascularity and predicting avascular necrosis in preoperative period after an intracapsular neck fractures. The use of this technique may change the approach towards management of such fractures as it provides more accurate and reliable prediction of femoral head vascularity and may provide better guidelines for definitive	Data suggest dynamic MRI is a good method to assess the vascularity of the femoral head in intracapsular neck fractures.

									management of these fractures."	
Hirata 2001 (score=3.5)										Prospective study. Data suggest dynamic MRI is appropriate for preoperative evaluation of femoral neck fractures.
Hossain 2007 (score=3.5)										Data suggest MRI is valuable to distinguish between those with and without occult hip fracture due to limitations of radiography.
Deleanu 2015 (score=3.5)										Data suggest MRI is best imaging tool for occult fractures of proximal femur.
Quinn 1993 (score=3.0)										Small sample. Data suggest MRI can identify hip fractures in negative or indeterminate radiographs.
Kim 2013 (Score=3.0)										Retrospective consecutive case series. Small sample. Data suggest MRI-CT is beneficial in evaluating isolated fractures

										of the greater trochanter.

Evidence for the Use of Radiography (X-ray) for evaluating hip fractures

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: X-ray, Radiography; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, subtrochanteric fractures, femoral neck fracture, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 512 articles in PubMed (Most Recent), 510 in PubMed (Best Match, went through first 100), 862 in Scopus (Went through first 100), 328 in CINAHL (Went through first 100), 265 in Cochrane Library (Went through fist 100), 18300 in Google Scholar (Went through first 100), and 8 from other sources. We considered for inclusion 6 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 8 from other sources. Of the 14 articles considered for inclusion, 14 diagnostic studies and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/ Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
O'Toole 2013 (Score=7.0)	X-Ray/CT	Diagnostic	The authors declared no sponsorship or COI.	N=86 patients with femoral shaft fracture with or without femoral neck fractures.	No mention of age and sex.	Femoral neck fracture	Computed tomography: axial-view 3-, 40- to 60-mm section multidetector pelvis CT vs. plain radiography: AP-view pelvis plain radiography and femoral shaft plain radiography. All patients were included.	The three imaging technique indicated 94% high specificity, 95% 1 minus negative post-test high probability, 65% poor sensitivity, and 58% positive post-test poor probability.	Plain radiography and computed tomography have rates of missed femoral neck fractures that are similar and substantial, with a sensitivity of only 56%–64%. Our data emphasize the importance of intraoperative and postoperative imaging in detecting nondisplaced femoral neck fractures in association with femoral shaft fractures.	Data suggest both imaging techniques of CT and plain radiography have similar rates of missed femoral neck fracture (sensitivity 56%-64%) associated with femoral shaft fracture Data suggest importance of post and intraoperative imaging in detecting non-displaced femoral neck fracture.
Esmaeilzadeh, 2016 (score=6.5)	Radiography/US	Diagnostic	No COI and no mention of sponsorship.	N=54 patients with hip fractures	Mean age: 70.65 years; 0 males, 54 females.	Hip fracture	Group 1, women with hip fractures as cases for 6 months (n=18) Vs	BUA for distal forearm fracture had a sensitivity and specificity of .706 and .667	"It can be concluded that QUS variables, particularly BUA, and FRAX® major osteoporo	Pilot study (case control) data suggest the BUA and FRAX may accurately

							Group 2: control group with no hip fractures. (n=36)	while hip fracture had a sensitivity and specificity of .688 and .700. SOS for distal forearm fracture had a sensitivity and specificity of .588 and .545 while hip fracture had a sensitivity and specificity of .688 and .667. ORAI score for distal forearm fracture had a sensitivity and specificity of .588 and .606 while hip fracture had a sensitivity and specificity of .688 and .533.	tic fracture probability without BMD are good candidates for the identification of both hip and distal forearm fractures. ”	identify distal forearm and hip fractures without the use of BMD.
Stevens 2003 (score=6.0)	X-ray/CT/MRI	Diagnostic	No mention of sponsorship or COI.	N= 45 patients with stage I and stage II osteonecrosis of the femoral head	Mean age: 47.8 years; 32 males, 13 females.	Hip fracture	All patients had a surgical core decompression of the hip – alone or with rhBMP-2 on an	MR imaging has a sensitivity of 38% and a specificity of 100% while unenhanced	“CT reveals more subchondral fractures in osteonecrosis of the femoral head than unenhanc	Data suggest CT better than MRI and both better than radiography in detecting subchondral

							absorbable collagen sponge (rhBMP/ACS) implanted in the decompression site. They were then evaluated with radiography and MR imaging. 2 weeks after surgery, CT and MR were performed. 6 and 12 months after surgery, radiography, CT, and MR were performed. (n=45)	radiography has a sensitivity of 71% and a specificity of 97%, when compared to CT.	ed radiography or MR imaging. The high-signal-intensity line seen on T2-weighted MR images appears to represent fluid accumulating in the subchondral fracture, which may indicate a breach in the overlying articular cartilage."	fractures in femoral head osteonecrosis.
Duane 2008 (Score=5.5)	CT/X-ray	Diagnostic	No mention of sponsorship or COI.	N=1388 patients sustained blunt trauma.	Mean age: 38.8 years; no mention of sex.	Pelvic fracture	Clinical examination (CE) vs. Plain films (PXR) vs. CT of the pelvis. All patients were included.	168 out of 1388 patients were diagnosed with pelvic fracture by CT scans; the incidence of fracture was 12.1%. Clinical examination indicated 96.43% sensitivity, 99.03% negative predictive value,	"In conclusion, clinically significant pelvic fractures are diagnosed better by CE than PXR compared with CT, eliminating the need for routine pelvic radiographs. The majority of	Data suggest CE>CT>plain radiographs in diagnosing pelvic fractures.

								50.25% specificity, and 21.07% positive predictive value. CT was considered as the gold standard.	patients with blunt trauma undergo CT making additional plain films unnecessary and therefore a wasted expense."	
Rosenberg, 2011 (score=5.5)	Radiography	Diagnostic	No mention of sponsorship or COI	N=36 patients with 38 complete subtrochanteric and diaphyseal femoral fractures	Mean age: 62.6 years; 7 males, 29 females.	Femoral hip fractures	Group 1, hip fractures treated with bisphosphonate therapy for 4-10 years (n=17 with 19 fractures) Vs. Group 2, hip fractures associated with major trauma, and not treated with bisphosphate therapy. (n=19 and 19 fractures)	The sensitivity, specificity, and overall accuracy for diagnosing bisphosphonate-related fractures were 94.7%, 100%, and 97.4% for reader 1; 94.7%, 68.4%, and 81.6% for reader 2; and 89.5%, 89.5%, and 89.5% for reader 3.	"Radiographs are reliable for distinguishing between complete femoral fractures related to bisphosphonate use and those not related to bisphosphonate use. Focal lateral cortical thickening and transverse fracture are the most dependable signs, showing high odds ratios and the highest accuracy for diagnosing these fractures."	Retrospective case series. Data suggest radiographs may accurately distinguish between complete femoral fractures related to bisphosphonate versus those which are not and the best predictors appear to be the presence of focal lateral thickening and/or transverse fracture.
Harley 1982 (Score=5.5)	X-Ray/CT	Diagnostic	No mention of sponsor	N=26 patients with suspicion of	Age range: 17 to 66 years	Acetabular fracture	Computed tomography: 5mm slice thickness	For detecting sacroiliac joint abnormali	"Sensitivity of both examinations for abnormali	Small sample. Data suggest suspicion

			ship or COI.	posterior femoral head dislocation or acetabular fracture.	; 21 males, 5 females.		with GE 8800 with scan time 9.6 seconds vs. plain radiography. All patients were included.	ties by CT and plain radiography, the preponderance of false-negative errors was statistically significant (p=0.05 vs. p=0.01). CT accurately identified all the sacrum fractures, but plain radiography incorrectly interpreted or missed some cases, but the differences between the two instruments was not statistically significant.	ties of the sacroiliac joint was relatively poor, but examinations were highly specific. Determination of the stable fracture fragment(s) was readily accomplished by CT scanning in all 26 patients; in five patients incorrect determinations were made with conventional radiographs alone."	of either femoral head dislocation or an acetabular injury should be followed up with CT.
Isida 2015 (Score=5.5)	CT/X-ray	Diagnostic/ prospective consecutive case series	No mention of sponsorship. The authors declared no COI.	N=110 patients with proximal femur fracture in trochanter.	Mean age: 85 years; 22 males, 88 females.	Trochanteric fracture	A/P pelvis plain X-rays vs. Computed tomography. All patients were included.	CT scans detected 93% lesser trochanter fractures, 94% greater trochanter fracture, and 51% lateral wall ruptures; while X-rays detected 81%, 75% and 35%	"The current results of this study suggest that comminution contributes to instability and that this finding is not taken into account in the AO	Data suggest standard X-rays underestimate the complexity of trochanteric fractures and show poor reproducibility.

								of the three fractures respectively. Thus, the X-ray indicated 48% sensitivity and 29% negative predictive value. CT indicated 95% sensitivity and 79% negative predictive value.	classification, which is not well suited for this type of fracture and raises the question of how to best evaluate and treat these fractures. "	
Almazedi, 2011 (score=5.0)	Radiography	Diagnostic	No mention of sponsorship or COI.	N=359 patients diagnosed with proximal femoral fractures.	Mean age: 81.1 years; 130 males, 229 females.	Hip fracture	Group 1, blinded reviewers assessed anteroposterior (AP) and later lateral views of femoral fracture radiographs (n=359) Vs Group 2, all of the same patients with intra-operative diagnosis as the control (n=359)	The sensitivity of an AP view alone was 52.6% with a specificity of 88.5%. Sensitivity improved to 90.9% and specificity to 90.6% after adding a lateral view.	"This study provides statistical evidence that one view is adequate and safe for the majority of hip fractures. The lateral radiograph should not be performed routinely in order to make considerable savings in money and time and to avoid unnecessary patient discomfort."	Retrospective case series of proximal femoral fractures. Data suggest in the majority of proximal femoral fractures, lateral radiographs need not be performed except when determining displacement in intracapsular fractures.

Riaz 2016 (score=5.0)	Radiography	Diagnostic	No sponsorship or COI.	N= 320 patients diagnosed with proximal femoral fractures.	Mean age: 81.5 (SD ± 9.3) years; 112 males, 208 females.	Hip fracture	Group 1, blinded reviewers assessed anteroposterior (AP) (n=320) Vs Group 2, blinded reviewers assessed anteroposterior (AP) and the lateral views of femoral fracture radiographs (n=320)	With intracapsular fractures, the sensitivity of an AP view alone was 54.3% with a specificity of 89.8%. Sensitivity improved to 92.1% and specificity to 91.4% after adding a lateral view. With extracapsular fractures, correct diagnoses rate were not improved with lateral x-ray (p=.29).	"This study provides statistical evidence that one view is adequate and safe for majority of proximal femoral fractures. The lateral radiograph should not be performed on a routine basis thus making considerable saving in time and money, and avoiding unnecessary radiation exposure and discomfort to the patient."	Consecutive Case Series. Data suggest in most cases, lateral X-rays are not required.
Davis 2013 (Score=5.0)	CT/X-ray	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=15 patients with OTA 62-A1 (isolated unilateral posterior wall) acetabular fracture.	No mention of age or sex.	Acetabular fracture	Plain radiography (high quality anteroposterior, oblique) vs. axial computed tomography. All patients were included.	Poor agreement of interobserver reliability arose among subjects (k=0.12). The correct percentage of assessment of wall fracture	"Orthopedic traumatologists expert in acetabular fracture care cannot adequately determine hip stability status for fractures involving	Small sample. Data suggest hip stability cannot be reliably determined using only plain radiographs and CT. If diagnosis is uncertain

								size range and hip dislocation history was only 53% for initial review and 52% for second review. Sensitivity was 100% for initial review and 57% for the second. Specificity was 13% for initial and 47% for second review.	20%–50% of the posterior wall using plain radiographs, computed tomography, and the patient's hip dislocation status."	ORIF may be the best treatment option.
Fairclough 1987 (score=4.5)	Bone scans/Radiography	Diagnostic	No mention of sponsorship or COI.	N = 43 elderly patients with suspected femoral neck fracture and negative bone scans.	Mean age: 77 years; No mention of gender.	Hip Fracture	43 patients with negative bone scans had an isotope scan. 30 patients had normal scans and 13 had specific bone scan abnormalities later shown to be fractures.	Bone scans resulted in zero false-positives and no false-negatives after three months.	"This study shows that isotope bone-scanning is highly reliable in the identification of "occult" fractures of the hip and may allow the surgeon to operate before displacement occurs, thus improving the prognosis.	Data suggest that if there is a strong index of suspicion that an elderly patient has a hip fracture (even though it is radiographically negative), a bone scan should be performed.
Resnik 1991 (Score=4.0)	CT/ X-ray	Diagnostic/ consecutive	No mention of sponsor	N=50 patients with posterior portion of	Mean age: 36 years	Pelvic fracture	CT: iliac crests-acetabular roofs for 10 mm	CT detected 80% of hip joint fragments,	"We conclude that the efficacy of plain	Data suggest plain radiographs detect

		case series	ship or COI.	pelvis injuries.	; 36 males, 14 females.		intervals and then pubic rami for 3 to 4 mm intervals vs. Anteroposterior plain radiography of pelvis. All patients were included.	10% sacroiliac diastasis, 16% of sacral fractures, 21% iliac fractures, 7% acetabular fractures, 3% superior pubic ramus, and 9% inferior pubic ischium. On the other hand, plain films indicated 9% misdiagnosis frequency of acute pelvic dislocations and fractures.	radiographs in detecting pelvic fractures in patients with acute pelvic trauma is sufficient to identify virtually all clinically important fractures and dislocations."	most clinically significant pelvic fractures.
Cesme 2016 (score=3.5)										Combination hip and/or distal forearm fractures case control with small sample size. Baseline differences between groups variable timing of testing.
Hadji 2014 (score=3.5)										Cross sectional case comparison. Unclear if

										all patients given all US test. Data suggest not all ultrasonometry devices are able to detect hip fractures. The Achillies, Sahara, and Insight QUS appear comparable to DXA.

Evidence for the Use of Ultrasound (US) for evaluating hip fracture patients

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Ultrasound; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, subtrochanteric fractures, femoral neck fracture, diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 782 articles in PubMed, 213 in Scopus, 20 in CINAHL, 7 in Cochrane Library, 282,200 in Google Scholar, and 0 from other sources. We considered for inclusion 22 from PubMed, 5 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 27 articles considered for inclusion, 24 diagnostic studies and 1 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Esmaeilzadeh, 2016 (score=6.5)	Radiography/US	Diagnostic	No COI and no mention of sponsorship.	N=54 patients with hip fractures	Mean age: 70.65 years; 0 males, 54 females.	Hip fracture	Group 1, women with hip fractures as cases for 6 months (n=18) Vs Group 2: control group with no hip fractures. (n=36)	BUA for distal forearm fracture had a sensitivity and specificity of .706 and .667 while hip fracture had a sensitivity and specificity of .688 and .700. SOS for distal forearm fracture had a sensitivity and specificity of .588 and .545 while hip fracture had a sensitivity and specificity of .688 and .667. ORAI score for distal forearm fracture had a sensitivity and specificity of .588 and .606 while hip fracture had a sensitivity and specificity of .688 and .533.	"It can be concluded that QUS variables, particularly BUA, and FRAX® major osteoporotic fracture probability without BMD are good candidates for the identification of both hip and distal forearm fractures."	Pilot study (case control) data suggest the BUA and FRAX may accurately identify distal forearm and hip fractures without the use of BMD.
He 2000 (score=5.5)	Ultrasound	Diagnostic	No mention of sponsorship or COI.	N=68 subjects that	Mean age: 74.8±7.2 years; 0	Hip Fracture	Quantitative Ultrasound (QUS-Hologic, the Sahara: vs	Standard CV for BUA between Sahara and UBA 575+ were	"[O]ur study indicated that the calcaneal QUS variables,	Data suggest QUS measurements of calcaneus in

				sustained hip fracture	males, 68 females		Quantitative Ultrasound (QUS-Walker Sonix UBA 575+ All patients were also evaluated with Dual X-ray Absorptiometry (DXA).	significant ($p<0.05$); however mean difference between two measurements were not with paired t-test ($p=0.6$-0.95). QUS and DXA measurements were lower in fractured patients compared to controls ($p<0.001$). BUA and speed of sound correlation between Sahara and UBA 575+ were $r=0.92$ and $r=0.91$, respectively. Correlation between DXA and QUS were $r=0.28$-0.44. QUS measurement of calcaneus showed better discrimination (OR+2.7-3.2).	as measured by the Sahara system can discriminate hip fracture patients equally as well as hip DXA."	elderly women as good as DXA in identifying hip fracture risk.
López-Rodríguez 2003 (score=5.5)	Ultrasound	Diagnostic	Sponsored by a grant from the Hospital Clinico Foundation.	N=300 patients with osteoporotic fractures	Mean age: 58±11 years; 19 males,	Fracture	Quantitative Ultrasound (QUS-Sahara Clinical Bone Sonometer) Vs	Sensitivity and specificity for QUI-T-score was -1.51 (sensitivity 68.9%, specificity	"In conclusion, calcaneus ultrasound appears as a useful technique for	Data suggest calcaneal US performs as well as DXA for identifying

			No mention of COI.		281 females		Dual X-ray Absorptiometry (DXA)	65.5%) compared to -1.53 (sensitivity 63.5%, specificity 76.7%) for DXA. DXA measurement prediction of fracture showed sensitivity and specificity of T-score≤-2.5 SD at lumbar spine and femoral neck. A lumbar spine *T*-score ≤-2.5 SD had 26.04% sensitivity and 92.65% specificity in the prediction of a femoral neck *T*-score ≤-2.5 SD. A femoral neck *T*-score ≤-2.5 SD had 62.5% sensitivity and 72.69% specificity in the prediction of a lumbar spine *T*-score ≤-2.5 SD.	the routine clinical practice, as its performance is similar to DXA for the discrimination of subjects with osteoporotic fracture."	osteoporotic fractures.
Durosier 2007 (score=5.0)	Ultrasound	Diagnostic	Spoonsored by INSERM-MSD-Chibret and by	N=12064 women with hip fracture and controls	Mean age: 79.3 years; 0	Hip Fracture	Quantitative Ultrasound (QUS) vs QUS-derived heel stiffness	Incidence rate of hip fracture was 7.32 per 1000 woman years.	"Combining clinical risk factors to heel bone ultrasound	The EPISEM study. Data suggest combining

			research grant from Geneva University Hospital. No mention of COI.		males, 12064 females		index (SI)-determined using speed of sound (SOS), degree of attenuation of the ultrasound (BUA)	Composite score showed sensitivity of 57% compared to 51.7% for the SI-age score, and 52.8% for the CRF score alone. Composite scores identified 163 women at high risk, which was 15 more than SI-age score and 12 more than CRF alone. Using SI alone, 38% were low risk and 52% were high risk. Using CRF alone, 34% were low risk, and 53% were high risk.	appears to correctly identify more women at low risk for hip fracture than either the stiffness index or the CRF alone; it improves the detection of women both at low and high risk."	clinical risk factors with US improves the ability to correctly identify women at both low and high risk for hip fractures.
Dargent-Molina 2003 (score=5.0)	Ultrasound	Diagnostic	Spoonsored by INSERM-MSD-Chibret. No mention of COI.	N=5910 women	Mean age: 80.5±3.8 years; 0 males, 5910 females	Hip fracture	Quantitative Ultrasound (QUS) with Lunar Achilles ultrasound system vs Dual X-ray Absorptiometry (DXA) with Lunar DPX-plus vs BMD Screening Alone vs QUS triage with BMD assessment vs BMD screening based on weight	QUS alone showed 5% of women as high risk of hip fracture. Average risk was 35.2 per 1000 woman years (95% CI 23.6-46.9) compared to 9.5 per 1000 woman years. Sensitivity was 15% and specificity was 95.4%. BMD	"With this combined strategy, women in the high risk group have one chance in ten of having a hip fracture over the next 4 years, whereas women in the low-risk group have only one chance in 40."	EPIDOS prospective study. Data suggest a combination of clinical risk assessment, QUS and BMD improves the sensitivity (53%) of fracture risk.

							by clinical evaluation (women with medium to low BMD)	alone sensitivity was 35.1% and specificity was 85.9%. Combining QUS, BMD, and clinical risk assessment showed increased identification of high risk women with a sensitivity of 53%.		
Ekman 2001 (score=5.0)	Ultrasound	Diagnostic	No mention of sponsorship or COI.	N=87 patients with hip fracture and N=195 controls	Mean age: 75.0 years; 0 males, 282 females	Hip Fracture	Dual X-ray Absorptiometry (DXA) vs Quantitative Ultrasound of the heel (QUS Achilles+) vs Quantitative Ultrasound of the fingers (QUS-DBM Sonic 1200) vs Radiographic Absorptiometry (RA)	BMD by DXA showed 62% of fractured patients and 19% of controls as osteoporotic. QUS of the heel showed 98% versus 72%, finger QUS showed 80% versus 85%, and RA showed 60% versus 51%. DXA showed highest sensitivity and specificity (T-score: -2.2) and then QUS of the heel (T-score:-3.4).	"[B]oth DXA of the hip and QUS of the heel have an independent, strong capability of discriminating female hip fracture patients from controls."	Population study. Data suggest hip DXA and heel QUS can distinguish hip fracture risk better than QUS and RA of phalanges.
Hans 2002 (score=4.5)	Ultrasound	Diagnostic	Sponsored by Diagnostic Medical System (DMS,	N=146 post-menopausal patients	Mean age: 61.5 years; 0 males,	Hip Fracture	Quantitative Ultrasound(QUS) -Achilles+: used wet system with transducer vs	Z-scores for the three tests were -2.9 for UBIS, -2.5 for Sahara, and -2.6 for	"In conclusion, no significant differences between QUS technologies	Data suggest time since fracture influences ability to

			France). No mention of COI.		146 females		QUS-UBIS 5000: used wet system with transducer vs QUS-Sahara: used ultrasonic gel, transducer, and placed in contact with heel	Lunar devices. UBIS fracture risk was OR=2.30, compared to Sahara BUA OR=2.30, and OR=3.5 for Achilles BUA. AUC were increased for BUA and decreased for SOS for all tests except the Lunar Achilles+.	were observed in their positive and significant ability to discriminate hip-fractured patient from controls. However, this statement is shadowed when taking into account the time since fracture which seems to negatively influence results obtained on dry versus wet QUS systems."	discriminate fractured versus non-fractured individuals not the type of QUS device measuring the calcaneus.
Karjalainen 2012 (score=4.5)	Ultrasound	Diagnostic	Sponsored by Finnish Cultural Foundation, International Graduate School in Biomedical Engineering and Medical Physics (iBioMEP), Finnish Funding Agency for Technology and	N=30 women with hip fractures	Mean age: 74.1±3.0 years; 0 males, 30 females	Femoral Neck Fracture	Quantitative Ultrasound (QUS): vs Dual X-ray Absorptiometry (DXA): All patients received both tests	Ultrasound measurement of BMD_{neck} showed 86% sensitivity and 100% specificity. AUC prediction of fracture was improved by combining BMD_{neck} and age. Combining BMDtroch, age, and weight showed highest AUC value of 0.88 compared to BMD_{neck} and age ($p<0.05$).	"For the first time, ultrasound backscatter measurements of proximal femur were conducted in vivo. The results indicate that ultrasound parameters, combined with patient characteristics, may provide a means for	Small sample. Data suggest a combination of specific patient characteristics and US measurements of the proximal femur may be predictive of an osteoporosis diagnosis.

			Innovation, and Kuopio University Hospital, Kuopio, Finland. No COI.					Cortical thickness at distal and proximal tibia showed estimate of r=0.86 (p<0.001).	osteoporosis diagnostics."	
Stewart 1994 (score=4.5)	Ultrasound	Diagnostic	Sponsored by grant from Scottish Home and Health Department, Arthritis and Rheumatism Council and Action Research. No mention of COI.	N=100 women with low or moderate hip trauma fractures	Mean age: 77.4 years; 0 males, 100 females	Hip Fracture	Dual Energy X-ray absorptiometry (DXA) of the spine and hip vs Broadband Ultrasound Attenuation (BUA) of the os calcis	BUA had the lowest mean Z-score for fracture patients (BUA=-0.96) except for DXA trochanter (L2-L4=-0.57; Neck=-0.82; Trochanter=-1.01; Wards area=-0.76). BUA compared to DXA Z-scores showed difference of p=0.014, DXA spine compared to DXA trochanter showed p=0.003), DXA trochanter and DXA wards showed p=0.009.	"[S]tudy shows that BUA is a better discriminator of hip fracture than DXA lumbar spine or DXA hip, which may have important implications for predicting those at risk of future hip fracture."	Data suggest BUA better than DXA for hip fracture risk.
Hans 1999 (score=4.5)	Ultrasound	Diagnostic	Sponsored by Sunlight Ultrasound Technologies. COI: One or	N=374 women with or without fracture of	Mean age: 72.1 years; 0 males,	Osteoporotic femur fracture	Quantitative Ultrasound (QUS): (0.5-2.0 MHz vs Radiation-based	SOS measurements (with QUS) were lower in hip fracture patients	"Our results demonstrate the encouraging potential of	Data would suggest that combining multiple bone site data

			more of the authors have received or will receive benefits for personal or professional use.	the proximal femur	374 females		Bone Densitometry techniques	compared to controls for both lower extremities such as patella and calcaneus (p<0.0001), upper extremities such as radius, and hand capitate (p<0.001), and spinous process (p<0.0002). Ability to discriminate hip fractures with QUS at all sites was p<.01 (ORs=1.4-3.0). Distal radius and calcaneus were OR=2.4 and OR=3.0, respectively showed best prediction of hip fracture from control.AUC was improved by 3% which increased sensitivity and specificity to 94%.	multiple-site ultrasonic measurements. Preliminary data gathered for this first generation device demonstrate good fracture discrimination for individual sites as well as a combination of sites."	improves hip fracture risk identification.
Krieg 2006 (score=4.0)	Ultrasound	Diagnostic	No mention of sponsorship. No COI.	N=7062 women with hip fracture	Mean age: 75.2±3.1 years; 0 males,	Hip Fracture	Achilles+: heel water-bath ultrasound ultrasound system (200-600 kHz) vs Sahara:	Hazard ratio was 2.3 (95% CI 1.7, 3.1) to 2.6 (95% CI 1.9, 3.4) for Achillies+, 2.2 (95% CI 1.7, 3.0)	"In conclusion, whereas the DBM Sonic 1200 AD-SOS was not predictive of hip fracture risk in	Data suggest QUS of the heel were predictive of hip fracture risk but QUS

					7062 females		dry system using oil-based coupling gel (200-600 kHz) vs DBM Sonic 1200: type of US that measure pulse through distal metaphysis of the first phalanges of the last four fingers of the hand (20 mV)	to 2.4 (95% CI 1.8, 3.2) for Sahara, and 1.2 (95% CI 0.9, 1.5) for DMB sonic 1200.	our elderly women population, the water-bath heel QUS Achilles+ and the dry system heel QUS Sahara showed similar predictive capacity in their assessment of hip fracture risk."	devices used of the phalanges were not.
Hans 1996 (score=4.0)	Ultrasound	Diagnostic	Sponsored by INSERM-MSD-Chibret. No mention of COI.	N=5662 women evaluated for hip fracture	Mean age: 80.4 years; 0 males, 5662 females	Hip Fracture	Ultrasonography vs Radiography: (dual-photon x-ray absorptiometry (DPXA)	Ultrasonographic variables predicted increasing risk of hip fracture similar to BMD from DPXA. Relative risk of hip fracture for 1 SD was 2.0 (95 % CI 1.6-2.4) for ultrasound speed of sound compared to BMD with 1.9 (95% CI 1.6-2.4).	"In conclusion, because ultrasound methods are less expensive, faster, and radiation free, and because they predict the risk of hip fracture as efficiently as DPXA, their use should be encouraged in the assessment of the elderly population. Ultrasonography is a useful tool in any programme directed towards prevention of hip fractures."	EPIDOS study. Data suggest US heel measurements do predict hip fracture in elderly women.

Määttä 2014 (score=4.0)	Ultrasound	Diagnostic	Sponsored by Finnish Funding Agency for Technology and Innovation, the Academy of Finland, and Tauno Tönning Foundation and Finnish Cultural Foundation. No mention of COI.	N=490 women at risk for osteoporosis and fractures	Mean age: 79.9 years; 0 males, 490 females	Fracture, Hip Fracture	Quantitative Ultrasound (QUS) vs Dual X-ray Absorptiometry (DXA)	Decreased V_{LF} showed an increased risk of hip fracture (OR=6.3). Low V_{LF} showed higher risk of hip fracture compared to high V_{LF} (OR=3.3). BMD predicted hip fractures with a ratio of HR=4.8 (95% CI 1.4-16.6) with a T-score≤-2.5. Low femoral neck BMD showed increased risk of hip fracture (OR=4.1; 95% CI 1.6-10.5) compared to normal femoral neck BMD.	"In conclusion, decreased low-frequency ultrasound velocity was associated to increased hip fracture risk despite the limited measurement precision."	Population study. Data suggest low frequency US velocity was associated with increased hip fracture risk.
Drozdzowska 2003 (score=4.0)	Ultrasound	Diagnostic	No mention of sponsorship or COI.	N=2466 female patients with osteoporotic fracture	Mean age: 60.3 years; 0 males, 2466 females	Fracture	Fractures: patients with non-traumatic fractures (n=583) vs Controls: patients without fractures (n=1883). All patients received quantitative ultrasound (QUS).	Negative Z-score was observed for fractures (-1.36 to -1.69) and also in controls (-1.0). AUC was 0.91 sensitivity and specificity for discriminating hip fractured patients from controls. Vertebral	Phalangeal QUS revealed the	"The present study demonstrates the ability of phalangeal QUS to discriminate between subjects with and without different types of nontraumatic fractures.	Data suggest QUS of phalanges can identify hip and spine fractured patients compared to controls.

								fractures had lower specificity and sensitivity of AUC=0.89, wrist fractures was 0.77, and other fractures was 0.70. Odds ratio for probability of having fracture was 3.49 (95% CI 1.57-7.75) for hip, 3.25 (95% CI 1.94-5.45) for spine, 2.24 for wrist (95% CI 1.86-2.70), and 1.81 for other fractures (95% CI 1.36-2.40).	best sensitivity and specificity in discriminating hip- and spine-fractured patients from controls."	
Cesme 2016 (score=3.5)										Combination hip and/or distal forearm fractures case control with small sample size. Baseline differences between groups variable timing of testing.
Hadji 2014 (score=3.5)										Cross sectional case comparison. Unclear if all patients given all US test. Data suggest not all

										ultrasonometry devices are able to detect hip fractures. The Achillies, Sahara, and Insight QUS appear comparable to DXA.
Alenfeld 1998 (score=3.5)										Data suggest US measurements of proximal phalanges can distinguish between healthy and osteoporotic women helping to predict fracture risk.
Njeh 2000 (score=3.5)										Data suggest all 6 calcaneal QUS devices performed with similar diagnostic sensitivity to identify hip fractures.
Schott 1995 (score=3.5)										Data suggest US better correlated to fracture type compared to DXA and provides

										fracture risk information.
Mautalen 1995 (score=3.5)										Data suggest in individuals with hip fractures, US of the OS calcis has diagnostic sensitivity.
Welch 2004 (score=3.5)										EPIC. Norfolk Cohort. Data suggest BUA varies in men versus women and is impacted by numerous variables such as HRT, smoking status, height and weight.
Zhang 2015 (score=3.5)										Cross-sectional. Data suggest QUS of calcaneal bone is associated with trochanteric cancellous bone.
Khaw 2004 (score=3.0)										EPIC-Norfolk population study. Data suggest total and hip fracture risk can be

										determined via QUS of the calcaneus.
Damilakis 2004 (score=3.0)										Cross-sectional study. Data suggest BMD is better at discriminating hip fractures than BUA measurement of the calcaneus.

Evidence for Ergonomic Interventions

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Ergonomic Interventions; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 13 in Scopus, 1 in CINAHL, 3 in Cochrane Library, 88700 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the Use of Fall Protection

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Fall protection, fall prevention; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 42 articles in PubMed, 3011 in Scopus (Went through first 100), 105 in CINAHL, 68 in Cochrane Library, 17,600 in Google Scholar (Went through first 100), and 20 from other sources. We considered for inclusion 9 from PubMed, 2 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 2 from other sources. Of the 19 articles considered for inclusion, 14 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Arnold 2010 (score=5.5)	Fall Protection	RCT	Sponsored by Saskatchewan-Canadian Institutes of Health Research regional Partnerships Program (Sask-CIHR RPP) provided a 2 year fellowship grant for the primary author, and the Physiotherapy foundation of Canada. No COI mentioned.	N = 79 Patients with hip OA	Mean age: 74.4; 23 males, 56 females.	Aquatics and education (n=28) (aquatic exercise twice a week with once a week group education for 11 weeks) Vs aquatics only (n=26) (2 times a week aquatic exercise for 11 weeks.) Vs control (n=25) (usual activity no added on exercise program.)	No follow up mentioned.	No significant difference in physical activity level among the three groups (one-way ANOVA; p=0.73) MANCOVA for change in fall risk factors for the intention-to-treat analysis was significant, F(5, 68) = 2.8, p=.038.	"The combination of aquatic exercise and education was effective in improving fall risk factors in older adults with arthritis."	Data suggest combining aquatic exercise with education is beneficial in fall prevention for older adults with hip OA.
Sjoberg, 2013 (score=5.5)	Fall Protection	RCT	Sponsored by the Swedish National Board of Health and Welfare. No COI.	N = 199 individuals with hip fractures over the age of 65 who had undergone surgery for hip fracture.	Mean age: 84.5 years; 67 males, 132 females.	Control Group: treated with treated with fracture-preventing drugs, such as calcium and Vitamin D; bone-active drugs, such as bisphosphonates, estrogen receptor modulators, and parathyroid hormones; fall-risk-increasing drugs identified according to the	Follow-up at 12 months after discharge.	The amount of participants that were treated with fracture-preventing drugs increased to 51% for the intervention group and 29% for the control group participants. Comparatively, the fall-risk-increasing displayed no significant difference between the two groups; the amount of drugs provided at admission was	"Medication reviews performed and conveyed by a physician increased treatment with fracture preventing drugs but did not significantly decrease treatment with fall-risk-increasing drugs in older adults with hip fracture. Prescribing physicians	Data suggest physician preformed medication reverses increased treatment with fracture preventing drugs but did not significantly lower the treatment with fall-risk increasing drugs in the elderly. Also it was noted that reviews show

						appropriate drug treatment for the (n = 99) Vs Intervention Group: treated with 50% more fracture-preventing drugs, such as calcium and Vitamin D and double the bone-active drugs, such as bisphosphonates, estrogen receptor modulators, and parathyroid hormones; fall-risk-increasing drugs identified according to the appropriate drug treatment for the (n = 100).		(P=.97) and declined to (P=.63) to the corresponding 12-month figures.	appreciated this intervention."	doctor are more likely to add new drugs than to withdraw old ones.
Berggren, 2008 (score=5.5)	Fall Protection	RCT	Supported by the Vårdal Foundation, the Joint Committee of the Northern Health Region of Sweden (Visare Norr), the JC Kempe Memorial Foundation, the	N = 199 patients operated on for femoral neck fracture.	Mean age: 82.15 years; 51 males, 148 females.	Control Group: specialist orthopedic department with conventional care used at the department, geriatric wards for patients who needed longer	Follow-up at 4 and 12 months.	Fall incidence rate at admission was 6.30/1000 d in the intervention group and 9.07/1000 d in the control group; IRR was .55 (95% CI: 0.27–1.12, p=0.100) vs 4.16/1000 d and 6.43/1000 d at the 12-month post	"A team applying comprehensive geriatric assessment and rehabilitation, including prevention and treatment of fall-risk factors, reduced inpatient falls and injuries,	Data suggest a non-statistically significant trend towards reduction in inpatient falls and associated injuries was found one-year post full

			Foundation of the Medical Faculty, the Borgerskapet of Umeå Research Foundation, the Arneska Foundation, University of Umeå and the County Council of Västerbotten ("Dagmar", "FoU" , and "Äldre Centrum Västerbotten") and the Swedish Research Council. No mention of COI.			in-hospital stays (1.01 nurses/aids per bed in orthopedic ward, 1.07 nurses/aids per bed in geriatric control ward) (n = 97) vs Intervention Group: postoperative care ward in the geriatric rehabilitation orthopedic (1.07 nurses/aids per bed) (n = 102).		admission mark. Throughout the 4-12 following months, significant differences were not displayed; IRR was .85 (95% CI: 0.48– 1.50, p=0.577). At the 12 month point following admission, the intervention group sustained 138 between 44 participants and the control group sustained 191 fall between 55 participants.	but no statistically significant effects of the program could be detected after discharge. It seems that fall-prevention must be part of everyday life in fall-prone elderly."	prevention program.
Stenvall, 2012 (score=N/A)	Fall Protection	Subgroup Analyses of Bergren, 2008	Supported by the Vårdal Foundation, the Joint Committee of the Northern Health Region of Sweden, the Swedish Dementia Foundation, the Foundation of the Medical Faculty, University of Umea˚ and the County Council of Va¨sterbotten,	N = 64 patients with femoral neck fracture below or equal to the age of 70.	Mean age: 82.1 years; 17 males, 47 females.	Control Group: received specialized orthopedic care with conventional postoperative routines (1.01 nurses/aides per bed) (n = 36) vs Intervention Group: received specialized geriatric orthopedic care with early	Follow-up at 4 and 12 months.	4/6 participants in the intervention group were able to sustain a walking pace independently compared to 1/17 participants in the control group at 4 months (p=0.005). At 12 months, (p=0.140).	"This study demonstrates that patients with dementia who suffer a hip fracture can benefit from multidisciplinary geriatric assessment and rehabilitation and should not be excluded from rehabilitation programs."	Data suggest a multidisciplinary program improved the post hip fracture outcome in patients with dementia.

			the Swedish Research Council, Grant 2005/D1255-V and the National Society for Research on Aging in Sweden. No COI.			mobilization and daily training provided by physiotherapists (PT) and occupational therapists (OT) (1.07 nurses/aides per bed) (n = 28).				
Hill, 2015 (score=5.0)	Fall Protection	RCT	Supported by the WA Health Falls Prevention Community of Practice. COI, Anne-Marrie Hill, Steven M McPhail, and Terry P Haines receive salary support through career fellowships from the National Health and Medical Research Council (of Australia). Terry P Haines is also the Director of Hospital Falls Prevention Solutions and has a direct financial interest in the outcomes of this study.	N = 3606 hip fracture patients from eight publicly funded rehabilitation units in general hospitals in Australia.	Mean age: 81.75 years; 1396 males, 2210 females.	Control Period: did not receive individual education (n = 1623 admissions) vs Intervention Period: received individual patient education about fall prevention based on cognitive status (n = 1983 admissions)	No mention of follow-up time.	576 falls were sustained through 384 participants throughout the 50-week duration of the study, 197 of which caused injury. The control period demonstrated more falls when compared to the intervention period; overall rate of falls was 10.9 falls/1000 patient days. The impaired cognition of 1676 participants created a large effect for the final fall outcomes; incident rate ratio 0.64, 95% CI [0.48–0.86], (p=0.003).	"Individualised patient and staff education provided as part of ward clinical care reduces falls and injurious falls in wards where elderly patients are undergoing rehabilitation. Hospitals should incorporate this type of education into falls prevention programmes that are delivered in rehabilitation units."	Data suggest fall rates and serious falls can be reduced with fall prevention programs significantly.

Koike, 2008 (score=5.0)	Fall Protection	RCT	Supported by grants from the Health and Labour Sciences Research Grants for Comprehensive Research on Aging and Health (TK and KT), Japan and the Research Society for Metabolic Bone Diseases (TK), Japan. No COI.	N = 672 total patients from 76 individual nursing homes in Osaka, Japan.	Mean age: 85.25 years; 0 males, 627 females.	Control Group: patients received a leaflet and standard care in given nursing home (n = 327) vs Intervention Group: issued with three pairs of hip protectors and were encouraged to wear them day/night, as well as standard care in given nursing home (n = 345).	Follow-up at 352 person-years for interventio n group and 495 person-years for control group.	The intervention group of the study had 19 hip fractures occur due to falls between 19 participants, 7 of which occurred while wearing the wearing the hip protector, 7 of which occurred without the hip protector, 2 without falls, and 3 before the intervention period began. HR of hip fracture in the intervention group was 0.635 (95% CI, 0.37– 1.10; p=0.11) and 0.56 (95% CI, 0.31–1.03; p=0.06) after adjustments were made to it. Comparatively, the control group had 39 hip fractures occur due to falls between 39 participants; all of the fractures were results of these falls. Overall, the hip protector was seen to be effective for preventing hip fractures (n=202; HR, 0.375; 95% CI, 0.14–0.98 (p=0.05).	"Risk of hip fracture can be reduced by hip protectors among elderly women with fall history and low BMI."	Data suggest use of a hip protectors reduces hip fracture risk in elderly nursing homes woman but total falls were similar between groups.

Elley, 2008 (score=4.5)	Fall Protection	RCT	Sponsored by the New Zealand ACC, the New Zealand Lotteries Commission, the Wellington Medical Research Foundation, the University of Otago, and the Hutt Valley District Health Board. No COI.	N = 312 community-living participants over the age of 75 years who had fallen in the past year.	Mean age: 80.75 years; 97 males, 215 females.	Control Group: participants received usual care and were offered two social visits from an accredited provider (n = 157) vs Intervention Group: participants were seen at home and used a standardized health assessment and an evidence-based algorithm to assess risk of falls and refer participants to their family physician (n = 155).	Follow-up at 12 months.	Incidence of falls for the intervention group was 1.91 (1.70-2.16) and 2.91 (1.79-2.25) in the control group. Incidence ratio of the intervention group compared to the control group was .96 (95% CI = .70-1.34).	"This nurse-led intervention was not effective in reducing falls in older people who had fallen previously. Implementation and adherence to the fall-prevention measures was dependent on referral to other health professionals working in their usual clinical practice. This may have limited the effectiveness of the interventions."	Usual care bias. Data suggest each of efficacy.
Louie, 2012 (score=4.5)	Fall Protection	RCT	No mention of sponsorship or COI.	N = 134 patients with hip fracture and hip osteoarthritis /avascular necrosis.	Mean age: 78.26 years; 25 males, 109 females.	Patient and Carer Empowerment Progamme (PCEP): attend five one-hour-sessions of PECP for hip fractures (n = 63) vs Conventional hip fracture protocol: provided with	No mention of follow-up.	Both groups demonstrated improvement on hip fracture related knowledge (P<.01), ADL (P<.05), instrumental ADL independence (P<.01); fall efficacy on ADL (P<.05). PCEP participants demonstrated their application of the	"(P)articipants who underwent the PCEP were more ready to build up habit on adapted ADL skills use. Further studies to investigate carers' stress and hands-on caregiving skills after the programme were recommended."	Usual case bias. Data suggest both groups improved but those in PCEP group were more likely to translate skills learned through daily habits.

						remedial activities and individual ADL training according to the conventional hip fracture rehabilitation protocol (n = 71).		adapted ADL skills more frequently.		
Ooijen, 2016 (score=4.0)	Fall Protection	RCT	Sponsored by Vrije Universiteit Amsterdam and ForceLink. Melvyn Roerdink and Peter J. Beek are inventors of rehabilitation treadmills that include visual context for foot placement, manufactured by ForceLink, neither authors received funding or salary from ForceLink.	N = 70 adults with a recent fall-related hip fracture.	Mean age: 83.3 years; males, females.	Adaptability treadmill training (AT): 30 training session of 40-min each, alternately practiced and rested throughout the training session, (2 participants: 1 physical therapist) (n = 24) vs Conventional treadmill training (CT): 30 training session of 40-min each, alternately practiced and rested throughout the training session, (2 participants: 1 physical therapist) (n = 23) vs	Follow-up at 4 weeks and 12 months.	All the measures of general walking ability improved (all p<.032) with most improvement during the intervention period. Significant differences among groups was seen only at the speed of walking at the four week mark (T1) (p=0.046). Walking speed while dual-tasking was seen higher in AT than in CT and UPT groups at T1 (p=0.017), r=0.394; (p=0.070), r=0.291. 46 participants then monitored their falls for 6 months after T1. Incidence rate ratios and relative were 0.63 (95% CI: 0.22–1.77, p=0.377) and	"Overall, adaptability treadmill training, conventional treadmill training and usual physical therapy resulted in similar effects on walking ability, fear of falling and fall incidence in older adults rehabilitating from a fall related hip fracture. Additional post hoc subgroup analyses, with stratification for pre-fracture tolerated walking distance and executive function, revealed several intervention effects in favor of adaptability and conventional	All 3 groups involved some type of exercise training. Data suggest significant improvement in walking ability, fear of fallings and general health over time in all 3 groups. Differences between the 3 groups were found on walking speed from the conventional treadmill training and adaptability treadmill training.

						Usual physical therapy (UPT): 30 sessions of conventional physical therapy, including exercises of leg strength, balance, transfers, walking, and daily living activities (n = 23)		0.51 (95% CI: 0.20–1.29, p=0.159) for AT training and 0.59 (95% CI: 0.22–1.64, p=0.314) and 0.56 (95% CI: 0.24–1.29, p=0.285) for CT training.	treadmill training, indicating superiority over usual physical therapy for certain subgroups. Future well-powered studies are necessary to univocally identify the characteristics of individuals who will benefit most from a particular intervention."	
Yamashita 2012 (score=3.5)										Data suggest chair rising exercise is better than the standing exercise for increasing dynamics body balance at 1-month post intervention.
Pekkarinen, 2013 (score=3.5)										Data suggest a falls prevention program may reduce fracture risk in elderly Finnish women.

Ward, 2010 (score=3.5)										Usual care bias. Data suggest implementation of falls prevention programs are particular challenging in patients with dementia. This study used hip protectors and vitamin supplements but showed lack of efficacy.
Tseng, 2016 (score=3.0)										Usual care bias. Data suggest both the interdisciplinary and comprehensive care models benefit hip fracture patients by improving the trajectory of good physical function post hospitalization.
Shyu, 2011 (score=2.5)										Usual care bias. Sparse methods. Data suggest comprehensive care and subacute care programs can improve QoL after hip

										fracture surgery compared to usual care.

Evidence for the Use of Bed Rest

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: bed rest; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 11 articles in PubMed, 68 in Scopus, 5 in CINAHL, 3 in Cochrane Library, 5850 in Google Scholar, and 0 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 1 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:
Endo 2013 (Score=4.5)	Bed Rest	RCT	No sponsorship. No COI.	N = 81 patients admitted to the hospital with acute fractures whom were 35 years of older.	Mean age: 75.34±12.17; 17 males, 64 females.	Group 1, patients received skin traction utilizing a foam 3kg rubber boot. (n=41) vs Group 2, received no traction and had their leg rested on a pillow comfortably (n=40)	Baseline, 1 hr after traction, and four times a day until surgery admission (approximately 7.5 days), after surgery.	Mean±SD for Group 1 vs group 2, pain scores at baseline, day 1, and day 7: 4.2±0.6, 2.8±0.4, 1.5±0.3 vs 4.8±0.6, 2.5±0.3, 2.3±0.4 (p=0.48). Mean±SD for Group 1 vs group 2, number of analgesics per day: 0.3-0.8 vs 0.6-1.0 (p=0.33).

Evidence for the Use of Bisphosphonates

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Diphosphonates, bisphosphonate ; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 77 articles in PubMed, 100 in Scopus, 345 in CINAHL, 36 in Cochrane Library, 97,000 in Google Scholar, and 3 from other sources. We considered for inclusion 10 from PubMed, 3 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 2 from other sources. Of the 21 articles considered for inclusion, 10 randomized trials and 4 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Black 2011 (score=6.0)	Bisphosphonates	RCT	Sponsored by Novartis Pharma AG, Basel, Switzerland. No mention of COI.	N = 1233 women who had received three ZOL or placebo infusions in the HORIZON-PFT study.	Mean age: 75.5 years; 0 males, 1233 females.	Patients who received 3 years of placebo annually after the initial 3 years of Zoledronic acid 5 mg annually (Z3P3, n= 617) vs patients who received 6 years of Zoledronic acid 5 mg annually total (Z6, n= 616)	Follow up at baseline and year 1, 2, 3, 4, 5, and 6 years.	Femoral neck BMD percentage change from year 3 to 6 remained constant in Z6 and dropped in Z3P3 (Between-treatment difference = 1.04%; 95% confidence interval 0.4 to 1.7; p=0.0009). New morphometric vertebral fractures were n=14 vs Z6 and n=30 for Z3P3 (odds ratios = 0.51; p=0.035).	"In summary, our study showed that continuing annual ZOL over 6 years maintained BMD and reduced vertebral fracture risk. Although discontinuation after 3 years showed an increase in morphometric vertebral fractures, there was also evidence of substantial residual benefits. These residual benefits after discontinuation suggest that after 3 years, many patients may discontinue infusions for up to 3 years, decreasing costs and possible adverse effects while maintaining efficacy. However, women at high risk of fracture,	Data suggest continuation of annual ZOL over 6 years reduced fracture risk by maintaining BMD.

									particularly vertebral fracture, may benefit from continuing annual infusions."	
Ito 2018 (score=5.5)	Bisphosphonates	RCT	Sponsored by Asahi-Kasei Phrama, Astellas Pharma, Chugai Pharmaceutical, Daiichi-Sankyo, MSD, and Ono Pharmaceutical. COI, one or more of the authors have received or will receive benefits for personal or professional use.	N = 102 female Japanese patients from the Zone study diagnosed with primary osteoporosis based on the Diagnostic Criteria for Primary Osteoporosis by the Japanese Society for Bone and Mineral Research	Mean age: 73.4 years; 0 males, 102 females.	Once yearly intravenous infusion of Zoledronic acid 5 mg group (n= 49) vs placebo group (n= 53) for two years.	Follow up at baseline, 12 and 24 months.	Cortical thickness of the femoral neck at baseline vs percent change at 24 months was 1.64 vs 4.09 for the Zoledronic acid group ($p<0.01$) while it was 1.58 vs 0.52 for the placebo group ($p>0.05$). Similar results of improvement in the zoledronic acid group were seen in the cortical CSA and total CSA at the interochanteric region and shaft, total vBMD at all sites, cortical vBMD at the neck and shaft, SM and CSMI at the shaft and BR at the intertrochanteric region and neck.	"The results demonstrated that once-yearly intravenous infusion of zoledronic acid improved volumetric bone mineral density (vBMD), cortical bone geometry parameters, and CT-derived biomechanical parameters at the femoral neck, intertrochanteric region, and shaft; particularly at the intertrochanteric region, significant improvements in cortical bone geometry parameters and CT-derived biomechanical parameters, compared with those in the placebo group, were detectable early, at 12 months. The present data	Data suggest yearly infusions of zoledronic acid may reduce hip fracture risk in Japanese women.

									suggest that zoledronic acid has a possibility to reduce the risk of hip fractures in Japanese patients with osteoporosis."	
Flodin 2014 (score=5.5)	Bisphosphonates	RCT	Sponsored by Sanofi AB and Fresenius Kabi. No COI.	N = 79 patients with recent hip fractures who were ambulatory before fracture.	Mean age: 79 years; 23 males, 56 females.	Weekly risedronate 35 mg for 12 months group (B, n= 28) vs weekly risedronate 35 mg with nutritional supplement 40g protein and 600 kcal for the first 6 months group (BN, n= 26) or control group (C, n = 25)	Follow up at baseline, 6 and 12 months.	Complete cases showed a 1.1% increase in total hip BMD of 0.7% in the BN group, a 1.1% decrease in group B and a 2.4% decrease in group C (p=0.071 between groups). BMD between baseline and 12 months was +0.06% for BN vs -0.3% for group B vs -1.8% for group C (p=0.009)	"Protein-and energy-rich supplementation in addition to calcium, vitamin D, and bisphosphonate therapy had additive effects on total body BMD and total hip BMD among elderly hip fracture patients."	Data suggest oral administration of bisphosphonates in addition to nutritional supplements increases BMD.
Unnanuntana 2017 (score=5.5)	Bisphosphonates	RCT	Sponsored by the Medical Association of Thailand Research Fund. No COI.	N = 140 postmenopausal women or men older than 50 from the metabolic bone disease clinic of Siriraj Hospital who met the indication	Mean age: 73.7 years; 16 males, 154 females.	Generic alendronate 70 mg/week for 12 months group (Bonmax, n= 70) vs brand alendronate 70 mg/week for 12 months group (Fosamax, n= 70)	Follow up at baseline, 3, 6, and 12 months.	Lumbar spine BMD at 1 year post treatment was 5.4% for the generic vs 5.5% for brand with no significant difference between the two (p=0.900). Similar for total hip BMD at 1 year, 2.5% for both generic and brand (p=0.952). Femoral neck BMD at 1 year increased 1.9% for generic vs 4.4% for brand,	"Generic and brand alendronate produced similar gains in BMD and reduction in bone turnover markers. Both medicadoitions were also equally well-tolerated. Based on these findings, generic alendronate (Bonmax®) is a viable alternative to	Non-inferiority study. Comparable efficacy. Data suggest benefit from both brand name and generic alendronate/

				s for osteoporosis treatment.				though not significant (p=0.163)	the original brand of alendronate"	
Magaziner 2014 (score=5.0)	Bisphosphonates	RCT	Sponsored by Novartis Pharma AG. COI, one or more of the authors have received or will receive benefits for personal or professional use.	N = 1486 patients older than 50 years old with minimal-trauma hip fracture operations within the last 90 days.	Mean age: 73.2 years; 347 males, 1139 females.	Zoledronic acid 5 mg every 12 months for up to 3 years group (n= 745) vs placebo group (n= 741)	Follow up at baseline, 12 and 24 months.	Treatment difference ZOL vs placebo in total hip BMD was 3.6% at 12 months and 5.4% at 24 months. Treatment difference ZOL vs placebo in femoral neck BMD was 2.5% at 12 months and 4.3% at 24 months	"In conclusion, a yearly ZOL 5-mg infusion demonstrated similar effects in terms of greater improvements in TH and FN BMD versus placebo over 2 years in the patient subgroups who sustained hip fracture. Our findings in this comparatively older and less healthy subpopulation who have already sustained a hip fracture offer further evidence of the beneficial effects of ZOL in improving BMD regardless of patient demographics and baseline characteristics."	Data suggest improved BMD in lowest tertile body mass group to the greatest extent at 12 months.
Adachi 2010 (score=4.5)	Bisphosphonates	RCT	Sponsored by Novartis Pharma AG. COI, one or more of	N = 2127 patients 50 years or older within 90 days of	Mean age: 74.5 years; 508 males,	Zoledronic acid (ZOL) 5 mg annually for 3 years group (n = 1065) vs	Follow up at baseline, 6, 12, 24, and 36 months and at end of study.	Change in EQ-5D VAS measurements at baseline vs 24 months were 9.26 in the ZOL group vs	"In conclusion, infusions of ZOL 5 mg in patients with a recent hip fracture leads to improved HRQoL, as	Data suggest ZOL significantly improves QoL compared to placebo in patients with

			the authors have received or will receive benefits for personal or professional use.	surgical repair of a hip fracture sustained with minimal trauma and ambulatory before the hip fracture.	1619 females.	placebo group (n= 1062)		6.17 in the placebo group (p=0.0024).	measured by the EQ-5D VAS, when compared with placebo. This was true for all patients and in the subset of patients with clinical fractures, non-vertebral fractures, and clinical vertebral fractures. Summary utility scores, however, did not show differences between treatment and placebo and, while not statistically significant, the mobility, self-care, and usual activities domains showed extreme difficulty in the placebo group compared with ZOL group."	low trauma hip fracture.
Bauer 2014 (score=4.5)	Bisphosphonates	RCT	Sponsored by Merck & Co. COI, one or more of the authors have received or will receive benefits for personal or professional use.	N = 1099 postmenopausal women with low femoral neck BMD.	Mean age: 74 years; 0 males, 1099 females.	Oral alendronate sodium 5 mg/day for 2 years then 10 mg/day after group (n= 662) vs placebo group (n= 437)	Follow up baseline, after 1 to 3 years, and 5 years.	After 5 years, 94 of 437 (22%) of the placebo group had 1 or more fracture. Placebo group who had fractures after the first year had mean age of 76.2 vs 73.1 for those who didn't (p<0.001). After adjusting for age, risk of fracture in the lowest tertile	"Among postmenopausal women who discontinue alendronate therapy after 4 to 5 years, age and hip BMD at discontinuation predict clinical fractures during the subsequent 5 years. Follow-up	Data suggest it is patient age and BMD which are predictive of fracture risk not termination of alendronate therapy.

								of baseline total hip BMD was 87% higher vs with that in the other two tertitles (RHR 1.87[1.20,2.92]).	measurements of DXA 1 year after discontinuation and of BAP or NTX 1 to 2 years after discontinuation are not associated with fracture risk and cannot be recommended."	
Unnanuntana 2017 (score=4.5)	Bisphosphonates	RCT	Sponsored by Siriraj Research Fund. No COI.	N = 100 patients who underwent hemiarthroplasty for femoral neck fracture at Siriraj Hospital.	Mean age: 76.6 years; 20 males, 80 females.	Risedronate 35 mg/week starting 2 weeks after hemiarthroplasty group (n= 49) vs Risedronate 35 mg/week starting 12 weeks after hemiarthroplasty group (n= 51)	Follow up at baseline, 2 weeks, 3 months and 1 year.	Changes in scores for DEMMI, Barthel Index, EQ-VAS and visual analog scale from baseline to 3 months and 3 months to 1 year after surgery were not significantly different between the groups (p>0.05).	"In conclusion, no significant differences in short-term functional recovery or significant adverse events were observed between the week 2 and week 12 bisphosphonate initiation groups. As such, initiation of bisphosphonate therapy may be considered as early as 2 weeks after femoral neck fracture. It is important to emphasize that low serum calcium and vitamin D status must be corrected with	Data suggest no significant differences between groups in terms of timing of bisphosphonate initiation after femoral neck fracture.

									calcium and vitamin D supplementation prior to or at the time of bisphosphonate initiation. Further studies in a larger population are needed to confirm the results of our study."	
Beaupre 2011 (score=3.5)										Some baseline differences such as pre-fracture health. Usual care bias. Data suggest oral bisphosphonates may reduce post hip fracture mortality.
Flodin 2015 (score=3.5)										Lack of efficacy. Data suggest bisphosphonates with protein supplements were no better than vit D and calcium.

Evidence for the Use of Calcitonin

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: calcitonin; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 97 articles in PubMed, 233 in Scopus, 30 in CINAHL, 8 in Cochrane Library, 6360 in Google Scholar, and 1 from other sources. We

considered for inclusion 3 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 4 articles considered for inclusion, 4 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Huusko 2002 (score=8.5)	Calcitonin	RCT	Sponsored by Central Finland Healthcare District, Kuopio University Hospital, University of Kuopio, Emil Aaltonen Foundation, Uulo Arhio Foundation, and Novartis Finland Ltd. No mention of COI.	N = 260 Acute hip fracture	Mean age: 80.1 years; 64 males, 165 females	Intranasal salmon calcitonin 200 IU daily vs. placebo nasal spray for 3 months.	3 months	At 3-month follow up, median intensity of pain on VAS scale 0mm in calcitonin group vs. 4mm in placebo (p = 0.15). Median change in IADL score from baseline to 3 months: -1 calcitonin vs. -2 placebo (p = 0.74). "The mean change in calcaneal bone mineral density from baseline to 3 months was not statistically significant between the groups -0.004 (95% CI -0.008 to -0.001) in the calcitonin group and -0.007 (95% CI -0.012 to -0.003) in the placebo group (P = 0.28)."	"[I]ntranasal calcitonin might be useful for hip fracture patients but the clinical significance of this finding needs to be confirmed by studies with more participants, a longer treatment period, a longer follow-up, and perhaps a higher dose of calcitonin."	Data trend towards suggesting weak efficacy.

Henriksen 2016 (Score=6.5)	Calcitonin	RCT	Sponsored by the Danish Research Foundation. No mention of COI.	N=4665 postmenopausal patients with osteoporosis.	Mean age: 66.8 years; 0 males, 4665 females.	SMC (salmon calcitonin) group: patients received daily 0.8 mg salmon calcitonin treatment for 36 months (n=2334) vs. Placebo group: patients received placebo for 36 months (n=2331).	No mention of follow-up.	For lumbar spine bone mineral density (BMD), the SMC021 group indicated higher increase (1.02%) than the placebo group (0.18%) ($p<0.0001$). The frequency of adverse events (AEs) was higher in SMC021 group (17.25%) than placebo group (10.81%) ($p<0.05$).	"In summary, this large phase III fracture efficacy trial of oral salmon calcitonin (SMC021) failed to meet the primarily endpoints, and no clinical benefit of the treatment could therefore be demonstrated."	Data did not demonstrate efficacy as both treatment and placebo groups had comparable results.
Binkley 2014 (Score=4.5)	Calcitonin	RCT	Sponsored by Tarsa therapeutics, Inc. Two of the authors have received or will receive benefits for personal or professional use.	N=129 postmenopausal patients with bone mineral density score: -2.5 <T-score <-1.0 at femoral neck, lumbar spine, trochanter, or hip.	Mean age: 67.2±6.4 years; 0 male, 129 females.	Calcitonin group: patients took once daily 600 mg calcium citrate with breakfast (n=86) vs. Placebo group: patients took once daily vitamin D in 1000 international unit (IU) with breakfast (n=43).	No mention of specific follow-up time length.	In calcitonin group, The total bone mineral density (BMD) loss in proximal femur reduced at 28th and 54th weeks ($p=0.05$), and that in placebo group was reduced at 54th week ($p=0.048$). The bone biomarker CTx-1 in calcitonin group was reduced at 28th ($p<0.001$) and 54th weeks ($p=0.041$), and that in placebo group indicated no significant	"In summary, based on modest effects on bone resorption and BMD, oral calcitonin may provide a useful alternative for postmenopausal women for whom other therapeutic classes are contraindicated or poorly tolerated."	Data suggest oral calcitonin may be beneficial to women with low bone mass.

								reduction (p=0.058).		
Tsakalakos 1993 (Score=4.0)	Calcitonin	RCT	No mention of sponsorship or COI.	N=40 patients with recent hip fracture.	Mean age: 77.4 years; 16 males, 24 females.	Group A: patients received 1200 mg daily calcium with diet (n=20) vs. Group B: patients received 100 international unit (IU) daily salmon calcitonin and 1200 mg daily calcium for 2 weeks (n=20).	No mention of follow-up.	Urinary calcium increased significantly in group A (P<0.01), while group B with calcitonin treatment indicated significant decrease in urinary calcium (p<0.01). For urinary hydroxyproline, group A indicated significant increase (p<0.01) and group B indicated significant decrease (p<0.05).	"[I]mmobilization resulting from a hip fracture, and possibly surgery itself, causes significant changes in biochemical markers of bone resorption. Calcitonin successfully reverses these changes and may also be effective in preventing subsequent bone loss, particularly in patients who cannot be remobilized immediately."	Data suggest short term calcitonin administration reverses some metabolic markers in elderly hip fracture patients which could potentially prevent subsequent bone loss.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar from January 1st, 2008 to January 1st, 2018 using the following terms: Transcutaneous Electircal Nerve Stimulation, TENS; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 4 articles in PubMed, 200 in Scopus, 459 in CINAHL (Went through first 100), 2 in Cochrane Library, 3680 in Google Scholar (Went through first 100), and 1 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 1 from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Lang 2007 (score=8.0)	Transcutaneous Electrical Nerve Stimulation (TENS)	RCT	No mention of sponsorship or COI.	N = 72 Hip fractures	Mean age: 80.4 years; 5 males, 58 females.	Group 1 – patients received TENS for at site of emergency and was left in place until arrival at hospital (n=30) vs. Group 2 – patients received sham TENS during emergency transport (n=33).	No follow up.	VAS pain (baseline/after transport): TENS (89±9/59±6) vs. placebo (86±12/79±11), p <0.01. Heart rate 67±11 vs. 99±8 (p <0.01). Blood pressure trended towards higher in placebo (e.g., diastolic 86±18 vs. 97±12, NS).	"TENS is a valuable and fast-acting pain treatment under the difficult circumstances of "out-of-hospital rescue." Because of its lack of side effects, it could also be a valuable tool in the hospital."	Post hoc excluded 9 from data analyses due to non-fractures. Baseline TENS group's pain trended towards shorter duration. Data suggest TENS reduces pain in emergency transport setting.
Manglone, 2010 (score = 5.5)	Transcutaneous Electrical Nerve Stimulation (TENS)	RCT	Sponsored by NIH/NICHD/NIA 1 R03 HD041944-01A1, 2002, (Mangione, Principal Investigator). No COI.	N = 26 patients with partial or total hip replacement or open reduction internal fixation of a hip fracture.	Mean age: 81 years; 5 males, 21 females.	CON Group – received TENS and mental imagery twice weekly for 10 weeks (N = 12) vs Exercise Group – received high intensity leg strengthening exercises twice weekly for 10 weeks (N = 14).	1 year post fracture.	The usual gait speed in the CON group and the exercise group were the following: baseline (0.66 ± 0.17, 0.70 ± 0.19), post intervention (0.70 ± 0.22, 0.81 ± 0.17, and p=.150), and 1 yr post fracture (0.67 ± 0.21, 0.81 ± 0.17, and p=.020, effect size=0.56), respectively. The effect sizes were the following: summed LE torque = 0.79. usual gait speed = 0.56, fast gait speed 0.41, six minute walk distance =0.49, physical performance test =	"A 10-week home-based progressive resistance exercise program was sufficient to achieve moderate to large effects on physical performance and quality of life and may offer an alternative intervention mode for hip fracture patients who are unable to leave home at 6 months after the fracture. The effects were maintained at 3 months after	Data suggest 10 week twice weekly home based exercise program showed sustained results for increased strength, walking, performance and general improved function one year post hip fracture.

								0.81, and SF-36 physical function = 0.30.	completion of the training program."	

Evidence for the Use of Acupressure for Transporting Patients

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar from January 1st, 2008 to January 1st, 2018 using the following terms: Acupressure; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 articles in PubMed, 87 in Scopus, 3 in CINAHL, 2 in Cochrane Library, 2700 in Google Scholar (Went through first 100), and 1 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Barker 2006 (score=8.5)	Acupressure for Transporting Patients	RCT	No mention of sponsorship or COI.	N = 38 Acute hip fractures	Mean age: 86.2±4.2 years;	Intervention Group: received bilateral auricular acupressure at 3 auricular acupressure points for hip pain (n=18) vs. Sham Group: received sham acupressure at sham points (n=20)	No mention of follow-up.	Heart rate (baseline/post): acupressure 95.4±8.3/72.5±9.4 vs. sham 92.3±11.7/90±8. (p = 0.0001 for true intervention). VAS pain ratings. VAS pain ratings reduced in true acupuncture group.	"The authors encourage physicians, health care providers, and emergency rescuers to learn this easy, noninvasive, and inexpensive technique for its effects in decreasing anxiety and pain during emergency transportation."	Study suggests acupressure may reduce pain in hip fracture patients during transport to hospital.

Evidence for the Use of Fascia Iliaca Compartment Block (FICB)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Fascia Iliaca Compartment Block, FICB; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 16 articles in PubMed, 31 in Scopus, 11 in CINAHL, 1 in Cochrane Library, 856 in Google Scholar, and 0 from other sources. We considered for inclusion 7 from PubMed, 4 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 13 articles considered for inclusion, 10 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Beaudoin 2013 (score= 7.0)	Fascia Iliaca Compartment Block (FICB)	RCT	Sponsored by the Emergency Medicine Foundation and the Emergency Medicine Residents' Association. No COI.	N = 36 patients with hip fractures	Mean age: 82 years; 12 males, 24 females	Group 1: Pain treated with Femoral Nerve Block (FNB) (n = 18) vs Group 2: Pain treated with Parenteral Opioid Analgesia (Standard Care group; SC) (n = 18)	4 hours	Mean NRS Pain Scores after 4 hours was 4.0 for FNB group (baseline score 8.3) and 8.0 for SC group (baseline score 8.0) (p<0.001). Mean rescue morphine needed was 0mg (range 0-6mg) for FNB group and 5mg (range 0-21mg) for SC group (p=0.028).	"Ultrasound-guided femoral nerve block as an adjunct to [standard care] resulted in 1) significantly reduced pain intensity over 4 hours, 2) decreased amount of rescue analgesia, and 3) no appreciable difference in adverse events when compared with [standard care] alone."	Data suggest US-guided 3-in-1 femoral nerve block was superior to SC in reducing pain intensity, decreased rescue analgesia, and the SC group reported ineffective pain control.
Kumar 2014 (score = 6.5)	Fascia Iliaca Compartment Block (FICB)	RCT	No mention of sponsorship or COI.	N = 60 patients posted for Open Reduction and Internal Fixation	Mean age: not given; 47 males, 13 females	Group B: Received 38ml of 0.25% bupivacaine with 2ml saline (n=30) vs Group BD: Received 38ml of 0.25% bupivacaine with 2ml dexamethasone (8mg) (n=30)	none	Mean duration of analgesia for group with bupivacaine only was 7.85 hours and for group with bupivacaine and dexamethasone was 16.33 (p<0.001). Mean total doses of rescue analgesia for group with bupivacaine only was 2.1 and for group with bupivacaine and dexametha was 0.9 (p<0.001)	"[A]dding Dexamethasone (8mg) to Bupivacaine for FICB significantly prolonged the duration of block and decreased the requirement of rescue analgesics as compared to patients who received Bupivacaine alone."	Data suggest that the addition of dexamethasone to bupivacaine in FICB blocks results in prolonged anesthesia and also decreases rescue analgesic requirements
Diakomi 2014 (score = 5.5)	Fascia Iliaca Compartment Block (FICB)	RCT	No COI. No mention of sponsorship.	N = 41 patients scheduled for hip fracture surgery	Mean age: 78 years; 8 males, 33 females	Group 1: Received IV Fentanyl (IVFE) (n=20) vs Group 2 Received an fascia iliaca compartment block (FICB) using 40mL ropivacaine	24 hours	Mean pain, recorded with NRS Scores, after positioning were 5.5 for IVFE group and 1.6 for FICB group (p<0.001). Patient satisfaction reported was 25% for IVFE group and 100% for FICB group (p<0.001). Mean postoperative morphine consumption was 94.7% in	"Performing an FICB before positioning for SA provides superior pain management compared with IVFE administration, facilitates spinal performance, and yields satisfactory postoperative analgesia and wide patient acceptance, hence	Data suggest FICB group showed superior pain management compared to IVFE as a significant decrease in morphine consumption was noted 24 hours post-op.

						(n=21)		IVFE group and 42.9% in FICB group (p<0.001).	improving overall quality and efficiency of care."	
McRae 2015 (score= 5.0)	Fascia Iliaca Compartment Block (FICB)	RCT	Sponsored by NSW Ambulance. No mention of COI.	N = 24 patients with suspected hip or femur fractures	Mean age: 82 years; 8 males, 16 females	Group 1: Received loading dose of intravenous morphine and then FICB using lidocaine with epinephrine (n = 11) vs Group 2: Standard Care group, received intravenous morphine only (n = 13)	15 minutes	Patients in FICB group had a 50% reduction in pain score and patients in the standard care group had a 22% reduction (p=0.025).	"The study suggests that FICB can be performed by trained paramedics for patients with suspected femoral fractures."	Data suggest patients reported lower pain scores in FICB group compared to the opioids (SC) group.
Newman 2013 (score= 4.5)	Fascia Iliaca Compartment Block (FICB)	RCT	No sponsorship or COI.	N = 107 patients presenting with isolated femoral neck fracture	Mean age: 82 years; 28 males, 79 females	Group 1: Received femoral nerve block (FNB) (n = 51) vs Group 2: Received fascia iliaca compartment block (FICB) (n = 56)	2 & 12 hours	Reduction in mean VAS pain score was 2.8 in FICB group and 3.7 in FNB group (p=0.047). Percentage of patients who needed no additional morphine in 12 hours after block was 46% in FICB group and 31% in FNB group (p=0.041).	"Femoral nerve block provided superior pre-operative analgesia for fractured neck of femur compared with fascia iliaca compartment block."	Data suggest femoral nerve block was better than fascia iliaca compartment block for decreasing pain pre-surgically and these patients required less morphine after the block.
Reavley 2014 (score= 4.5)	Fascia Iliaca Compartment Block (FICB)	RCT	Sponsored by grand from UK College of Emergency Medicine. No COI.	N = 178 patients with a femoral neck fracture	Mean age: 79 years; 47 males, 131 females	Group 1: Received a fascia iliaca compartment block (FICB) (n = 88) vs Group 2: Received 3-in-1 block for pain (n = 90)	60 minutes	Mean pain score, measured by VAS scale, was 38 in FICB group and 35 in 3-in-1 group (p=0.44).	"The fascia iliaca compartment block is equivalent to the 3-in-1 block for immediate pain relief in adult neck of femur fractures	Short follow-up. Data suggest equivalent efficacy
Nie 2015 (score= 4.5)	Fascia Iliaca Compartment	RCT	Sponsored by Funds of Guiyang Science	N = 104 patients with hip fracture	Mean age: 70 years; no mention of	Group 1: Received Fascia iliaca compartment block (FIB) (n=51) vs	2, 4, 6, 12, 24, and 48 hours	At 48 hours post-op, mean reported pain, measured with NRS, was 1.6 for PCIA group and 0.6 in FIB group (p=0.039). Mean total	"Continuous FIB is a safe and effective technique for postoperative analgesia after hip fracture surgery, making it	Data suggest decreased pain and less pain medication requirements occurred in the FIB group.

	Block (FICB)		and Technology Department. No COI.	s scheduled for open reduction and internal fixation surgery	gender specifications	Group 2: Patient-controlled intravenous analgesia (PCIA) (n=53)		morphine received was 65.8mg in FCIA group and 7.4mg in FIB group (p<0.0001).	an option for pain management in elderly patients with hip fractures."	
Yun 2009 (score= 4.0)	Fascia Iliaca Compartment Block (FICB)	RCT	No mention of sponsorship or COI.	N = 38 patients with an isolated femoral neck fracture	Mean age: 75 years; 12 males, 16 females	Group 1: Received intravenous analgesia with alfentanil for pain (IVA) (n=20) vs Group 2: Received fascia iliaca compartment block for pain (FIC) (n=18)	2, 4, 6, 12, and 24 hours	Mean VAS scores during positioning were 2.0 in FIC group and 3.5 in IVA group (p=0.001). Mean time to achieve spinal anesthesia was 6.9 minutes in FIC group and 10.8 minutes in IVA group (p=0.009).	"An FIC block is more efficacious than i.v. alfentanil in terms of facilitating the lateral position for spinal anaesthesia in elderly patients undergoing surgery for femoral neck fractures."	Data suggest use of an FIC block is better than the continuous IV infusion group with alfentanil
Madabushi 2016 (score= 4.0)	Fascia Iliaca Compartment Block (FICB)	RCT	No sponsorship or COI.	N=60 patients undergoing surgery for femur fracture	Mean age: 59.5 years; 32 males, 28 females	Group 1: Received fascia iliaca compartment block (FICB) with 30mL of 0.375% ropicavaine (n = 30) vs Group 2: Received intravenous fentanyl (IVF) at 0.5 µg/kg body weight for max of 3 doses (n = 30)	24 hours	Mean VAS scores post-procedure were 24.72 in FICB group and 61.22 in IVF group (p=0.01). Sitting angle improvement was 56.17° in FICB group and 21.38° in IVF group (p=0.01). Rescue analgesia was received by 13 patients in the FICB group and 25 patients in IVF group (p=0.04).	"Fascia iliaca block offers superior analgesia compared to IVF in patients with femur fracture before positioning for spinal anesthesia"	Data suggest decreased analgesia requirements in the FICB group with less pain reported post procedure.
Temelkovska-Stevanovska 2014 (score= 3.5)										Short follow-up. Data suggest better hip flexion and improved pain relief was best in the FNB group

Evidence for the Use of Surgical Treatment for Hip Fractures

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Surgery, surgical treatment, internal fixation, sliding hip screw, fixed nail plates, dynamic screws, compression hip screws, intramedullary hip screws, gamma nails, proximal femoral nails, pugh nails, percutaneous compression plate, nail plates, medoff sliding plates; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 870 articles in PubMed (Went through first 200), 16405 in Scopus (Went through first 200), 2247 in CINAHL (Went through first 200), 1092 in Cochrane Library (Went through first 200), 17000 in Google Scholar (Went through first 200), and 145 from other sources. We considered for inclusion 71 from PubMed, 9 from Scopus, 19 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 27 from other sources. Of the 130 articles considered for inclusion, 108 randomized trials and 22 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Nails										
Cameron 1992 (score=7.0)	Femoral Shaft Fractures	RCT	No mention of sponsorship or COI.	N = 88 Femoral shaft fractures	Mean age: 30 years; 63 males, 21 females	Grosse-Kempf vs. Russell-Taylor vs. Synthes (intermedullary)	10-31 months	Grosse-Kempf nail insertion faster (88 vs. 97 105 vs 97min). At first follow up, no difference found among techniques in terms of pain, limp, range of motion, or time to union.	"No nail showed significant advantage over the others. All nails have similar indication for use; however, Synthes nail were less satisfactory for proximal fractures. Factors other than performance claims should be considered when deciding which system to use."	No clinical difference in outcomes. Somewhat sparse data.
Kim 2005 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No sponsorship or COI.	N = 58 Unstable inter-trochanteric fractures	Mean age: 81.5 years; 14 males, 44 females	Cementless Calcar-replacement prosthesis vs. proximal femoral nail	6 weeks, 3, 6, and 12 months; and yearly thereafter.	Final mortality rate at 3 years 55% cementless vs. 17% proximal femoral nail (p = 0.006). Ability to walk with a walker 7.8±1.6 days post-operative for cementless vs. 8.8 ± 2.9 days for proximal femoral nail (p = 0.069). No difference in functional scores between treatments at last follow-up. Cementless patients mean hospital cost $11,048±$1216 vs. $5,150± $821 proximal femoral nail.	"No significant differences regarding functional outcomes, hospital stay, and general complications was found between the two groups. However, results showed no functional benefit of the arthroplasty at a minimum of two years postoperatively."	Lower mortality rate with PFN. Lower costs and trend towards earlier activity with PFN.
Starr 2006 (score=6.5)	Surgical Approach including Minimally Invasive	RCT	Sponsored by Suzanne and Aaron A. Hoffman, MD Orthopaedic Research	N = 34 Subtro-chanteric, intertro-chanteric or ipsilateral femoral neck/shaft fracture from high	Mean age: 34 years; 22 males, 12 females	Russell-Taylor Recon Nail (piriformis fossa starting point) vs. Howmedica Long Gamma Nail (trochanteric starting point)	1, 3, 6, 9, 12, 29 months	Estimated blood loss: recon nail group 328 (100-750) vs. long gamma nail 282(100-700), p = 0.15. Duration of surgery: recon nail: 106 vs. long gamma nail 88, p = 0.26. Harris Hip Score: recon nail 86, long gamma nail 84, p = 0.60. Returned to work: recon nail 15, long gamma nail 12, p = 0.46. Same job:	"Both devices yield predictably good results in these difficult fractures. We found no difference between the two devices with regard to incision length, duration of surgery, blood loss, reduction, ease of use, union rate, complication rate, or outcome."	Both groups had high complaints of painful implants after union, with 8/17 in recon and 4/17 in long gamma nail undergoing elective implant removal within 13 months.

			Fund. No COI.	energy injury				recon nail: 12 vs. long gamma nail 12, p = 1.0.		
Schipper 2004 (score=6.0)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by Stykerowmedica and Mathys Medical Nederland. No COI.	N = 424 Unstable trochanteric fractures	Mean age: 82.4 years; 75 males, 349 females	Gamma nail vs. proximal femoral nail	4 weeks, 4 months, 1 year	No significant differences between quality of reduction for both types of implant and types of fracture. Peri-operative data for both groups: Mean (SEM) blood loss (mL): PFN = 220(13); GN = 287(18). General complications were comparable for both groups. No differences in symptoms or limitations at 1 year (None: 77.6 vs. 76.5%, NS).	"[N]o important differences between the results of treatment with either the GN or the PFN. The general complications and mortality rates did not reveal any surprising results and are in range with the results of other studies…A skilled surgeon may treat the demanding unstable trochanteric fractures with any type of fixation device, as long as he or she remembers that the fixation device will never make up for surgical failures."	Study suggests interventions have comparable efficacy regarding major outcomes.
Cai 2016 (score=5.5)	Surgical treatment	RCT	Sponsored by the National Natural Science Foundation of China. No COI.	N=222 patients aged over 65 years with stable intertrochanteric fractures (Evans grades I and II).	Mean age: 75.9 years; 82 males, 140 females.	Extramedullary group: received dynamic hip screw fixation. (n=92) Vs intramedullary group: received gamma nail placement and proximal femoral nail antirotation (PFNA) (n=106)	Follow up at 6 and 12 months with the Functional Recovery Score (FRS) questionnaire and a radiological evaluation.	In both groups, hidden blood loss was more than the observed blood loss (528.37 ± 386.91 mL versus 135.54 ± 36.48 mL and 720.51 ± 408.91 mL for extramedullary group vs. 138.92 ± 37.69 for intramedullary group). FRSs at baseline, 6, and 12 months for both group were similar (40.64 ± 2.47, 33.78 ± 3.04, and 35.96 ± 1.99 vs 40.43 ± 2.72, 34.25 ± 2.91, and 36.10 ± 2.38; p = 0.577, p = 0.26). Time to union was not significantly different between both groups (13.29 ± 1.22 vs. 12.18 ± 1.30	"Extramedullary fixation (such as DHS placement) significantly reduces perioperative blood loss in patients with stable intertrochanteric fractures. Such fixation affords functional outcomes and times to union similar to those associated with intramedullary fixation. In view of the morbidity and complications associated with acute anaemia and transfusion, extramedullary fixation may be a	Data suggest extramedullary fixation reduces perioperative blood loss but both methods result in similar outcomes regarding union of the fractured bone.

								weeks, respectively, p = 0.526).	good choice in such patients."	
Reindl 2015 (score=5.5)	Surgical treatment	RCT	No mention of sponsorship. COI: One or more of the authors received payments or services, either directly or indirectly, from a third party in support of an aspect of this work. In addition, one or more of the authors, or his or her institution, has had a financial relationship, in the thirty-six months prior to submission	N = 204 Patients with an unstable intertrochanteric hip fracture	Mean age: 81.1 years; 88 males, 116 females.	Extramedullary/ Dynamic Hip Screw group: a lateral incision is made proximally over the femur. The fascia lata is split, exposing the vastus lateralis. The fascia of that muscle is opened and retracted anteriorly to make the femur visible. With fluoroscopic guidance, the femoral head screw is placed in a center position inside the femoral head. A side plate (ranges in length from two to six holes) is attached to the hip screw. The dynamic hip screw was used in all patients. (n=92) Vs Intramedullary/ Nails Group: incision is made in the gluteal area in line with the proximal part of the femur. A guidewire is placed into the greater trochanter and down the medullary canal. Trochanter is then drilled. The nail is inserted and if fixed into the femoral head with either a single or double screw(s) or a helical blade. The nail is then locked distally. (n=112)	Follow up at 12 months	Baseline preinjury LEM scores in DHS and nail groups was 74.5 and 71.0 points. Scores did not return to their preinjury level in either group over the 12 month period (p<.05) Radiographic parameters were better in the intramedullary treatment arm. No significant differences between the two groups when regarding either the primary or the secondary clinical outcome tools.	"In conclusion, the current literature regarding intertrochanteric fracture treatment does not clearly favor one implant over another10. In an attempt to define fracture types for which the intramedullary implants might be superior, we restricted our study to patients with an unstable AO/OTA 31-A2 fracture type. The intramedullary devices led to significantly less shortening across the fracture site. This did not translate to a significant difference in extremity or general function as measured with the LEM and FIM, respectively."	Data suggest similar functional outcomes with a trend towards favoring intramedullary devices due to less femoral shortening via radiograph.

			of this work, with an entity in the biomedical arena.							
Vaquero 2012 (score= 5.0)	Surgical treatment	RCT	Supported by the AO Foundation and a financial grant from Synthes, GmbH, Switzerland. Study was designed in cooperation with the AO Foundation and Synthes, but authors declared No COI.	N = 61 Patients with an isolated, unstable, closed or type 1 open trochanteric fracture	Mean age: 83.6 years; 8 males, 53 males.	Gamma3 Group: standard implant was a 180 mm nail of 11 mm diameter. Surgery performed by standard protocol. (n=30) Vs Proximal Femoral Nail Antirotation Group: standard implant for nail was 200 mm in length and 11 mm in diameter. Surgery performed by standard protocol. (n=31) Both nails had a standard neck-shaft angles (125 or 130 degrees) and were inserted using percutaneous technique.	Follow up at 3, 6, and 12 months.	Similar mean time between trauma and surgery and time taken from incision to closure in both groups (2±1 days, p = 0.228; 35±10 vs. 37±10 min, p = 0.445). There was no significant difference in the amt of blood loss between the two groups (p=.913). Highest score of independence in ADL was reported in over 40% in both groups. Over 30% in both groups reported severe functional impairment. There was a significant difference between baseline pain compared to pain at 6 and 12 months of the fracture site, middle thigh and knee (p<.0001).	"The results of our study showed that there is no significant difference in the overall clinical outcome and risk of complications between the PFNA- and the Gamma3-treated patients during the first postoperative year. Both helical blade and screw proximal femoral nails were found to be suitable treatment options for aging patients with an unstable proximal femoral fracture."	Data suggest similar adverse events and comparable ROM, clinical and radiological outcomes.
Zhou 2012 (score=5.0)	Surgical treatment	RCT	No sponsorship. No mention of COI.	N = 64 patients who had an OTA Type 31A proximal femoral fracture	Mean age: 72.5 years; 30 males, 34 females.	Less Invasive Stabilization System (LISS) Group: Patients positioned in supine on fracture table. Reduction of fracture visualized using an image intensifier. After reduction, a 4 to 6 cm long incision was made over the tip of the great trochanter. A sub	Follow up at 1, 3, 6, and 12 months.	There was a significantly longer operative time in LISS group than in PFNA group (P=.006). Intraoperative blood loss and hospital stay after surgery was not significantly different when compared with the two groups (P=.179; P=.457). All	"In summary, the femoral LISS is a safe and satisfactory option for the treatment of proximal femoral fractures. It fulfills the requirements for internal fixation of proximal femoral fractures with regard to the biologic mechanisms and	Data suggest comparable outcome efficacy but surgical time was greater in LISS group.

						muscular tunnel was made on the surface of the femur. An appropriate length distal femoral LISS plate was chosen and inserted between the vastus lateralis muscle and the shaft of the femur from the proximal end to distal end of the femur. The first guidewire was inserted through hole A and placed just above the inferior cortex of the femoral neck on the anteroposterior view and in the center of the femur neck on the lateral view. Plate was approximated to the shaft of the femur and then through guide handle, using the pulling device. Screws were placed in D, E, and F holes. (n=28) Vs Femoral Nail Anti-rotation (PFNA) Group: Shaft angle of 130-degrees and 12mm diameter. Nail inserted according to the surgical technique recommended by the manufacturer. (n=36)		fractures showed union within 6 months. No wound infections. All fractures showed union within 6 months.	anatomic structures. There were no major differences in functional outcome or major complications between LISS and PFNA. An intramedullary nail still is the implant of choice in most unstable proximal femoral fractures. For the fractures more unstable than Type 31A2.2 in which nailing may be difficult, the reverse LISS may be a good alternative. Mastering the techniques of indirect reduction, properly placing the guide pin in Hole A, and avoiding early weightbearing are keys to successful treatment."	
Chechik 2014 (score=5.0)	Surgical treatment	RCT	No mention of sponsorship. No COI.	N = 60 patients who had a unilateral extracapsular hip fracture.	Mean age: 83.1 years; 14 males, 46 females.	Dynamic Hip Screw (DHS) Group: Introduced through a vastus lateralis split approach. A 135-degree plate was used and 3 diaphyseal screws were inserted. The femoral head scew was inserted in a central-central or a central-inferior position. A tip apex of less than 25 mm was used. (n=31) Vs Exandable Proximal Femoral Nails (EPFN) Group:	Follow up at 6 and 12 weeks, 3, 6 and 12 months.	Blood tranfusions occurred more in the DHA group than the EPFN group (p=.08). Surgical incision was also longer in DHS group (p=.02). EPFN patients had better functional results in the HHS score and HHS support subscore was significantly better (p<0.05)	"We conclude that the EPFN is a promising technology for the treatment of pertrochanteric fractures, allowing for good and stable fixation and maintenance of reduction until fracture union. The EPFN seems to be associated with low rates of cut out and fractures distal to the nail tip. Fracture progression	Data suggest EPFN group experienced fewer cases of shaft medialization and/or femoral neck shortening otherwise results are comparable.

						introduced through a percutaneous trochanter approach. Either a 10mm or a 12mm nail with a 130-degrees nail-peg angle was used. EPFN inflated to a max. of 70mmHg. (n=39)			is a possible complication, and surgeons should inflate the EPFN under fluoroscopic control. Further studies are needed to determine the applicability of this technology in larger populations and in focus on specific fracture patterns."	
Fritz 1999 (score=4.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 80 Unstable trochanteric fractures	Mean age: 79 years; 17 males, 80 females	Gliding nail vs. gamma nail	6 months	No differences in operative time, EBL or hospital stay (9.2 vs. 10.4 days, NS). Intraoperative complications in GLN 2.5% vs. 17.5%. Deaths were (before discharge/during first 6 mo.): GLN (0/15%) vs. GAN (7.5/5%).	"We found no differences concerning the operation time, blood loss, period of stationary treatment or social situation. Also, the anatomic reconstruction and the long-term function according to the Merle d'Aubigne score were comparable."	Most data comparable.
de Grave 2012 (score=4.0)	Surgical treatment	RCT	No sponsorship. No mention of COI.	N = 112 patients with pertrochanteric femoral fractures resulting from a low-energy fall	Mean age: 74.9 years; 67 males, 45 males.	Gamma 3 Group: 11-mm distal diameter, 180-mm length, 4° valgus curvature, 120°, 125° or 130° neck angle, the set screw (antirotation) and one distal locking screw were used in all cases. (n=61) Vs ACE Group: 11-mm distal diameter, 200-mm length, 5° valgus curvature, 125° or 130° neck angle, only one distal locking screw was used (n=51). All patients were given one dose of cefuroxime before the operation and low-molecular-weight heparin for 4 weeks post surgery.	Follow up clinically and radiographically on a regular basis between 6 weeks to 1 year.	26 patients died within the first postoperative year. Mean postoperative hip scores in Gamma 3 and ACE group were not significantly different (p=.92). Walking was restored adequately in about 80% of the patients.	"In conclusion, the results of the present study show that both the Gamma 3 nail and the ACE nail provide effective methods of treatment for pertrochanteric hip fractures. no significant differences were found in functional outcome, or complication – and failure – rate."	Data suggest comparable outcomes and 80% of total population had restoration of walking ability.
Moein 2010 (score=4.0)	Surgical treatment	RCT	No mention of	N = 19 patients with an	Mean age: 28.9 years;	Unreamed Femoral Nail (UFN) Group: straight in the frontal plane (n=10) Vs Antegrade	Follow up at 6, 24, and	Patients reported some limitations for intensive daily activities in both groups. The	"Anatomical localization of the entry point	Small sample likely underpowered. Data

			sponsorship. No COI.	isolated femoral shaft fracture	18 males, 1 female.	Femoral Nail (AFN) Group: has a 6_-degree proximal lateral bend in the frontal plane. (n=9) All fractures were reduced by closed means under image intensifier control on the fracture table with boot traction or distal femoral skeletal traction. All nails locked proximally and distally.	52 weeks.	mean VAS score for pain for the UFN group and AFN group was 4.6 (1.6) and 3.7 (2.2). MRI and EMG showed signs of iatrogenic abductor musculature lesions and superior gluteal nerve injury in both groups.	seems to be important for per-operative soft tissue damage and subsequent functional impairment. However, the results of this study did not show appreciable differences between femoral nailing through the greater trochanter tip and nailing through the trochanteric fossa.	suggest comparable results.
Sahin 2016 (score=4.0)	Surgical treatment	RCT	No mention of sponsorship. No COI.	N = 72 elderly patients with AO/OTA 31A2 and 31A3 proximal femur fractures	Mean age: 75.7 years; 29 males, 35 females.	Manual traction group: Hip elevated 30-degrees. Fracture reduction and preservation of the reduction was done with longitudinal traction and manipulation. (n=36) Vs Traction table group: Both lower extremities were fixed to the traction table with the foot apparatus. The contralateral extremity was brought into abduction to allow the C-arm fluoroscopy device to be positioned between legs for optimal AP and lateral view. The fracture fragments were reduced with manipulation. Traction table was fixed into an appropriate position by locking the connections. (n=36)	Follow up at 6 months.	The difference observed between 31A2 and 31A3 fractures and the amount of blood loss was not statistically significant. In the manual traction group, there was a significant time gain in the positioning and preparation period (18.0 min in MT group, 29.0 min in TT group, $p < 0.05$).	"Manual traction and traction table facilitated intramedullary fixation of intertrochanteric fractures revealed similar results. Intramedullary nailing for unstable intertrochanteric femoral fractures could be performed by both methods effectively and safely. However, manual traction reduced the preparation time and total anaesthesia duration, despite an increase in number of surgical assistant."	Data suggest both anesthesia and prep time are reduced with manual traction but more surgical assistants are required but no differences were found in outcomes.
Chen 2010 (score=4.0)	Surgical treatment	RCT	No mention of sponsorship or COI.	N = 16 patients with Pipkin type 1 fractures	Mean age: 37.5 years; 13 males, 3 females	Conservative Group: treated with immediate closed reduction of the fracture dislocation. Limb was put into skeletal traction for 6 weeks after. (n=8) Vs Surgical Group: treated with closed reduction	Follow up from 25 to 52 months.	Functional outcome of conservative group was worse than the surgical group (p=.032). The interval between injury and successful closed	"This study showed the outcome of closed reduction followed by surgical fragment excision for Pipkin type 1 fractures is better than closed reduction alone. The	Small sample (n=16). Data suggest surgical excision of fragments post pipkin type 1 fractures appears to be effective after

						(same as conservative group) followed with fragment excision (a Smith-Petersen approach) (n=8)		reduction was 4.0±2.14 hours. Student's t tests failed to reach statistical significance for age (p=0.967) and the average interval between injury and successful closed reduction (p=0.894) between groups.	incidence of heterotopic ossification was high; treatment such as indomethacin or low-dose radiation could be used to minimise heterotopic ossification. Successful closed reduction within six hours of trauma, followed by surgical fragment excision, is a safe and effective for treating Pipkin type 1 fractures associated with posterior dislocation of the hip."	closed reduction compared to closed reduction alone.
Hopp 2016 (score=3.5)										Data suggest no significant difference in outcomes. Data suggest reduction of fracture and proper positioning of the implant is key.
Chaudhary 2012 (score=3.5)										Small sample. Sparse methods.
Lin 2013 (score=3.5)										Small sample. Data suggest a high AVN rate with poor outcomes in those patients who underwent emergent ORIF of Pipkin Type 1 Femoral Fxs.
Xue 2013 (score=3.5)										Sparse methods. Data suggest no difference between groups.

Sonmez 2017 (score= 3.5)										Data suggest these are advantages and disadvantages to both strategies.
Liu 2015 (score=3.5)										Data suggest ORIF better thancapsulotomy reduction & internal fixation.
Herrera 2002 (score=2.5)										Both techniques had significant limitations, but the study suggests PFN superior to Gamma nail.
Plates Vs Nails										
Miedel 2005 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by grants from Trygg-Hansa Insurance Company, the Swedish Orthopaedic Association, Styker Howmedica, Sweden, and Swemac, Sweden. No COi.	N =217 Unstable trochanteric and subtrocha n-teric fractures	Mean age: 84 years; 41 males, 176 females	Gamma nail vs. Medoff sliding plate	4, 12 months	Mean operating times SGN 61 (22 to 127) vs. MSP 65 minutes in the MSP group. Blood loss was SGN 276ml (50 to 1000) vs. 402mL (25 to 2400) (p <0.01). Reduction "good" in 63% SGN vs. 40% MSP (p <0.005). Mean stays 6 days both groups. No post-operative fractures. No differences in ADLs between groups at any of follow-up. Hip function and HRQOL according to EQ-5D did not differ. Reduction in HRQOL between prefracture and both follow-up exams was significant in both groups (p <0.005).	"[U]se of the SGN gave good results in both trochanteric and subtrochanteric fractures. The limited number of intra-operative femoral fractures did not influence the outcome or require further procedures. Moreover, the group with an SGN showed a reduced number of serious general complications and wound infections compared with the NSP group. The negative influence of an unstable trochanteric or subtrochanteric fracture on the quality of life was substantial regardless of the choice of implant."	Combined mortality rate at 1 year=55/217 (25.3%). Mean age 86. Both intervention groups had lower quality of life after fractures. Author conclusion supports gamma nail based on incidence of severe general complications, although data do not support clear advantage of either technique. Study underpowered for revision rates and failures.
Ekström 2007 (score=7.0)	Hip Screw/Nail vs.	RCT	No mention of	N = 203 Unstable tro-	Mean age: 82 years; 49 males,	Proximal femoral nail vs. Medoff sliding plate	6 weeks, 4, 12 months	Mean operative time for subtrochanteric group for MSP longer: 82±25 vs. 62±29	"No major differences in functional outcome or major complications between	One year mortality rate 33/203 (16%). 40% lost/dropout

	Other Approaches		sponsorship or COI.	chanteric and sub-tro-chanteric fractures	151 females			minutes for trochanteric group (p = 0.004). Fluoroscopy time longer in PFN 7±4 min vs. 5±5 min for MSP (p <0.001). Less EBL in PFN: 230±185 mL vs. 527±565 mL in MSP (p <0.001). No difference in number of blood transfusions. Follow up lost to general health problems or death 20% at 6 weeks, 28% at 4 months, and 41% a 1 year. No difference in total or major complication rates.	proximal femoral nail or Medoff sliding plate. Walking ability in early rehabilitation period was slightly better for the proximal femoral nail group."	rate at 1 year. Data suggest comparable efficacy.
Guo 2013 (Score=5.5)	Surgical Treatment/Plates vs. Nails	RCT	No mention of sponsorship. No COI.	N=90 patients older than 60 years of age with intertrochanteric fractures.	Mean age: 72.9±8.2; 35 males, 65 females.	Group 1, (PCCP) surgically received a percutaneous compression plate (n=45) vs. Group 2, (PFNA) surgically received a proximal femoral nail anti-rotation (n=45)	Baseline, 3, 6, 9, and 12 months. Then yearly thereafter.	PCCP vs PFNA, operating time, min (mean±SD): 53.0±9.4 vs 66.5±18.1 (p<0.0001). PCCP vs PFNA, intraoperative blood loss, mL (mean±SD): 100.7±23.5 vs 138.2±51.8 (p<0.0001). PCCP vs PFNA, perioperative blood loss, mL (mean±SD): 916±44 vs 1111±42 (p<0.0001). No significant difference between post-op hip flexion, walking ability, Oxford hip score, and Harris hip score.	"In summary, based on our findings, the PCCP and PFNA appeared to have similar clinical effects in treating elderly patients with intertrochanteric fractures. The PCCP was shown to require shorter operation times and less blood loss than the PFNA."	Data suggest both surgical intervention resulted in comparable outcomes at one year. Unclear if all 90 patients were available for final follow-up or alive.
Tao 2013 (Score=5.0)	Surgical Treatment/Plates vs. Nails	RCT	No mention of sponsorship or COI.	N=100 patients over the age of 65 with an intertrochanteric femoral fracture.	Mean age: 80.0±7.4; 33 males, 54 females.	Group 1, (PFNA) surgically received a proximal femoral nail anti-rotation (n=45) vs Group 2, (rLISS) surgically received a reverse less invasive stabilization system (n=42)	6, 13, 26, and 52 weeks.	PFNA vs rLISS, operating time, min (mean±SD): 66.9±13.7 vs 92.9±3.9 (p<0.0001). PFNA vs rLISS, intraoperative blood loss, mL (mean±SD): 228±100 vs 242±124 (p=0.565). PFNA vs rLISS, Harris hip score (pts) (mean±SD): 82.8±9.5 vs 82.0±10.4 (p=0.717).	"In conclusion, the results of the present study show that both the PFNA and the reverse LISS provide effective methods of treatment for intertrochanteric hip fractures. PFNA is superior to reverse LISS in terms of surgical time, weight-bearing, and perhaps fluoroscopy time."	Data suggest similar outcomes between implant designs.

Haq 2014 (Score=4.5)	Surgical Treatment/Plates vs. Nails	RCT	No mention of sponsorship or COI.	N=40 patients over the age of 18 with unstable intertrochanteric fractures with unstable lateral wall.	Mean age: 54.75±15.78; 28 males, 12 females.	Group 1, (PFN) surgically received a proximal femoral nail (n=20) vs Group 2, (DFLCP) surgically received contralateral reverse distal femoral locking compression plate (n=20)	2 weeks, 6 weeks, 3 months, 6 months, 1 year.	PFN vs DFLCP, operating time, min (mean±SD): 64.30±21.40 vs 80.95±22.57 (p=0.022). PFN vs DFLCP, intraoperative blood loss, mL (mean±SD): 316±143.98 vs 441±131.34 (p=0.008). PFN vs DFLCP, Harris hip score at 1 year, (mean±SD): 81.53±13.21 vs 68.43±14.36 (p=0.018). PFN vs DFLCP, Short Form-12 Physical component score & mental component score, 1 year (mean±SD): 41.83±12.28 vs 31.18±9.99 (p=0.002) & 57.52±3.99 vs 53.74±3.87 (p=0.007).	"In summary, the results of our study show that duration of surgery, blood loss during surgery and fluoroscopy time was less in the PFN group compared to the reverse-DFLCP group. At one-year follow up, the PFN group had better functional outcome than the reverse-DFLCP group as assessed by Harris hip score and Short Form-12."	Data suggest PFN group ad better outcomes at 1 year (16/17 complete unions) compared to DFLCP group (11/17 unions) although this study is underpowered.
El-Desouky 2016 (Score=4.5)	Surgical Treatment/Plates vs. Nails	RCT	No mention of sponsorship. No COI.	N=46 patients with subtrochanteric fractures who were above the age of 18.	Mean age: 44.3±17.7; 34 males, 12 females.	Group 1, (open) surgically received a proximal femoral locked plate with anatomical reduction (n=24) vs Group 2, (biological), surgically received proximal femoral locked plate without anatomical reduction (n=22)	2 weeks, 6 weeks, 3 monts, 6 motnhs, and 1 year.	Open vs biological, operating time, min (mean±SD): 129±16.9 vs 91±8 (p<0.0001). open vs biological, intraoperative blood loss, mL (mean±SD): 756±1551.3 vs 260±39.6 (p<0.0001). open vs biological, duration of healing, weeks (mean±SD): 18.3±3.7 vs 16.5±4 (p=0.058). open vs biological, final harris hip score, number for excellent, (% & chi squared p-value): 13 (54%) vs 12 (57%) (p=0.766).	"PF-LCP provided a strong and feasible construct for fixation of the comminuted subtrochanteric fractures either by open or biological method. Low patient compliance is an influential factor for implant failure in both techniques of fixation."	Data suggest similar results in both groups.
Varela-Egocheaga 2009 (Score=3.0)										Sparse methods. Data suggest comparable efficacy.
Plates Vs Screws										

Olsson 2001 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by grants from Stig and Ragna Gorthon Foundation, Helsingborg, and from the clinical research foundation of Malmöhus County Council, Lund. No COI.	N = 114 Inter-trochanteric fractures	Mean age: 84 years; 34 males, 80 females	Medoff sliding plate vs. compression hip screw	4 months	Operating time: MSP=58 vs. CHS=55 minutes, p = 0.23. Hospital stay: MSP = 11 vs. CHS=12 days, p = 0.07. Intraoperative bleed: MSP = 225 vs. CHS = 200mL, p = 0.07. Femoral shortening: MSP=15 vs. CHS = 11mm, p = 0.03. Lag screw sliding: MSP = 7 vs. CHS=14mm, p = 0.0004. Number of post-operative fixation failures: MSP = 0 vs. CHS = 5, p = 0.03.	"The marginally greater femoral shortening seen with the MSP compared with the CHS appeared to be justified by the improved control of impaction of the fracture. Biaxial dynamisation in unstable intertrochanteric fractures is a safe principle of treatment, which minimizes the rate of postoperative failure of fixation."	Greater failure rate of compression hip screw. Failures occurred in unstable fractures.
Kosygan 2002 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 111 Inter-trochanteric fractures	Mean age: 82 years; 21 males, 90 females	Percutaneous compression plate vs. classic hip screw	6 months	Durations of operative time were: PCCP 58±15.3 vs. CHS 49±13.1, p = 0.001. Transfusions were: 1.2±1.3 vs. 1.7±1.4U, p = 0.05. Hospital stays did not differ. Mortality rates did not differ.	"The PCCP gives results which are similar to those obtained with a conventional device. Its suggested advantages seem to be theoretical rather than practical and, being a fixed-angle implant, it is not universally applicable."	Data suggest overall comparable efficacy.
Brandt 2002 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 71 Peri-trochanteric fractures	Mean age: 80.9 years; no mention of sex.	Percutaneous compression plating vs. dynamic hip screw	1, 3, 8 months	Differences in operation time between treatments (PCCP 46.6 vs. DHS 69.2 minutes, p <0.001); 6 patients in PCCP and 10 in DHS experienced post-operative general complications (p = 0.13). 24 DHS patients required	"PCCP seems similar to DHS regarding bone healing and stability despite relatively small number of patients and short follow up. PCCP device was significantly better than DHS regarding blood loss, soft tissue healing and operation time."	Study followed until fracture union. No long-term follow-up. Suggest PCCP technique is as effective as DHS; though trend towards more

								transfusions vs. 6 in PCCP (p <0.001).		complications in DHS.
Lunsjö 2001 (score=6.0)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by grants from Thelma Zoéga Foundation and the Stig and Ragna Gorthon Foundation, Helsingborg, the Clinical Research Foundation of Malmöhus County Council, Lund, and the Swedish Medical Research Council, Sweden. No mention of COI.	N = 569 Unstable inter-trochanteric fractures	Mean age: 82 years; 152 males, 417 females	Medoff sliding plate vs. DHS vs. DHS/stabilizing plate vs. dynamic condylar screw	12, 15 months	DHS/stabilizing plate, dynamic condylar screw and Medoff sliding plates had longer median operation time (DHS 45 vs. DHS/TSP 70 vs. DCS 70 vs. MSP 60) and EBL compared to dynamic hip screw. Dynamic condylar screw had longer median hospital stay (14 vs. DHS 9 vs DHS/TSP 11 vs. MSP 9 days).	"No superiority for Medoff sliding plate over the other 3 techniques. However, it may be a suitable method for treatment of unstable intertrochanteric fractures due to low fracture rate and biaxial dynamization principle."	Study found some comparison data, but authors' purpose was to utilize Medoff vs. the other 3 groups as one group.

Janzing 2002 (score=6.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 115 Inter-trochanteric fractures	Mean age: 82.5 years; 14 males, 69 females	Percutaneous compression plate vs. dynamic hip screw	1, 3, 7 days, 1 year	Surgical times: PCCP 49 minutes vs. DHS 65 minutes, p = 0.005. Intra-operative problems: DHS 0% vs. PCCP 6%, p = 0.18. Unplanned operations: 3% vs. 8%, p = 0.53. One-year mortality 19% vs. 21%, p = 0.96. Mean VAS pain scores first week: PCCP 3.2±1.2 vs. DHS 4.2±1.3.	"Minimal invasive treatment of pertrochanteric fractures with the PCCP reduces operation time and postoperative pain."	Operative time was less with PCCP, but efficacy appears comparable.
Hardy 1999 (score=5.5)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by Smith and Nephew Richards, Memphis, Tennessee. No COI.	N = 160 Inter-trochanteric fractures	Mean age: 80.6 years; 23 males, 77 females	Intramedullary hip screw (IMIS) vs. compression hip screw plate (CHSP)	1 year	IMIS group significantly better functional outcome, particularly mobility score at 1 and 3 months. Significantly better ability to walk outside observed for IMIS group at 1 year. CHSP patients had significantly higher sliding of lag screw (10.2mm± 11.76) compared to IMHS (5.6 mm ± 4.32).	"Use of intramedullary hip-screws cannot be recommended for the treatment of intertrochanteric femoral fractures. However, this device is a promising alternative for comminuted fracture with subtrochanteric extension or a reverse oblique pattern because of the decreased shortening of the limb and the possibility of early weight-bearing."	Follow-up with increased sample size to 1998 study. Conclusion appears inconsistent with presented findings.
Watson 1998 (score=5.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 160 Inter-trochanteric fractures of which 114 are unstable fractures	Mean age: 76 years; 61 males, 117 females	Compression hip screw with 4-hole side plate (Dynamic Hip Screw) vs. Medoff sliding plate	6 weeks, 6 months	All stable fractures with no differences in union (mean 3 months) or loss of fixation. Time to union for 114 unstable fractures not different. No differences in hospitalization (mean 9 days), return to ambulatory status, or post-op pain. Medoff plate had higher blood loss (350 vs. 213mL, p = 0.0001) and operating time	"Based on the results of this study, the authors think that the compression hip screw device remains the implant of choice of stabilization of stable intertrochanteric fractures."	Pseudo-randomization on medical record number. Substantial difference in group sizes apparently a consequence. Some data support each approach.

								(135 vs. 90 minutes, p = 0.0001); 10 (5.6%) patients died during hospitalization. Overall failure rate for unstable fracture 9.6%; failure rate with use of compression hip screw 14%, (p = 0.01) than with Medoff plate (2%, 2 patients).		
Esser 1986 (score=4.5)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by a grant from the Gwynedd Research Committee. No mention of COI.	N = 98 Trochanteric fractures	Mean age: 81.7 years; 0 males, 98 females	Jewett nail-plate (JNP) vs. Dynamic hip screw (DHS) (both 135°)	6 weeks, 3, 6 months	Operative difficulties occurred more frequently with DHS vs. JNP (10 % vs. 1%, p <0.01). DHS better radiographic results at 6 months (p = 0.02). More with DHS mobile 6 months (73% vs. 57%); by chance more in DHS less mobile before fracture. With initial mobility taken into account, corrected percent of mobile patients 61% JNP vs. 88% DHS, p <0.05. Technical complications at fixation more with DHS (24%) vs. JNP (2%), p <0.05.	Over the years the Jewett fixed-angle nail-plate has served both our patients and surgeons well and we see no reason why it should be rejected completely; it has also allowed our trainee surgeons and theatre nurses to become adept in one technique of trochanteric fixation rather than less skilled in several. However, on the basis of this study we feel that we should now bias our training and equipment towards the DHS system."	Allocation not described and baseline comparison missing, with note that DHS group were less mobile than JNP before surgery. Data suggest DHS superior to JNP.
Qiang 2014 (score= 4.5)	Surgical Treatment	RCT	No mention of sponsorship or COI.	N = 121 elderly patients w/ intertrochanteric femur fractures (type	Mean Age: 75.3 years; 50 males, 71 females.	Percutaneous Compression Plating Group: (Orthofix Inc. USA plate) A guiding frame was connected parallel to the plate through which all drills and screws were introduced (n = 65) vs Dynamic Hip Screw Group: operated upon a	Follow up at 6, 9, 12, 18 and 24 months.	Outcome measures such as surgery time (P<0.01), blood loss (P<0.01), blood transfusion rate, mean VAS score (P<0.028) and Harris hip score (P< 0.05) were	"In conclusion, the present study demonstrates that, when compared with the conventional DHS approach, the PCCP procedure provides significant advantages such as less blood loss, fewer blood	Data suggest PCCP better than DHS for less adverse events and blood loss but no significant differences in LOS,

				AO/OTA 31.A1-A2, Evans type 1)		standard lateral approach in accordance with the manufacturer's (Richards Inc. USA) instructions. (n=56)		more favorable in the PCCP group than the DHS group.	transfusions, decreased pain, faster recovery of function and less postoperative morbidity. The PCCP should be considered as a minimally invasive and viable therapeutic alternative for intertrochanteric fractures (type AO/OTA 31. A1-A2, Evans type 1) in elderly patients."	healing or mortality rates
Yang 2011 (score= 4.5)	Surgical Treatment	RCT	No sponsorship. COI: One or more of the authors have received or will received benefits for personal or professional use.	N = 66 patients with an A1 or A2 AO/OTA intertrochanteric proximal femoral fracture.	Mean Age: 77 years; 19 males, 47 females.	Sliding Hip Screw Group: Standard technique (n=33) vs Percutaneous Compression Plating Group: Reduction of the fracture, lateral incision at the level of the lesser trochanter, bone hook/clamp secures plate to femoral shaft, main guide is drilled to within 5mm of the articular surface, neck screw is captured in the sleeve and locked at a 135 degree angle, cortical shaft screws are placed, and superior neck screw is placed. (n=33)	Follow up for Sliding Hip Group at 2 weeks, 2 weeks, and every month after up to a year. Follow up for PCCP group at 12 months.	Operative times (forty-eight vs. seventy-eight minutes), incision length (56 vs. 82 mm), and blood loss (41 vs. 101 mL) significantly favored the PCCP group ($p < 0.001$). Mortality at 12 month follow up in the sliding hip screw group was nearly twice than the PCCP group (27.3% vs. 15.2%) (P=.022).	"In conclusion, the Gotfried PCCP system provides a minimally invasive approach for the treatment of intertrochanteric proximal femoral fractures that compares favorably with the surgical treatment of these fractures with use of the sliding hip screw. Compared with the sliding hip screw, the PCCP resulted in a shorter operative time, a smaller total incision, and decreased blood loss, while maintaining at least equivalent functional results."	There was less blood loss and shorter operative times with the plate. Data suggest compression plate led to more independently walking patients, less pain and improved QoL but this was not a significant difference
Buciuto 1997 (score=3.5)										The role of the implant position and subsequent removal

										and incidence of fracture are unclear.
Buciuto 1998 (score=3.5)										Trends of better healing rates and lower technical failures, but more deaths in the FAB group.
Dhamangaon-kar 2013 (score=3.0)										Sparse methods. Data suggest a proximal femoral locking plate was better than dynamic hip screws for prevention of limb shortening and shaft medialization
Calder 1995 (score=2.5)										Study to ascertain usability of mailed follow-up surveys for assessing outcomes. Higher participation rate for younger more active patients; 67.4% response rates/potential response biases may invalidate conclusions, especially adverse outcomes.

Pitsaer 1993 (score=2.5)										Sparse study details. Recommendation against McLaughlin Nail plate not based on functional outcomes but on complications (implant breakage).
Bannister 1990 (score=2.5)										One-year mortality rate 37%. Most data aggregate, limiting conclusions on relative value of devices. Data suggest DHS superior.
Screws vs Nails										
Hoffman 1996 (score=7.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 67 Intertro-chanteric fractures	Mean age: 80.9 years; 16 males, 51 females	Gamma nail vs. Ambi hip screw	6 months, 2 years	Blood loss 42% greater in Gamma nail group (p = 0.006). Mobility ranked worse in Gamma nail group at 2 weeks (p = 0.038), 6 weeks (p = 0.039), and 3 months (p = 0.015). No patients admitted from home died during study. Time to full weight-bearing no different between groups.	"Gamma nail is not recommended for routine use by inexperienced orthopaedics due to findings of longer intensifier screening times, greater blood loss, increased numbers of technical complications and perhaps a poorer rehabilitation."	No advantage of either technique at 6 months.

Saudan 2002 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	No sponsorship or COI.	N = 206 Peri-trochanteric fractures	Mean age: 83.4 years; 46 males, 160 females	Sliding compression hip screw vs. intramedullary nailing.	3, 6, 12 months	No differences between treatment groups in operation duration, fluoroscopy time, requirement of reduction of fracture before fixation, and technical problems with implants. No difference in post-operative data. At 1 year 29/206 (14%) had died.	"There is no advantage to an intramedullary nail versus a sliding compression hip screw for low-energy pertrochanteric fractures. AO/OTA 31-A1 and A2, specifically with its increased cost and lack of evidence to show decreased complications or improved patient outcome."	Both treatments were equally effective.
Sadowski 2002 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	No sponsorship or COI.	N = 39 Oblique and transverse intertro-chanteric fracture	Mean age: 78.5 years; 12 males, 27 females	Dynamic condylar screw vs. proximal femoral nail	3, 6, 12 months	Operative time 166±48 (Dynamic Condylar Screw) vs. 82±53 (Proximal Femoral Nail), p <0.001. Blood transfused DCS 2.95±1.7 vs. PFN 1.45±1.5, p = 0.006. No. of patients receiving blood DCS 18 vs. PFN 11, p = 0.008. Type of reduction: Open 19 (Dynamic Condylar Screws, 5 (Proximal Femoral Nail). No differences in general complications, p = 0.83. Hospital stay: DCS 18±7 vs. PFN 13±4 days, p = 0.01. Rehabilitation protocol identical for both groups. Orthopaedic complications 8:1 (Dynamic Condylar Screws), p = 0.007. Functional results, p = NS.	"Our results clearly confirm the advantages of intramedullary fixation over fixed-angle screw-plate fixation, including a shorter operating time, easier reduction of the fracture, less blood loss, fewer units of blood transfused, fewer patients needing a blood transfusion, and a shorter hospital stay. More importantly, in this fragile elderly population the intramedullary nail provided significantly lower rates of implant failure and delayed healing, thereby lessening the need for revision surgery."	7 dynamic condylar screw patients with non-union or device fracture excluded, which may have biased outcome comparisons. Data suggest PFN superior to DCS.

O'Brien 1995 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 102 Intertro-chanteric fractures	Mean age: 80.1 years; 26 males, 75 females	Gamma nail vs. dynamic hip screw	11-82 weeks	No differences between groups. Length of surgical procedure, not including set-up and fracture reduction, longer for GN (mean 59 minutes) vs. DHS group (mean 47 minutes). No differences in length of stays.	"Effective treatment of intertrochanteric fractures was found for both gamma nail and dynamic hip screw. Dynamic hip screw was associated with lower risk of local complications and recommended to be considered for implant choice for patients with intertrochanteric fractures."	Comparable efficacy, though duration of operation and use of fluoroscopy shorter for dynamic hip screw.
Adams 2001 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by research fund Scottish Orthopaedic Research Trust. No COI.	N = 400 Intertro-chanteric fractures	Mean age: 81.0 years; 88 males, 312 females	Gamma nail vs. dynamic hip screw and plate	3, 6 months, 1 year	Mean operation time less for Gamma nails 55.4 minutes (52.7-58.2) vs. hip screw 61.3 min (58.2-64.4) (p = 0.008). 37% dropout rate. No difference in fixation failure between groups in stable or unstable fractures; 1-year mortality 120/400 (30.0%).	"Study confirms evidence that Gamma nail should not be adopted for routine treatment of intertrochanteric femoral neck fractures."	Data suggest DHS has fewer complications.
Pajarinen 2005 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 108 Peri-trochanteric fracture	Mean age: 80.6±9.9 years; 27 males, 81 females	Dynamic hip screw vs. proximal femoral nail	4 months	Median operation time in minutes: 45(20 to 105) DHS, 55(35 to 200) PFN, p = 0.011. Restoration of walking ability was achieved more often in the patients treated with a PFN (76.2%) compared with those treated with a DHS (53.7%; p = 0.040).	"[T]he use of a PFN in the treatment of trochanteric femoral fracture may have a positive effect on the speed of restoration of walking, when compared with patients treated with a DHS."	Lack of blinding did not likely have a strong influence on outcome as it was simple classification of walking status. Data favor proximal femoral nail.
Ahrengart 2002 (score=6.0)	Hip Screw/Nail vs. Other	RCT	Sponsored by grants form the Karolinska Institute	N = 426 Inter-trochanteric fractures	Mean age: 80 years; 123 males, 303 females	Compression hip screw vs. gamma nail	6 months	Compression hip screw operation time for fracture type 1 50 (20-100) minutes, p <0.01; type 2 45 (23-135), p <0.01; type 3 55 (25-115)	"Surgical treatment should be chosen according to the type of intertrochanteric fracture. Compression hip screw method may be faster and safer for less	23% drop out (mortality, complication). Study used two types of compression hip

	Approaches		Foundation, Lund University, Skane County Council and Styker-Howmedica. No mention of COI.					minutes, p <0.05; type 4 59 (22-240) min, p <0.05. CHS EBL for type 1 fractures 175 (0-600) mL, p <0.05. Overall GN operations 60 vs. 50 minutes for CHS, (p = 0.0001). Overall wound infections 9%. Lag screw in lower 1/3 of femoral head 17% of GN vs. 24% CHS, p <0.05. Distal locking in 14% GN. Death rate 18% within 6 months; 6 month findings Gamma nail/compression hip screw: fracture healed in peri-operative position 72%/55%; sliding of lag screw 3mm (0-25mm)/ 5mm (0-27 mm), p <0.01; Cut-out of lag screw 14/4 patients, p <0.05; pain at top of greater trochanter 20%/6%, p <0.001; External hip rotation of fractured leg 20°(0°-70°)/ 30°(0°-70°), p <0.001.	comminuted fractures. Comminuted fractures may experience more surgical difficulties parallel to the fracture complexity. Care must be taken to put the femoral head screw centrally in the femoral head to avoid cut-out."	screws (dynamic hip screw and Richards classic) without details of how many or related outcome measures.
Leung 1992 (score=6.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 225 Peri-trochanteric fractures	Mean age: 79.6 years; 55 males, 131 females	Dynamic hip screw vs. gamma nail	6, 12 months	Mean duration of operation lower with GN, p >0.05. Mean EBL lower with GN for unstable fractures 837.85 (497.17) vs. 1012.29 (477.18) ml, p = 0.047. Mean duration of hospital stay not different. Mean time to full weight bearing for stable fractures GN 1.3 (0.88) weeks vs. 1.9	"Gamma nail demonstrated similar final outcomes to dynamic hip screw but occurs with less surgical time, less screening time, less blood loss and earlier rehabilitation."	Gamma nail showed modest advantages over dynamic hip screw in reduced fluoroscopy time, shorter incision, and less intra-operative blood loss for unstable fractures. Gamma nail had

								(0.89) for dynamic hip screw p = 0.453; for unstable fractures 1.2 (0.64) weeks GN vs.1.7 (0.76) p = 0.0009. Post-op mobility not different. Hip ROM for unstable fractures, hip pain, thigh pain, not different. Similar functional results in both groups.		higher operative complications (14% vs. 10%, p <0.05).
Bridle 1991 (score=6.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 100 Inter-trochanteric fractures	Mean age: 81.9 years; 16 males, 84 females	Dynamic hip screw vs. gamma nail	No mention of follow-up.	Operative times not different (DHS 33.5 vs. GN 36 minutes). Gamma nail obtains a more central position of screw, otherwise no difference between groups.	"Routine use of the Gamma nail device is not recommended until the secondary femoral fractures problem has been resolved; however, in the case of difficult fractures where other forms of fixation are less satisfactory, such as subtrochanteric extension or reversed obliquity, the Gamma nail may prove useful."	High mortality rate (36%) at 6 months
Parker 2012 (score=6.0)	Surgical Treatment	RCT	No sponsorship. COI: one or more of the authors have received or will receive benefits for personal or	N= 598 patients with trochanteric fractures of the hip	Mean Age: 82 years; 121 males, 477 females	Sliding Hip Screw Group: Undertaken via a lateral incision which was the length of the plate to be used. Femur was approached posterior-laterally and vastus lateralis elevated (n=300) vs Targon Proximal Femoral Group: undertaken through three stab incisions. The standard nail was 220mm long, with a 130° angle telescoping screw and barrel and anti-rotation pin. (n=300)	Follow up at 6 weeks, and 3, 6, 9, and 12 months.	Operative difficulties were more common with the intramedullary nail. There was a tendency to fewer revisions of fixation or conversion to an arthroplasty in the nail group, although the difference was not statistically significant (nine *versus* three cases, p = 0.14). The extent of shortening, loss of hip flexion, mortality and degree of residual pain were	"In summary, the results of our study indicate that both methods of fixation produce comparable results. The nail used was found to be more technically demanding to insert but there was as tendency to regain better mobility for those treated with the nail."	Data suggest comparable efficacy but a trend towards increased mobility in nail group.

			professional use from a commercial party related directly or indirectly to the subject of this article.					similar in both groups. The recovery of mobility was superior for those treated with the intramedullary nails (p = 0.01 at one year from injury).		
Bretherton 2016 (score=6.0)	Surgical Treatment	RCT	No sponsorship. COI: One or more of the authors have received or will receive benefits for personal or professional use from BBrawn, Tuttlingen, Germany, related directly or indirectly to the	N = 538 patients presenting with a trochanteric hip fracture	Mean Age: 80.6 years; 102 males, 436 females.	Targon Proximal Femoral Group: (n=260) vs Sliding Hip Screw Group (SHS): A standard SHS was used with a 135-degree plate. The standard nail was 220 mm long, with a 130-degree angle telescoping screw and barrel and antirotation pin, locked with a single screw distally. (n= 272) All patients with fractures were reduced using a fracture table to achieve either a valgus or anatomical reduction.	Follow up at 1 year.	Patients with .50% medialization had worse pain (P =0.012) and mobility scores (P = 0.013) at 1 year. They also had more fracture healing complications (P = 0.021) and required more revision procedures (P = 0.014). Fractures treated with SHS were more likely to medialize .50% compared with intramedullary nail (P, 0.001). A2 and A3 fractures were more likely to medialize, and A3 fractures were more likely to undergo .50% medialization (P, 0.001).	"Our study demonstrates the previously theoretical predisposition for unstable hip fractures treated with SHS to undergo femoral medialization and correlates this with worse functional outcomes. It supports the use of intramedullary nails for A3 fractures, which have a significant tendency to medialize."	Data supports using intramedullary nails for A3 fractures

			subject of this article.							
Matre 2013 (score=6.0)	Surgical Treatment	RCT	Sponsorship and COI: one or more authors received payments or services from a third party in support of an aspect of this work or has had a financial relationship with an entity that could have potential influence.	N = 684 elderly patients with a trochanteric or subtrochanteric fracture	Mean Age: 84.1 years; 171 males, 513 females.	INTERTAN Group: A short or long version of the INTERTAN nail with distal locking was used w/ two integrated screws inserted into the femoral head-neck fragment (n=341) vs Sliding Hip Screw Group: Two different implants were used - the Compression Hip Screw and the Dynamic Hip Screw. A trochanteric stabilizing plate, either as an integrated part of the sliding hip screw or added as a separate device onto the sliding hip screw, was also used. (n=343)	Examined at day 5 if still at hospital. Follow up at 3 and 12 months.	Patients treated with an INTERTAN nail had slightly less pain at the time of early postoperativemobilization (VAS score, 48 versus 52; p = 0.042), although this did not influence the length of the hospital stay and there was no difference at three or twelve months. Regardless of the fracture and implant type, functional mobility, hip function, patient satisfaction, and quality-of-life assessments were comparable between the groups at three and twelve months. The numbers of patients with surgical complications were similar for the two groups (twenty-nine in the sliding-hip-screw group and thirty-two in the INTERTAN group, p = 0.67).	"In conclusion, we found similar results regarding pain, function, complications, and reoperation rates at one year in this randomized controlled trial comparing the INTERTAN nail and the sliding hip screw for the treatment of intertrochanteric and subtrochanteric fractures. Patients treated with the INTERTAN nail had slightly less pain at the time of initial postoperative mobilization and received fewer blood transfusions. However, this did not influence the length of the hospital stay, function, or complication rate."	Data suggest comparable efficacy
Zehir 2015 (score=6.0)	Surgical Treatment	RCT	No mention of sponsorship. No COI.	N= 198 Patients with AO type 31.A2 fracture on plain radiographs and aged	Mean Age: 77.0; 76 males, 122 females.	Group 1: received a Dynamic Hip Screw. DHS plates were made of stainless steel, including 25 or 38 mm barrels and 3–12 holes within the shaft with the shaft length ranging from 62 to 206 mm (n=96) vs Group 2: received a	Follow a 4 and 6 weeks, and 6 months.	Operative and fluoroscopy times were significantly shorter and blood loss was significantly lower in Group 1 than those in Group 2. Complication rates, mean	"In conclusion, PFNA seems to be an optimum choice in patients submitted to surgery for unstable trochanteric fractures, since it offers faster recovery. Further developments in its design should be focused on	Data suggest similar postoperative adverse events but recovery is better in proximal femoral nail anti-rotation group

				above 65 years		Proximal Femoral Nail Antirotation (PFNA) The PFNA nails used in this study were made of a solid titanium nail ranging from 200 to 240 mm in length and 9.0 to 10.0 mm in diameter (n=102)			better purchasing within the bone to reduce complication rates."	
Vidyadhara 2007 (score=6.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 73 Unstable trochanteric fractures	Mean age: 69±6.4 years; 37 males, 36 females	Single femoral neck screw vs 2 femoral neck screws (gamma nail vs. ace nail)	4 months, 1, 2 years	Good fracture reductions in 57% Gamma nail vs. 89% Ace. Delay in walking Gamma 1.6±0.9 vs. Ace 2.5±1.3 days. Hip pain at 1 month GN 10% vs. Ace 6%. Fifty-three patients had anatomical reduction; 13 acceptable, 7 poor reductions on post-op radiographs. All patients walked weight bearing from 2.3+/-1.2 days; good post-op recovery without pain at 4 weeks.	"This study shows that the osteoporosis of the proximal femur does not have a bearing on the choice of single or two-femoral neck screws along intra-medullary nails in the management of trochanteric fractures with respect to clinical outcome."	No long term functional differences although improved radiologic healing and some short term outcomes favored 2 screws.
Fornander 1994 (score=5.5)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by the Swedish Medical Research Council and the Medical Faculties of Lund University and Karolinska	N = 209 Trochanteric fractures	No mention of mean age or sex.	Gamma nail vs. sliding hip screw	6 months	Gamma nails mean (median) blood loss 300 (250) vs. 440 (300) ml (p <0.01) for sliding hip screw. Subtrochanteric bleeding GN 480 (500) vs. 1,090 (880) ml (p <0.05) SHS. Pertrochanteric bleeding for GN 285 (240) vs. 365 (280) ml (p <0.01) SHS. Pertrochanteric fractures mean (median) operating time for GN 68 (65) vs. 56 (45) minutes (p <0.01) SHS.	"Gamma nail may be useful for unstable, especially subtrochanteric, fractures in fragile subjects."	Study is early report of Gamma nail usage. Data suggest technique may be most beneficial for subtrochanteric fractures (reduced operating time and blood loss).

			Institute. No mention of COI.					Subtrochanteric fractures operating times 70 (70) GN vs. 109 (107) minutes (p <0.05) SHS. No differences in complication rate between 2 treatments. Radiological fracture positions, healing, ambulation and returning home similar.		
Goldhagen 1994 (score=5.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 75 Peri-trochanteric fractures	Mean age: 78 years; 22 males, 50 females	Compression hip screw vs. Gamma nail	6 months	No significant differences for operative time (intertrochanteric GN 72 vs. CHS 47); (subtrochanteric GN 82 vs. CHS 99), EBL, fluoroscopy time or transfusions. No differences for follow-up ambulatory status, range of motion, pain or return to preinjury functional level.	” Clinical results can be produced by GN equal to CHS for the fixation of intertrochanteric fractures. Gamma nail may be superior to CHS for certain subtrochanteric fracture fixation; although, gamma nail is more technically demanding.”	Study suggests Gamma Nail is more technically demanding and requires significant learning curve to reduce per-operative complications.
Dujardin 2001 (score=5.5)	Hip Screw/Nail vs. Other Approaches	RCT	No sponsorship or COI.	N = 60 Trochanteric fractures	Mean age: 83.5 years; 12 males, 48 females	Dynamic hip screw vs. experimental intramedullary nail with 2 non-parallel cervicocephalic screws	1 month, 6 weeks, 6 months	Trochanteric hip screw had longer procedure time 46±9 vs. 24±7 minutes for experimental nail (p <0.001). Total EBL higher in trochanteric hip screws (329±161) vs. experimental nail (90±75) (p <0.001); 6 weeks, pain better with nails Salvati and Wilson score (p <0.01). Painless mobilization in trochanteric hip screw 8.2±3.7 vs. 4.3±1.3 weeks for nail group (p <0.001).	“The experimental nail had shown advantages but not all possible disadvantages were able to be evaluated.”	Experimental nail group had disproportionate number of unstable fracture compared to the hip screw (p <0.01), which further strengthened data suggesting strengthens that experimental nail superior.

								Effective weight-bearing 8.3±4 trochanteric hip screw vs. 5.8±2.1 weeks nail group (p <0.02). Final telescoping trochanteric hip group 10mm vs. 0mm for nail group (p <0.001).		
Stern 2011 (score=5.5)	Surgical Treatment	RCT	No sponsorship. No mention of COI.	N = 335 patients with extra-capsular hip fractures classified according to AO/OTA [23] as 31-A1 and A2 (pertrochanteric fractures), and 31-A3 (intertrochanteric fractures), in persons over the age of 60 years caused by a low-energy injury.	Mean Age: 86.3; 78 males, 257 females.	Group 1: received either a DHS screw or Gamma nail (n=172) vs Group 2: patients treated with a DHS blade or PFNA (n=163)	Follow up at 1 year.	There was no significant difference concerning mean tip-apex distance, percentage of patients with a tip-apex distance >25 mm, and patients with a centre–centre position of the cephalic implant. There were 137 patients in the screw group and 132 in the blade group available for follow-up. They did not differ regarding rates of reoperation or cut-out (screw group=2.9%; blade group=1.5%).	"In conclusion, our clinical study found that both a screw and a blade performed equally well with a SHS or IM nail for stabilisation of trochanteric fractures in the elderly. It remains that the most important factor in achieving a good result and avoiding cephalic implant cut-out in hip fracture surgery is careful technique respecting accurate tip-apex distance."	Data suggest comparable performance from both the screw vs helical blade for femoral head placement and reoperation rates.

Papasimos 2005 (score=5.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 129 Unstable trochanteric fractures	Mean age: 81.2 years; 47 males, 73 females	AMBI dynamic hip screw vs. gamma nail (TGN) vs. proximal femoral nail (PFN)	1 year	Operative times favored TGN (AMBI 59.2 vs. TGN 51.3 vs. PFN 71.2, p <0.05). Anatomical reductions were achieved in AMBI 92.5%, TGN 90% and PFN 85%, p <0.05. Estimated blood loss 282.4 vs. 250 vs. 265mL, p >0.05. Hospitalization 9.9 vs. 8.6 vs. 8.8days, p >0.05. Technical complications 1 vs. 5 vs. 10 (mostly locking difficulties).	"The three methods are comparable in the treatment of unstable trochanteric fractures. The AMBI remains the gold standard for the fractures of trochanteric region. We consider that the PFN is a highly accepted minimally invasive implant for unstable proximal femoral fractures but future modification of the implant to avoid Z-effect phenomenon, careful surgical technique and selection of the patients should reduce its high complication rate."	Data suggest proximal femoral nail may be inferior to dynamic hip screw.
McLaren 1991 (score=5.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 100 Inter-trochanteric fractures	Mean age: 80.2 years; 19 males, 81 females	Pugh nail vs. dynamic hip screw	6 months, 14 months	No differences between number of early deaths (Pugh 10 vs. DHS 6), operation time (53 vs. 57 minutes), and the number of unsatisfactory fixations (7 vs. 4). Length of stay in ward was similar in each group. No difference in walking ability at 6 months.	"[W]ith both the Pugh and the DHS devices, there is a low incidence of long-term problems even if the fracture has been quite grossly malreduced. Because we found no specific disadvantages for the Pugh nail and because of the price difference between it and the DHS, we have elected to use the Pugh device for fixing future intertrochanteric fractures in our unit."	No clear differences. By chance, slightly more unstable fractures in the DHS group (27/50 vs. 22/50), yet that group tended to have fewer unsatisfactory fixations (4 vs. 7). Statistically, no preference shown.
Hardy 2003 (score=5.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 80 Inter-trochanteric fractures	Mean age: 77.1 years; 30 males, 50 females	Two screws transfixing the nail in 2 separate holes (Group A) vs. nail locked with 1 screw passing through slot (Group B)	1, 3, 6 months, 1, 2, 3 years	No differences in intra-hospital mortality (2 vs. 3). Statistical significance (p = 0.029) found for tolerance to dynamically locked nails with 1 patient in Group B having cortical hypertrophy of	"The use of two static locking screws is correlated with a relatively high rate of cortical hypertrophy and that the use of a dynamically locked nail significantly reduces the prevalence of this complication."	High mortality rate reduced power of study(20% at 1 year follow up)

								femur at level of tip of nail when compared to 6 patients in Group A.		
Little 2008 (score=5.0)	Surgical Treatment	RCT	No sponsorship or COI.	N = 190 patients with a low-energy extracapsular intertrochanteric fracture.	Mean Age: 83.4 years; 28 males, 157 females.	Holland Nail Group: Nail has a proximal diameter of 13 mm and the long nail is available with a 9 mm or 12 mm distal diameter. It can be locked proximally into the femoral neck with two 7 mm partially threaded cannulated screws to achieve rotational stability and distally with two 4 mm static locking partially threaded bolts. A standard operative technique either recommended by the manufacturer or by previous studies was used. (n=92) vs Dynamic Hip Screw Group: A standard operative technique either recommended by the manufacturer or by previous studies was used. (n=98) Each patient was given a single-dose antibiotic and gentamicin at induction.	Follow up at 6 weeks, 6 months, and 1 year post-operatively.	The mean anesthetic and operation times were shorter in the DHS group than in the Holland nail group (29.7 vs 40.4 minutes, $p < 0.001$; and 40.3 vs 54 minutes, $p < 0.001$, respectively). There was an increased mean blood loss within the DHS group versus the Holland nail group (160 ml vs 78 ml, respectively, $p < 0.001$). The mean time to mobilisation with a frame was shorter in the Holland nail group (DHS 4.3 days, Holland nail 3.6 days, $p = 0.012$). More patients needed a post-operative blood transfusion in the DHS group (23 vs seven, $p = 0.003$) and the mean radiation time was shorter in this group (DHS 0.9 minutes vs Holland nail 1.56 minutes, $p <0.001$).	"We conclude that the DHS can be implanted more quickly and with less exposure to radiation than the Holland nail. However, the resultant blood loss and need for transfusion is greater. The Holland nail allows patients to mobilise faster and to a greater extent. We have therefore adopted the Holland nail as our preferred method of treating intertrochanteric fractures of the hip."	Data suggest Holland Nail group led to quicker mobilization than dynamic screw. The screw can be implanted quicker but is associated with increased blood loss.
Davis 1988 (score=4.5)	Hip Screw/Nail vs. Other	RCT	Sponsored by Northern Regional Health Authority.	N = 230 Inter-trochanteric fractures	Mean age: 80.6 years; 40 males, 190 females	Küntscher-Y nail vs. sliding hip screw	6 weeks, 3, 6 months, 1 year	After control for age and mental status, expected 1-year mortality rate slightly lower for K-Y subgroup (11%) than for sliding hip screw subgroup (13%) in those with good walking ability (NS).	"Study suggests that sliding hip screw is a better for the fixation of intertrochanteric fractures of the femur compared to Küntscher-Y nail. Sliding hip screw was associated with a	High mortality at 1 year (40% vs. 35% SHS), $p >0.05$. Study did not exclude severely debilitated or demented

	Approaches		No mention of COI.					Total 1-year mortality rates 40% vs. 35% (NS). High complication rates both groups.	significantly lower mortality for patients with good preoperative walking ability compared to Küntscher-Y nail."	patients (frequently excluded in other comparison studies).
Utrilla 2005 (score=4.5)	Hip Screw/Nail vs. Other Approaches	RCT	No sponsorship or COI.	N = 210 Trochan-teric fractures	Mean age: 80.2 years; 66 males, 144 females	Trochanteric gamma nail vs. compression hip screw	12 months	Post-operative mortality over 12 months TGN 19 vs. CHS 21, NS. No differences in medical complications or local wound complications. No intra-operative or post-operative femoral shaft fractures. A lag screw cutting through femoral head occurred in 1 TGN vs. 2 CHS. In all cases, original hip screw placed superiorly in femoral head. No differences in intra-operative and post-operative complications or rate of fixation failure. Fluoroscopy time (minutes) TGN = 2.2±1.2; CHS = 2.7± 1.2, p = 0.006. Transfused (no.) TGN = 28; CHS = 44; p = 0.029. Transfusion (unit) TGN = 0.6±1.0; CHS = 0.9±1.2; p = 0.046.	"[T]he new Gamma nail appears to offer some advantages over the CHS, namely less blood loss, less fluoroscopy time, and similar intraoperative complication rate… we found a better walking ability score with the TGN. We believe that the indication for either TGN or CHS is similar in stable fractures, but we recommend the use of the TGN for unstable trochanteric fractures."	Data suggest comparable efficacy and no major differences in major complication rates. The better walking ability in the TGN group requires repeating.
Barton 2010 (score=4.5)	Surgical Treatment	RCT	No sponsorship or COI.	N = 210 patients presenting with an AO/OTA 31-A2 fracture of the proximal	Mean Age: 83.2; 44 males, 166 females.	Long Gamma Nail Group: the femur was reamed to 1 mm greater than the diameter of the nail, and a 130- degree nail of the appropriate length was inserted; all nails were locked distally with two screws. (n=100) vs Sliding Hip Screw Group: a four-hole, 135-degree plate was inserted.	Follow up at 3,6, and 12 months (clinically & radiographically)	The long-gamma-nail group included a significantly higher proportion of patients with a reduced mini-mental score (p = 0.04). There was no significant difference between the two groups with regard to the rate of the reoperation (p = 0.67). There was no difference between the two groups in terms of the mean tip-apex distance	"In conclusion, our study identified no difference in the reoperation rate following the fixation of AO/OTA 31-A2 fractures of the proximal part of the femur with a long gamma nail or a sliding hip screw. Furthermore, no difference was	Data suggest comparable outcomes but sliding hip screw is less costly

				part of the femur		(n=110) In all cases, efforts were made to achieve optimum positioning of the tip of the screw in the subchondral bone of the femoral head with a combined tip-apex distance measuring <25mmon anteroposterior and lateral radiographs.		(p =0.51). The mortality rate at one year was 32% in the long-gamma-nail group, compared with 22% in the sliding-hip-screw group (p = 0.045; odds ratio = 1.71). However, there was no significant difference between the two groups in terms of the mortality rates after controlling for the mini-mental score (p = 0.26).	identified between the two groups with regard to quality of life as measured with EuroQol 5D outcome scores at one year. We conclude that the sliding hip screw should remain the gold standard for the treatment of such fractures."	
Aktselis 2013 (score=4.5)	Surgical Treatment	RCT	No sponsorship or COI.	N= 80 patients with a 31-A2.2 or A2.3 Arbeitsgemeinschaft für Osteosynthesefragen /Orthopaedic Trauma Association (AO/OTA) intertrochanteric fracture	Mean Age: 83.0 years; 15 males, 56 females.	Gamma Nail Group: Gamma nail was inserted through a small incision proximal to the greater trochanter under image intensifier. Reaming was performed up to 15.5 mm proximally. The angle of the Gamma nail was 125°, except for three cases in which it was 130 (n=40) vs Sliding Hip Screw Group: AMBI was applied onto the femur through a standard lateral approach. Angles were 135° in 21 cases and 130° in 14. Three-hole plates were used in 28 patients, four-hole plates in four and five-hole plates in three (n=40)	Follow up at 1, 3, 6, and 12 months.	There was no significant difference in one year mortality rate between two groups. From the first to the 12th month, there was a significant improvement in Barthel Index (p <0.05), EQ-5D (p <0.05) and Parker score (p <0.001) w/ the exception from 3 months to 6 months, where QoL remained unaltered in the AMBI group (p =0.253). At 12 months, the Gamma nail group approached but did not normalise to its pre-operative Barthel Index values (p =0.043). AMBI group values at 12 months lagged significantly to pre-operative values (p <0.001). At 12 months, Parker	"Few failures occur when unstable 31-A2.2 and A2.3 AO/OTA fractures are fixed with a sliding hip screw. Nevertheless, an intramedullary nail seems superior in reconstituting patients to their pre-operative state."	Data suggest no statistically significant difference between groups although the gamma nail group required less surgical time and was associated with less self-reported pain

								mobility scores remained significantly lower to pre-operative values in both groups (p <0.001).		
Park 1998 (score=4.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 60 Inter-trochanteric fracture	Mean age: 73.0 years; 24 males, 36 females	Gamma AP nail vs. compression hip screw	12, 18.5 months	No mechanical complications. Time to union similar with 1 non-union in CHS. Greater decrease in femoral neck shaft angle in CHS group. Mean operative time: GN 79 minutes vs. CHS 94 minutes, p = 0.03. Mean blood loss (mL): Gamma nail EBL 462mL vs. CHS 622 mL, p = 0.01. Average Ceder post-op mobility scores: 5.10 GN vs. 4.73 CHS (NS). Post-op complications similar, but patterns different.	"[T]he Gamma AP locking nail is more efficient than the CHS in the treatment of intertrochanteric fractures in geriatric patients."	No details on mortality or drop-outs. Study used Gamma (AP) Nail designed for Asian-Pacific population with smaller dimensions than traditional Gamma Nail.
Butt 1995 (score=4.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 95 Peri-trochanteric fractures	Mean age: 78.5 years; 29 males, 66 females	Dynamic hip screw vs gamma nail	No mention of follow-up.	Operative times: GN mean 53 minutes vs. 62 minutes DHS. Hospital stays averaged 22 vs. 23 days. Times to union averaged 150 vs. 142. Overall total number of complications GN 17/47 (36.2%) vs. DHS 26/48 (54.2%). Fractured femoral shafts in 8 GN vs. 0 DHS.	"We do not recommend the gamma nail for the treatment of peri-trochanteric femoral fractures."	Sparse details of statistical analysis weakens conclusion regarding complications. Study suggests DHS is superior to Gamma nail.
Zou 2009 (score=4.0)	Surgical Treatment	RCT	No sponsorship or COI.	N = 121 patients with low-energy trochanteric femoral fractures	Mean Age: 65 years; 27 males, 96 females.	Proximal Femoral Nail Antirotation Group: performed according to the surgical technique described by Simmermacher et al (n=58) vs Dynamic Hip Screw Group: performed according to the	Follow up at 6 weeks, 3, 6, and 9 months, and then	The mean ± SD operative time was significantly longer in the DHS group (93 ±13 min) than in the PFNA group (52 ± 10 min) ($P < 0.05$), whereas the mean ± SD fluoroscopy time was significantly longer in the	"In conclusion, the PFNA is an intramedullary load-bearing device that allows for immediate postoperative weightbearing, with a sliding helically shaped column-blade permitting controlled	Sparse methods. Data suggest comparable outcome efficacy.

						surgical technique described by Hoffman and Haas (n=63)	annually.	PFNA group (7 ± 3 min) compared with the DHS group (5 ± 2 min) ($P < 0.05$). The mean ± SD external blood loss during surgery was significantly lower in the PFNA group (156 ± 24 ml) compared with the DHS group (410 ± 65 ml) ($P < 0.05$). No statistically significant differences were found in the complication rate between the two treatment groups or for different types of fracture.	impaction of the metaphyseal fracture zone. The PFNA device reduced iatrogenic tissue trauma and re-operation rate, although it was associated with higher X-ray exposure compared with the DHS. The present study showed that the PFNA device can be used effectively to treat trochanteric fractures and may be the best choice particularly in unstable trochanteric fractures because of its low re-operation rate."	
Garg 2011 (score=4.0)	Surgical Treatment	RCT	No sponsorship or COI.	N = 81 patients with unstable fracture of the proximal part of the femur	Mean Age: 62.2 years; 59 males, 22 females.	Dynamic Hip Screw Group: fracture reduced then fixed with the compression hip screw-side plate assembly (135° and 4-8 holes upon fracture extent) (n=39) vs Proximal Femoral Nail Antirotation Group: closed reduction. 5 cm incision proximally from tip of greater trochanter. Femur opened w/ a 17mm reamer. A PFNA was mounted and inserted in to the femur. The lateral cortex was opened with an 11 mm drill. 11 mm cannulated reamer used to ream the head and neck in non-osteoporotic bones. A blade was attached to the impactor and inserted. Locked blades. (n=42)	Follow up at 3, 6, 12 months and then annually.	The mean Harris hip score on final evaluation was 81 in the PFNA group, and in the DHS group it was 76 points (p <0.05). The mean surgical time for patients treated with PFNA was 25 min (range 19 - 56 min) and was significantly lower than in those treated with sliding hip screw where the mean time was 38 min (range 28 - 70 min). Similarly, the intra-operative radiation exposure was significantly lower in patients fixed with PFNA (mean 180s, range 100 - 340s) as compared to sliding hip screw fixation (mean 260s, range 100 -410s). The intra operative blood loss was around 110 ml in	"We believe that the PFNA is biomechanically and biologically superior to dynamic hip screw for fixation of unstable inter-trochanteric fractures as it provides stable intramedullary fixation resistant to varus collapse and fixation failure, with relatively less operation time, fluoroscopy exposure and blood loss."	Data suggest better functional outcomes in PFNA group vs DHS group with less radiological exposure, less blood loss, and fewer implant failures.

								the PFNA group while in the DHS group it was around 250 ml.		
Verettas 2010 (score=3.5)										Data suggest comparable results.
Benum 1994 (score=3.0)										Abstract. Details sparse. Large sample size.
Hogh 1993 (score=3.0)										Abstract. Sparse details.
Bajpai 2015 (score=2.5)										Sparse methods. Data suggest comparable efficacy.
Ekeland 1993 (score=2.5)										Abstract
Kazemian 2014 (score=2.5)										Limited details. Data suggest similar outcomes.
Madsen 1996 (score=2.0)										Abstract
Aune 1993 (score=1.5)										Abstract
Michos 2001 (score=1.5)										Abstract

Saudan 1999 (score=0.5)										Short abstract.
Mott 1993 (score=0.5)										Short abstract.
Plates vs Plates										
Griffiths 2015 (score=3.5)										Small sample data suggest LAP provides more axial stiffness to achieve better bicortical proximal construct fixator.
Total Hip Arthroplasty (THA)										
Kim 2012 (score=5.0)	Surgical Treatment	RCT	No sponsorship or COI.	N = 140 patients with an acute Garden III or IV fracture of the femoral neck.	Mean Age: 75.45 years; 36 males, 104 females	Short Stem Group: short, anatomical metaphyseal-fitting cementless femoral stem ith a 36 mm Biolox delta ceramic modular head (n=70) vs Conventional Stem Group: conventional diaphyseal-fitting fully porous coating cementless with the 36 mm Biolox delta ceramic modular head stem (n=70)	Follow up at 3 months, one year, and then yearly after. Mean follow up is 4.5 years.	No statistically significant differences between the short anatomical and the conventional stems with regard to the mean Harris hip score (85.7 (66 to 100) *versus* 86.5 (55 to 100); p = 0.791), the mean Western Ontario and McMaster Universities Osteoarthritis Index (17 (6 to 34) *versus* 16 (5 to 35); p = 0.13) or the mean University of California, Los Angeles	"Our study demonstrated that despite the poor bone quality in these elderly patients with a fracture of the femoral neck, osseo-integration was obtained in all hips in both groups. However, the incidence of thigh pain, pulmonary microemboli and peri-prosthetic fracture was significantly higher in the conventional stem group than in the short stem group."	Data suggest osseo-integration may be achieved in both groups.

								activity score (5 (3 to 6) *versus* 4 (3 to 6); p = 0.032).		
Roy 2010 (score=4.0)	Surgical Treatment	RCT	No sponsorship or COI.	N = 56 patients with a displaced femoral neck fracture	Mean Age: 82 years; 11 males, 45 females.	Mini-incision surgery (MIS) group: 8 cm incision centered over the posterior aspect of the greater trochanter. The short external rotators and capsule were taken as a unit and tagged for later repair. The quadratus femoris, piriformis tendon and anterior capsule were spared, as well as the femoral insertion of the gluteus maximus. (n=25) vs Standard incision group (STD): an incision equal to or greater than 16 cm. The quadratus was released in the standard technique, and part of the gluteus maximus insertion was released as needed (n=31)	Follow up at baseline, 4 days post-surgery, 3,6, and 12 weeks and 6, 12, and 24 months.	The evaluation of the HHS did show a significant difference at 24 months, the p-value being 0.05. The detailed results are as follows: 12 months (p = 0.06) and 24 months (p = 0.05). There was also significant difference between the two groups for the PF scale of the SF-36 at 24 months with a better score for the standard incision group (p = 0.01).	"Based on the results of the present study, we cannot recommend the use of a minimally invasive approach over a standard approach in the implantation of a cemented endoprosthesis."	Baseline differences in age of groups. Data suggest comparable efficacy.
Total Hip Arthroplasty Vs Open/Closed Reduction										
Blomfeldt 2005 (score=7.5)	Hip Screw/Nail vs. Other Approaches	RCT	Sponsored by the TryggHansa Insurance Company, the Swedish Society for Medical Research,	N = 102 Displaced femoral neck fractures	Mean age: 80.3 years; 20 males, 82 females	Total hip replacement (Exeter modular stem and Ogee cup) vs internal fixation with two cannulated screws (Olmed)	4, 12, 24, 48 months	Complication rates over 48 months 4% THR vs. 47% (p <0.001). Less pain 24 months THR group (p <0.005), borderline 48 months (p = 0.088). Walking rating favored THR 1st 24 months (p <0.05). 97% of THR vs. 57% fixation at 48 months had no hip complications (p <0.001). Reoperation rates	"Compared with internal fixation, primary hip replacement provides a better outcome…the complication and reoperation rates were significantly lower and hip function and health-related quality of life were at least as good as at four years after surgery."	Arthroplasty outcomes appear better. Re-operative rates substantially lower in THR group.

			the Swedish Orthopaedic Association, and the Stockholm County Council. No COI.					48 months 4% vs. 47% (p < 0.001). Death rates both 25%.		
Varley 1995 (score=6.0)	Wound Drainage Systems	RCT	No mention of sponsorship or COi.	N = 177 Patients undergoing AO dynamic hip screw or hemiarthro-plasty	Mean age: 80.2 years; 39 males, 138 females	Closed suction surgical wound drainage for 48 hours (1 deep to fascia lata alongside implant, 1 superficial to fascia lata) vs. no wound drainage	2, 5, 8, days, 6 weeks, 6 months	Infection rates were: drainage 6/86 (7%) vs. 12/91 (13.2%) (NS). Asepsis wound scores on day 8: drained, 1.33±3.49 vs. no drain 2.05± 4.62, p = 0.018. Drains were found to prevent early wound hematomas but not reformation after drain removal.	"Due to our study size we have failed to show a significant difference in overt wound infection rate, despite the fact that there were twice as many infections in the group without drains. This series shows that drains do significantly improve wound healing, and that the ASEPSIS score is a useful method of assessing wounds in orthopaedics. We therefore recommend the routine use of drains for up to 48 h postoperatively."	Results suggest drainage is effective for improved wound scores, but the study is underpowered for infections.
Liehu, 2014 (score=5.0)	Surgical Treatment (Total hip arthroplasty vs. closed/open reduction)	RCT	No mention of sponsorship or COI.	N= 285 patients with femoral neck fractures.	Mean age: 76 years; 132 males, 153 females.	CRIF Group: received closed reduction and internal fixation procedure performed (n=128) vs THA Group: received total hip arthroplasty (n=157)	Follow up annually for 5 years.	The closed reduction and internal fixation group had more complications than the total hip arthroplasty group in hip joint (P<0.01), general complications (P<0.01), and reoperation (P<0.05).	"For displaced fractures of the femoral neck in elderly patients, THA can achieve a lower rate of complication and reoperation, as well as better postoperative recovery of hip joint function compared with CRIF."	Data suggest THA superior to CRIF in elderly patients due to reduced adverse events and number of reoperations in addition to shortened recovery and better joint function.

Zielinski 2014 (score= N/A)										Data suggest patients who heal after internal fixative of a femoral neck fracture have better functional outcome than patients undergoing salvage arthroplasty after a failed internal fixation
Hemiarthroplasty vs Internal Fixation with Cannulated Screws										
Parker 2002 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 455 Intra-capsular fractures	Mean age: 82.3 years; 91 males, 364 females	Hemiarthroplasty (Austin Moore) vs. internal fixation (3 AO Stratec screws)	1, 2, 3 years	Trends towards worse survival for internal fixation for those 70-79, but better for internal fixation for those 80-89 or >90 years. Pain scores at 1 year hemi 2.41 vs. IF 2.22 (p = 0.91) and 3 years 1.79 vs. 1.92, p = 0.93.	"We recommend that displaced intracapsular fractures in the elderly should generally be treated by arthroplasty but that internal fixation may be appropriate for those who are very frail."	Large sample size.
Leonardsson 2009 (score=4.0)	Surgical Treatment	RCT	Sponsored by the Swedish Research Council, Malmö University Hospital Research Foundation and the Research and Development	N = 450 patients with displaced fractures of the femoral neck sustained between 1995 and 1997	Mean Age: 81.4 years; 126 males, 324 women.	Internal Fixation Group: received internal fixation (n=232) vs Replacement Group: received a total hip replacement/ hemiarthroplasty. (n=217)	Follow up at 4, 12, and 24 months, and 5 and 10 years	A significant difference between the groups with an overall total of 99 failures (45.6%) in the internal fixation group and 17 (8.8%) in the replacement group (chi-squared test, p < 0.001).	"We conclude that replacement should remain the treatment of choice for displaced intracapsular fractures of the femoral neck and that the apprehension of long-term complications can be discarded. Since replacement leads to a better patient-reported outcome during the first year this should be the treatment of choice even for patients	At both 5 and 10 years, pain was similar in both groups but data suggest replacement (either THR or hemiarthroplasty best for long term results)

			Council of Region Skåne, Sweden. No COI.						with a short remaining life expectancy in order to achieve more efficient reduction of pain and a better health-related quality of life."	
Bjornelv 2012 (score=3.5)										Data suggest both methods comparable with a trend towards cost-affectiveness in hemiarthoplasty group
Ozkayin 2015 (score=3.5)										Baseline comparability differences as hemiarthroplasty group older than nailing group. Data suggest hemiarthroplasty group better at 3 months but at 6 months both groups similar and at 12 months the nail group was better suggesting better activity in the end for nail group.

Sadr 1977 (score=2.5)										Variable length follow-ups of 3 to 17 months

Screws										
Moroni 2005 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	No sponsorship or COI.	N = 40 Pertro-chanteric fractures	Mean age: 80 years; 0 males, 40 females	Dynamic hip screw vs. external fixation device	1, 3, 6 months	Intra-operative time DHS 64±6 vs. EFD 34±5 minutes, p <0.005. All DHS had postoperative blood transfusion, with an average of 2.0±0.1 U vs. none in EFD group, p <0.0001. At 5 days, numbers reporting moderate or severe pain were: DHS 14/18(77.8%) vs. EFD 6/20 (30%), p <0.05. External fixation did not impede patient ability to sit or lie down in a supine or prone position. At 6 months, Harris hip score averaged DHS 62±19 vs. EFD 63±17 points (NS).	"[E]xternal fixation with the Orthofix pertrochanteric fixator and hydroxyapatite-coated pins should be considered as an option for the treatment of pertrochanteric fractures in elderly patients with osteoporosis."	Trial included only females with osteoporosis. Data suggest operative times, blood transfusions and pain ratings all favored external fixation.
Mattsson 2005 (score=7.0)	Other Surgical Studies	RCT	Sponsored by Stratec (Stockholm, Sweden) and Trygg Hansa. No COI.	N = 112 Unstable trochanteric fractures	Mean age: 81.6 years; 21 males, 91 females	Dynamic hip screw with vs. without cement augmentation	6 weeks, 6 months	Mean hospital stays 10.5 days with cement vs. 10.0 days without (NS). No re-operations. Two loosened plates at 6 months cemented group vs. 0. At 6 weeks, global pain scores 14±11 vs. 28±12 (p <0.003). Lower pain scores walking 10 or 50 feet at 6 weeks (p <0.01). No	Augmentation with calcium phosphate cement in unstable trochanteric fractures provides a modest reduction in pain and a slight improvement in the quality of life during the course of healing when compared with	Results suggest cement augmentation superior especially at 6 weeks, but also at 6 months in some measures.

								differences at 6 months in pain or walking scores. SF-36 scores also superior at 6 months for cemented.	conventional fixation with a sliding screw device alone.	
Vossinakis 2002 (score=7.0)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorhsip or COI.	N = 100 Peri-trochanteric fractures	Mean age: 77 years; 26 males, 74 females	Pertrochanteric fixator vs. sliding hip screw	6 months	Surgery time for pertrochanteric fixator (PF) (21.1±3.9 minutes) vs. sliding hip screw (SHS) (38.8±7.5 minutes), p <0.001. EBL PF (0 ml) vs. SHS (568±174), p <0.00001. Haemoglobin post-op PF (10.8±0.9mg/dL) vs. SHS (9.6±0.9mg/dL), p <0.0001. Decreased haemoglobin with PF. Hospitalization for PF (8±1.5 days) vs. SHS (16.7±2.2), p <0.00001. PF began walking on average 1 day earlier than SHS patients, no significant correlation between time walking began post-op and level of walking ability at final follow-up.	"Pertrochanteric fixator is an effective and safe device for treating pertrochanteric fractures. Pertrochanteric fixator had a reduced operating time, surgical trauma, blood loss and length of hospitalisation compared to sliding hip screw"	Study suggests percutaneous fixation superior to sliding hip screw. Relationship of advanced age and unstable fracture more prone to shortening, and no correlation between early walking after operation and load of walking ability 6 months later.
Baum-gaertner 1998 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 135 Inter-trochanteric fractures	Mean age: 79 years; 46 males, 89 females	Intramedullary hip screw vs. compression hip screw	6 weeks, 3, 6, 12, 24 months	Less EBL with intramedullary hip screw (HIS) (245 vs. 340 mL, p = 0.02). No difference in operating room charges, quality of reduction achieved or implant position. Surgical time greater with CHS. Greater operation time for CHS with unstable fractures (67 vs. 94 minutes, p <0.01), higher EBL (275 vs. 410mL, p	"Sliding hip screw and side plate should remain the preferred device for stable intertrochanteric fractures until the design/technique modifications of intramedullary hip screw can substantially reduce the rate of postoperative femoral shaft fractures. Results are applicable to a community	More higher functioning patients at baseline with SHS patients (74%) vs IHS (54%), biasing in favor of SHS. Noted use of new technique (new intramedullary nail) that

								<0.01), and operating room charges ($2105 vs. $2520, p <0.01). No difference between stable and unstable fracture patterns with intramedullary hip screw. Intramedullary hip screw patients had intra-operative complications exclusively.	orthopaedic surgeon's first experience with the device, and do not necessarily reflect the true potential of this intramedullary hip screw."	surgeons were less familiar with, providing possible bias against new implant if experience would mitigate complications.
Harrington 2002 (score=6.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 102 Unstable inter-trochanteric fractures	Mean age: 82.9 years; 21 males, 81 females	Compression hip screw vs. intramedullary fixation with an intramedullary hip screw	3, 6, 12 months	Mean operative times CHS (88) vs. IMHS (108 minutes), p = 0.001. Recovery of living status at 12 months in 19/30 (63.3%) IMHS vs. 22/33 (66.7%) CHS. No differences in transfusions (15 vs. 12 receiving 2 U) or time to mobilise after surgery. Post-operative stays 16.3 days CHS vs. 16.5 days IMHS (NS). No differences in radiological or functional outcome at 12 months.	"We have not shown that the theoretical advantages of intramedullary fixation devices have a significant effect on clinical outcome."	Twenty-five percent (25%) mortality rate at 6 months in the elderly population. Surgical procedures were performed by resident physicians.
Alobaid 2004 (score=6.0)	Surgical Approach including Minimally Invasive	RCT	No mention of sponsorship. No COI.	N = 48 Intertro-chanteric fractures	Mean age: 81.3 years; 17 males, 30 females	Minimally invasive vs. conventional surgical technique for placing dynamic hip screw (DHS)	6 months, 1, 2 years	Operative time significantly less in MIDHS (p <0.001). Mean 70 minutes control vs. 29 minutes MIDHS. Acetaminophen: MIDHS = 1.9g PO vs. Control = 5.4g, p = 0.03. Morphine: MIDHS = 15.1mg IM vs. control 25.2mg IM, p = 0.10.	"Minimal invasive technique significantly reduces blood loss and operative time for fixation of intertrochanteric hip fractures without sacrifice of fixation stability or bone healing."	Randomization not well described. Results favor MIDHS.

Hornby 1989 (score=6.0)	Surgery vs. Traction	RCT	Sponsored by a grant from the Newcastle District Research Committee. No COI.	N = 106 Trochanteric fractures	No mention of mean age; 78 males, 228 females	AO dynamic hip screw vs. traction	6, 12 months	Mean hospital stays: operation 53.0±56.5 vs. 79.7±62.9 days. Outcomes at 6 months included deaths (<75 years/75+years): operation (25%/35.9%) vs. traction (7.7%/51.4%). Complications of traction included track infection (16%), pin loosening (39%), traction sores (10%).	"Operative treatment gave better anatomical results and a shorter hospital stay, but significantly more of the patients treated by traction showed loss of independence six months after injury."	Suggests surgery is superior to traction in elderly. Data suggest worse outcomes particularly for older patients treated with traction.
Mattsson 2004 (score=5.5)	Hip Screw/Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 26 Unstable trochanteric fracture	Mean age: 82.8 years; 4 males, 22 females	Sliding screw augmented with calcium phosphate cement	1, 6 weeks, 6 months	No re-operations or post-operative wound infection during the study period. Augmented group had a smaller movement vs. controls. Rotation at fracture most pronounced around sagittal axis as varus angulation. Average varus angulation for controls was larger when compared with augmented fractures at all time points.	"Augmentation with calcium phosphate cement significantly improved the stability of unstable trochanteric fractures fixed with a sliding screw device. In addition, it could be shown that rotation at the fracture was limited not only in augmented fractures but also in fractures fixed with the sliding screw device alone."	Study had no clinical outcomes measures to determine if treatment was of benefit to patients. Small sample size.
Mehdi 2000 (score=3.0)										Abstract. Sparse study details
Hansen 1994 (score=1.5)										Abstract only. Details sparse. The groups are unequal for unknown reasons.

Harrington 1999 (score=1.0)										Study reported in 4 paragraphs which resulted in sparse details. Unclear if part of population Harrington 2002 above.

Evidence for the Use of Total Hip Arthroplasty

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Arthroplasty, Replacement, Hip; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 546 articles in PubMed, 3047 in Scopus, 1079 in CINAHL, 163 in Cochrane Library, 39500 in Google Scholar, and 7 from other sources. We considered for inclusion 34 from PubMed, 1 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 7 from other sources. Of the 45 articles considered for inclusion, 26 randomized trials and 19 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Total Hip Arthroplasty vs. Hemiarthroplasty										
Macaulay 2008 (Score= 5.5)	Arthroplasty	RCT	Sponsored by American Association of Hip and Knee	N=41 patients with femoral neck	Mean age: 79 years; 20 males, 21	Hemi group: patients received hemi arthroplasty surgery with unipolar /	Follow-up at baseline, 29, 34, and 42 months.	For primary outcome SF-36 24 months postoperatively, Less bodily pain was indicated in THA group (54.8±7.9) than that in hemi hip arthroplasty group (44.7±10.5) (p=0.03);	"This trial demonstrates the feasibility of conducting a well-designed research protocol in a higher functioning hip fracture population using a	Baseline differences in pain and function between groups. Data suggest both THA and hemiarthroplasty had comparable

			Surgeons and Orthopedic Research and Education Foundation grant. No mention of COI.	fracture.	females.	bipolar prosthesis (n=23) vs. THA group: patients received total hip replacement surgery with 28 mm femoral head implant protocol (n=18).		THA group also showed better mental health score (54.9±9.4) than that in hemi group (40.9±10.3) (p<0.01). For WOMAC scores, the two groups indicated significant differences in function subscale (THA=81.8 vs. Hemi=65.1; p=0.03). For Harris hip score, the two groups indicated no significant difference (p=0.64).	multicenter design. Using a performance measure such as the TUG, in addition to self-report measures, appears to be a valuable component of following functional outcomes in these patients but does complicate follow-up and statistical analysis."	complication but at 24 months, THA patients had significantly less pain suggesting THA as optional treatment in active independent individuals.
van den Bekerom 2010 (Score= 4.5)	Arthroplasty	RCT	No mention of sponsorship. The authors declared no COI.	N=252 over 70 years old patients with displaced femoral neck fracture.	Mean age: 81.1 years; 47 males, 205 females.	Hemi group: cemented hemiarthroplasty with 2mm increments femoral components (n=137) vs. THR group: cemented total hip arthroplasty with 32mm diameter modular head (n=115).	Follow-up at baseline, 1 and 5 years.	For primary outcome the modified Harris hip score (HHS), the mean score in THR group was 76.0, and 73.9 in hemiarthroplasty group, no significant difference (p=0.4). The HHS between two groups was still not significant at 5-year follow-up: THR group=75.2 vs. hemi group=71.9 (p=0.22).	Because of a higher intra-operative blood loss (p < 0.001), an increased duration of the operation (p < 0.001) and a higher number of early and late dislocations (p = 0.002), we do not recommend THR as the treatment of choice in patients aged ≥ 70 years with a fracture of the femoral neck in the absence of advanced radiological osteoarthritis or rheumatoid arthritis of the hip.	Data suggest THR should typically not be performed in patients 70 years of age and older due to higher intraoperative blood loss, longer surgical duration and more dislocations.
Tol 2017 (Score= N/A)	Arthroplasty	Follow-up study of	No mention of sponsorship. The authors	N=252 over 70 years old patients	Mean age: 81.1 years; 47	Hemi group: cemented hemiarthroplasty (n=137) vs. THR group:	Follow-up at baseline, 12 years.	At 12-year follow-up, the primary outcome Harris hip score (HHS) indicated no significant differences between the two groups: THA	"In the treatment of active elderly patients with an intracapsular fracture of the hip there is	12 years follow up study of van den Bekerom. Data suggest no difference in

		van den Berekom 2010	declared no COI.	with displaced femoral neck fracture.	males, 205 females.	cemented total hip arthroplasty (n=115).		group= 69.3±20.0 vs. hemi group=70.3±16.3 (p=0.85). The mortality rate indicated no significant differences between two groups: THA group=84% vs. hemi group=77% (p=0.13).	no difference in the functional outcome between hemiarthroplasty and THA treatments at 12 years post-operatively."	functional outcomes between groups.
Baker 2006 (Score= 6.5)	Total hip arthroplasty/hemiarthroplasty	RCT	The authors declared no sponsorship or COI.	N = 81 Displaced intra-capsular fractures	Mean age: 75 years old; 17 males, 64 females.	Hemi group: patients received hemi-arthroplasty with Zimmer endo femoral head (n=41) vs. THA group: patients received total hip arthroplasty with 28 mm cobalt femoral head with all polyethylene acetabular component (n=40).	Follow-up at baseline, 3 years.	Patients reported significant decrease in walking distance (p <0.001) after hemi-arthroplasty vs. increase (p = 0.023) after total hip arthroplasty. No wear evidence in cemented polyethylene cup any hip. 21/32 (66%) acetabular erosion for hemiarthroplasty. Total hip arthroplasty group had significantly superior cementing technique (p = 0.028). Mean oxford hip score (points) at time of final follow up: 22.3 (12 to 48) hemiarthroplasty compared to 18.8 (12 to 47) total hip arthroplasty, p = 0.033. Mean walking distance (mi, km) at final follow-up 1.17 (0 to 4), 1.9 (0 to 6.4) hemiarthro-plasty vs. 2.23 (0 to 25), 3.6 (0 to 40.2) total hip arthro-plasty, p = 0.039. Borderline for overall rate of revision or planned revision with 14.6% (6/41) hemiarthroplasty vs.	"Findings suggest that total hip arthroplasty is superior to hemiarthroplasty. Total hip arthroplasty was associated with better functional outcomes, fewer complications, fewer revisions after three years of follow-up."	Study suggests THR had more advantages in this healthy younger population.

								2.5% (1/40) total hip arthroplasty, p = 0.058.		
Avery 2011 (Score= N/A)	Arthroplasty	Follow-up study of Baker 2006	No mention of sponsorship. The authors declared no COI.	N=81 patients with non-pathological hip fracture.	Mean age: 75 years old; 17 males, 64 females.	Hemi group: patients received hemi-arthroplasty with Zimmer endo femoral head (n=41) vs. THA group: patients received total hip arthroplasty with 28 mm cobalt femoral head with all polyethylene acetabular component (n=40).	Follow-up at baseline, 7, 9, and 10 years.	For SF 36 scores, THR group indicated slightly further walk and better physical function (p=0.487, p=0.152 respectively). Both groups indicated deteriorated walking distance (THR group: p<0.001 & hemi group: p<0.02).	"There was lower mortality (p = 0.013) and a trend towards superior function in patients with a total hip replacement in the medium term."	7-10 year follow-up suggesting THR superior to hemiarthroplsty. The hemiarthroplasties had acetabular erosion and some required revision to THR.
Blomfeldt 2007 (Score= 7.0)	Arthroplasty / hemi arthroplasty	RCT	Sponsored by Stockholm county council, and Trygg-Hansa insurance company. The authors declared no COI.	N=120 patients with acute displaced intracapsular fracture.	Mean age: 81 years; 19 males, 101 females.	Hemi group: patients received hemiarthroplasty with 28mm Exeter femoral head (n=60) vs. THA group: patients received total hip arthroplasty with bipolar or DePuy ogee acetabular	Follow-up at baseline, 4 and 12 months.	Total hip arthroplasty (THR) group indicated better hip function score than hemiarthroplasty group did (28.8 vs. 31.9; p=0.021). Harris hip score (HHS) in THR group indicated significant improvement (p=0.001), but hemiarthroplasty group indicated no significant improvement in HHS (p=0.601).	"These results indicate that a total hip replacement provides better function than a bipolar hemiarthroplasty as soon as one year post-operatively, without increasing the complication rate. We recommend total hip replacement as the primary treatment for this group of patients."	Author's strong recommendation based on Harris hip scores which were statistically significant but maybe of questionable clinical difference.

						component (n=60).				
Hedbeck 2011 (Score= N/A)	Arthroplasty / hemi arthroplasty	Post-hoc analysis of Blomfeldt 2007	Sponsored by Trygg-Hansa insurance company, and Stockholm county council.	N=120 patients with acute femoral neck fracture.	Mean age: 80.6 years; 19 males, 101 females.	Hemi group: patients received hemi-arthroplasty bipolar bicentric / UHR head (n=60) vs. THA group: patients received total hip arthroplasty with DePuy / Johnson & Jognson acetabular component (n=60).	Follow-up at baseline, 4 years.	After 12 and 48 months, the total Harris hip scores in both groups indicated significant differences in dimension of pain ($p<0.001$) and dimension of function ($p<0.05$). Quality of life was higher in THA group than hemiarthroplasty group, and the difference was significant in 2nd year follow – up ($p=0.039$).	"These results confirm the better results in terms of hip function and quality of life after total hip arthroplasty as compared with hemiarthroplasty in elderly, lucid patients with a displaced fracture of the femoral neck."	Four year follow-up of Blomfeldt 2007. Data support THA superior to bipolar hemiarthroscopy for femoral neck fractures.
Parker 2002 (Score=6.5)	Arthroplasty / hemi arthroplasty	RCT	No mention of sponsorship. The authors declared no COI.	N=455 patients with proximal femur intracapsular fracture.	Mean age: 82.3 years; 91 males, 364 females	Hemi group: patients received hemiarthroplasty with uncemented Austin Moore anterior lateral approach (n=229) vs. Internal group: patients received percutaneous internal	Follow-up at baseline, 1, 2, and 3 years.	Trends towards worse survival for internal fixation for those 70-79, but better for internal fixation for those 80-89 or >90 years. Pain scores at 1 year hemi 2.41 vs. IF 2.22 ($p = 0.91$) and 3 years 1.79 vs. 1.92, $p = 0.93$.	"We recommend that displaced intracapsular fractures in the elderly should generally be treated by arthroplasty but that internal fixation may be appropriate for those who are very frail."	Large sample size.

						fixation with 3 parallel cancellous screws (n=226).				
Parker 2010 (Score= N/A)	Arthroplasty / hemi arthroplasty	Post-hoc analysis of Parker 2002	No mention of sponsorship. The authors declared no COI.	N=455 patients with proximal femur intracapsular fracture.	Mean age: 82.3 years; 91 males, 364 females.	Hemi group: patients received hemiarthroplasty with uncemented Austin Moore anterior lateral approach (n=229) vs. Internal group: patients received percutaneous internal fixation with 3 parallel cancellous screws (n=226).	Follow-up at baseline, 1, 9, and 11 years.	The survival of internal screw fixation was 3.2 years (95%CI: 2.5 to 3.9), while hemiarthroplasty group was 2.7 years (95%CI: 2.2 to 3.1), and the difference was not significant (p=0.424; 95%CI: 0.891 to 1.315). The hemiarhroplasty group indicated lower implant failure (p=0.001; 95% CI: 0.604 to 0.887).	"There was no difference in the degree of residual pain between groups neither was there any difference in the number of patients requiring institutional care. These results demonstrate that both treatment methods produce comparable final outcomes but internal fixation is associated with an increased re-operation rate."	Long term post hoc analysis of Parker 2002. Data suggest comparable results in both groups although revision surgery higher in internal fixation group.
Cadossi 2013 (Score= 4.5)	Arthroplasty	RCT	No mention of sponsorship. The authors declared no COI.	N=83 patients with intracapsular femoral neck fracture.	Mean age: 83.2 years; 21 males, 62 females.	HA group: patients received hemiarthroplasty with cemented or uncemented bipolar femoral head (n=42) vs. PCU-THR	Follow-up at baseline, 1, 2, and 3 years.	At 12 months' follow-up, hemiarthroplasty patients experienced significantly less pain (Harris hip score) than PCU-THR group (p=0.006), and HA group indicated less pain than PCU group at 24 months follow-up as well (p=0.019). The time of revision Harris hip score (HHS) was 49.4, and patients without revision	Based on our findings we do not recommend the use of the PCU acetabular component as part of the treatment of patients with fractures of the femoral neck.	Data suggest HA better than PCU group for both pain and lower numbers of surgical revisions.

						group: patients received large-diameter femoral head and uncemented conus stem (n=41).		indicated higher HHS 69.5 (P=0.008).		
Total Hip Replacement vs. Open Reduction and Internal Fixation										
Chammout 2012 (Score= 5.5)	Arthroplasty	RCT	No mention of sponsorship or COI.	N=100 patients with sustained femoral neck fracture.	Mean age: 78 years; 21males, 79 females.	THR group: patients received total hip replacement 28 mm chromium cobalt head and titanium alloy cemented femoral stem (n=43) vs. Control group: patients received internal fixation with 2 cannulated screws (n=57).	Follow-up at baseline, 3 months, 1, 2, 4, 11, and 17 years.	The primary outcome Harris hip score in total hip replacement group (14.7 points, 95%CI: 9.2 to 20.1) was higher than that in control group (p<0.001). The VAS in total hip replacement group indicated 1.2 points (95%CI: 0.4 to 2.0) (p<0.001).	"Over a period of seventeen years in a group of healthy, elderly patients with a displaced femoral neck fracture, total hip replacement provided better hip function and significantly fewer reoperations compared with internal fixation without increasing mortality."	Data suggest THR was better for fewer reoperations and better overall function and gait speed compared to ORIF group during the first year post-surgery.
Parker 2000 (Score= 4.0)	Arthroplasty	RCT	No mention of sponsorship or COI.	N=208 patients over 70 years old who	Mean age: 81.5 years; 46	HA group: patients received hemiarthroplasty with	Follow-up at baseline, 3 to 7 years.	Hemiarthroplasty group showed median survival time for 897 days (95%CI: 672 to 1122 days), and internal fixation group was 1427 days	"In conclusion, internal fixation and arthroplasty Produced comparable functional results. Internal fixation is associated with	Data suggest THA had lower reoperation rater, lower readmission rater (7/100 versus 24/100)

				experienced displaced cervical hip fracture.	males, 162 females.	uncemented Austin Moore and anterolateral surgical approach (n=106) vs. Fixation group: patients received internal fixation with 6.5 mm diameter cannulated screws and 32 mm thread (n=102).		(95%CI: 884 to 1970 days), and no significant difference showed (p=0.08). Pain in hemiarthroplasty rose at 2 years follow-up to 80% and 3 years follow-up to 87%, and internal fixation group at 2 years to 73% and 3 years to 75%	a markedly increased re-operation rate, but has a tendency to a lower mortality."	but surgical time was longer (47 minutes versus 22 minutes), and higher transfusion requirements due to blood loss (172 ml versus 23 ml).
Total Hip Arthroplasty										
Chammout 2017 (Score=8.0)	Total hip arthroplasty	RCT	No mention of sponsorship. The authors declared no COI.	N=69 patients with displaced femoral neck fracture.	Mean age: 72.5 years; 22 males, 47 females.	Cemented group: patients received cemented total hip arthroplasty with modular collarless polished tapered (CPT) stem and 32mm cobalt chromium head (n=35) vs.	Follow-up at baseline, 3, 12, and 24 months.	The relative risk of hip related complication after surgery in both groups was 7.95% (p=0.03; 95%CI=1 to 55). No significant difference in health related quality of life score (EQ-5D) was found between both groups (p>0.05).	"Based on our results and those of others, we do not recommend the use of uncemented stems for the treatment of displaced femoral neck fractures in elderly patients."	Cemented vs. uncemented femoral stems in THR. Data do not support uncemented femoral stem surgery in THR for displaced femoral neck fractures in the elderly.

						Uncemented group: patients received uncemented total hip arthroplasty with bi-metric stem and 32mm cobalt chromium head (n=34)				
Chiu 1993 (score=6.5)	Surgical Approaches	RCT	No mention of sponsorship or COI.	N = 120 Acute hip fractures	Mean age: 77.2 years; 28 males, 92 females	Drape group (operative site was covered with plastic adhesive drape after operation) vs. no-drape group (operation site was left uncovered).	6 months	No difference in post-op wound infection rates. Five swaps (4.2%) taken at wound closure positive for bacterial growth; 4 drape group, 1 no-drape group. Difference not statistically significant ($X^2 = 0.53$, $p > 0.25$).	The use of plastic adhesive drapes did not affect the wound infection rate after acute hip fracture operations.	Study suggests adhesive drapes do not provide advantage over no-drape at incision site.
Freund 2003 (score=6.5)	Comparisons between Different Cement Restrictors	RCT	No sponsorship. No mention of COI.	N = 70 Primary cemented hip replacement	No mention of mean age; 40 males, 29 females	Polyethylene vs. Shuttle Stop (degradable)	2 years	At 3 months, Shuttle Stop with 8 distortions or plug displacements and 13 cement leakages vs. 0 distortions/plug displacements and 3 with cement leakage in polyethylene group ($p < 0.01$). At 3 years, 2 failures and 1 probable loosening in Shuttle stop vs. no failures and 1 loosening in polyethylene group.	"We cannot recommend the Shuttle Stop for femoral canal sealing in total hip replacement."	Suggests biodegradable inferior.
Motobe 2004 (score=6.0)	Miscellaneous	RCT	No mention of sponsorship or COI.	N = 35 OA, RA and femoral neck	Mean age: 77.8 years; 8 males,	Femoral component inserted with vs. without cement. Endogenous	No mention of follow-up.	Sixteen patients in cemented group had a sudden decrease in systolic blood pressure of more than 20% at 2 minutes after prosthetic insertion vs. none in	"We have demonstrated for the first time significant increases in levels of ANA and 2AG, members of a newly identified class of	Study suggests endogenous cannabinoids are important vascular mediators, released by bone cement. A

				fracture, all <55 years	27 females	cannabinoids inserted using a conventional cementing technique vs. insertion without cement		non-cemented group (p = 0.0015). Sudden decrease in diastolic blood pressure also differed significantly at 2 minute interval (p <0.05). Significant difference in anandamide (ANA) and 2-arachidonylglycerol (2-AG) levels (p <0.05).	neurohumoral vascular mediators, in the course of cemented hip cement arthroplasty. This observation strongly suggests that ANA and 2AG are mediators of the hemodynamic variables associated with bone cement implantation shock. Therefore, targeting of the biosynthesis of, specific receptors for and biological degradation systems of endocannabinoids might be useful as new strategies for the prevention and clinical management of BCIS."	preventive therapy is unclear.
Inngul 2015 (Score= 5.5)	Cemented / uncemented arthroplasty / total hip arthroplasty	RCT	No mention of sponsorship. The authors declared no COI.	N=141 with acute displaced femoral neck fracture.	Mean age: 81.3 years; 42 males, 99 females.	Cemented group: patients received unipolar head / 32mm head with cemented Exeter stem hip replacement (n=67) vs. Uncemented group: patients received hip replacement with unipolar / 3 mm head and biometric stem with	Follow-up at baseline, 4 and 12 months.	Harris hip score (HHS) in cemented group was significantly better than that in uncemented group (p=0.004). The two groups indicated significant difference in health related quality of life score (EQ-5D), the cemented group indicated better score than that in uncemented group (p=0.001 at 4 months follow-up; p≤0.001 at 12 months follow-up).	"In conclusion, our data do not support the use of an uncemented hydroxyapatite coated stem for the treatment of displaced fractures of the femoral neck in the elderly."	Data suggest use of cemented versus uncemented arthroplasty for better function and significantly fewer adverse events like intra-operative fractures (0 versus 9).

						hydroxyapatitie coat (n=74).				
McCaskie 1997 (score=5.5)	Cementation Types, Techniques, and Pressurization	RCT	No mention of sponsorship. No COI.	N = 31 THR	No mention of mean age or sex.	Finger-packing vs. cement-gun technique femoral canal before cementing	No mention of follow-up.	Maximum pressure in cement insertion mean ± SD: Finger 96.4±15.9; gun 118.3±48.7. Oxygen saturation -4.5±4.9% vs. 0.78±0.97 (p = 0.006).	"Gun technique produced the highest pressure peaks and mean pressure. These results support that gun method promotes better interlock."	Higher pressures associated with gun use, but both better cement and less hypoxemia with gun use.
Berger 1997 (score=5.5)	Cementation Types, Techniques, and Pressurization	RCT	No mention of sponsorship or COI.	N = 60 THA	No mention of mean age or sex.	Femoral component inserted with vs. without distal centralizing device (PMMA) for primary hybrid total hip arthroplasty	No mention of follow up.	Prostheses of centralizer group valgus mean of 0.2°±1.2°. Range of angles 2.7° for valgus, 2.7° varus. Prostheses of uncentralizer group varus mean of 1.5°± 1.7°. Range of 2.6° of valgus to 5.6° of varus. 21% of centralizers vs. 16% of uncentralizers showed voids. Fewer cement mantle deficiencies with vs. without centralizer (p <0.001).	"Decreased incidence of cement mantle deficiencies and a more neutral prosthetic alignment four with distal centralizing device."	Centralizing device use improved overall cementing quality, but did not reduce voids.
Christie 1995 (score=5.0)	Femoral Canal Preparation	RCT	No sponsorship. No mention of COI.	N = 24 All femoral neck fractures	Mean age: 72.9 years; 5 males, 19 females	Minimal washout of the medullary canal before cement insertion vs. extensive washout by allocation of alternate cases to groups	No mention of follow-up.	Grade 3 or 4 maximal embolic responses of 50% in lavage group vs. 91.7% in control, p <0.05. Mean duration embolic response 270.4 vs. 421.9 sec, p <0.05. Mean number large emboli 2.3 vs. 7.1, p <0.05. Mean fall end-tidal CO2 1 vs. 5.5mmHg, p <0.05.	"We consider that thorough lavage should be an essential part of the preparation of the proximal femur before cement insertion."	Thorough lavage appears important.
Pabinger 2004 (score=4.5)	Femoral Components	RCT	No mention of sponsorship or COI.	N = 22 THR	Mean age: 75 years; no mention of sex.	CPS stem cemented conventionally using 3rd generation cementation technique vs.	2, 5, 7 years	Radiolucencies TRIOS/CPS: 2 years 75%/40%. Mean subsidence at 5 years (range) TRIOS/CPS: 4 years 2.29(0.1-8)/1.38 (0.4-2.9).	"Cementing titanium stems of this design cannot be recommended."	No benefit of the transprosthetic drainage system for cementation. However, high rates of subsidence with TRIOS stems.

						TRIOS cemented using transprosthetic drainage system				
Wykman 1992 (score=4.5)	Cementation Types, Techniques, and Pressurization	RCT	No mention of sponsorship or COI.	N = 19 Cemented THA	Mean age: 68.8 years; 7 males, 12 females	Continuous irrigation with Ringer solution during cement curing vs. no irrigation	No mention of follow-up.	Among those without irrigation, 9/11 (81.8%) exceeded 44ºC during 2.7 min. With irrigation, 2/8 (25%) exceeded 44ºC for 18s and 46s. Median maximum temperatures: irrigation 40.9 vs. no irrigation 48.8ºC, p = 0.007.	"Continuous water irrigation reduced the amount of heat at the bone-cement interface; median maximum temperature was 41 (37-48) ºC."	No long-term outcomes.
Thanner 1995 (score=4.5)	Cementation Types, Techniques, and Pressurization	RCT	Sponsored by IngaBritt and Arne Lundberg Research Foundation, Doctor Félix Neubergh Foundation and the Swedish Medical Research Foundation. No mention of COI.	N = 30 THA	Mean age: 71 years; 8 males, 22 females	Fixation of the prosthesis, using Boneloc vs. Palacos with gentamicin	6, 12 months	Cups fixed with Palacos displayed small lateral migration; cups fixated with Boneloc migrated medially (6 weeks, 6 and 12 months; p = 0.03). In group fixed with standard cement, mean proximal-distal migration of stem close to 0 throughout observation period. With Boneloc increasing subsidence recorded especially after 6 months (6 months vs. 12 months; p = 0.03, 6 weeks vs. 1 year; p = 0.002).	"The cold-curing cement provided an inferior fixation of both the acetabular and femoral components compared to standard cement."	Boneloc cement appeared inferior.
Thomsen 1992 (score=4.5)	Comparisons between Different Cement	RCT	No mention of sponsorship or COI.	N = 77 THA	Mean age: 71.2 years; no mention of sex.	Comparison of 3 plugs in THA: 1) bone plug made from femoral head; 2) Richards polyethylene plug ; 3) Thackray	No mention of follow up.	The quality of cement packing with Thackray polyethylene plug was significantly better compared to other 2 options (p = 0.02, p = 0.03).	"The Thackray polyethylene plug (38 mm, disc-shaped), with its large and flexible diameter, was best able to seal the femoral canal and produced significantly better cement packing compared to both the autologous bone plug and the Richard polyethylene plug."	Unclear if this is an RCT.

	Restrictors					polyethylene plug was 38mm				
Visser 2002 (score=4.0)	Comparisons between Different Cement Restrictors	RCT	No sponsorship. No mention of COI.	N = 93 THA	No mention of mean age or sex.	Biosem II plug vs. Cemlock plug vs. Thackray plug; all Stanmore prostheses	No mention of follow-up.	40/93 (43%) plugs migrated >1cm. Difference in migration between 3 plugs significant (p = 0.001). Biosem plug unstable in 78% (25/32); Cemlock in 32% (9/28); and Thackray 18% (6/33). Leakage of cement below plug most frequent in Thackray group (20 hips). Quantity of cement below plug varied between 0.5 and 4cm.	"Comparing the results, the most stable plug in our study was the Thackray plug; however, the difference with the resorbable Cemlock plug was not significant, with failure in 18% of cases. The Biosem plug was not able to resist the pressure during cementing and was abandoned in our clinic."	Polyethylene plug superior to 2 different biodegradable plugs.
Wembridge 2006 (score=4.0)	Comparisons between Different Cement Restrictors	RCT	No sponsorship. No mention of COI.	N = 32 THA	No mention of mean age or sex.	Ultra-high-molecular-weight polyethylene (Hardinge) vs. biodegradable (Amberflex Summit Medical) femoral cement restrictor	No mention of follow-up.	Mean migration of Hardinge was 6 times lower (0.5 vs. 3.0cm, p <0.002) than that of the biodegradable restrictor.	"Although there are theoretical advantages in avoiding UHMWPE restrictors, the current biodegradable alternative is actually inferior and its use cannot be endorsed."	Ultra-short term follow-up period of 5 days only.

Evidence for the Use of Hemiarthroplasty

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hemiarthroplasty; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 130 articles in PubMed, 1290 in Scopus, 110 in CINAHL, 28 in Cochrane Library, 3180 in Google Scholar, and 2 from other sources. We considered for inclusion 25 from PubMed, 18 from Scopus, 9 from CINAHL, 0 from Cochrane Library, 6 from Google Scholar, and 2 from other sources. Of the 60 articles considered for inclusion, 29 randomized trials and 9 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Hip Screw/Nail vs. Other Approaches										
Frihagen 2007 (score = 8.0)	Hemiarthroplasty	RCT	No sponsors hip. COI	N = 222 All displaced intracapsular femoral neck fractures with angular displacement	Mean age: 83 years; 57 Males, 165 Females	Group 1: Closed reduction and two parallel screws (n=112) vs. Group 2: bipolar cemented hemiarthroplasty. (n=110)	4, 12, and 24 months	Mean Eq-5d index score at 24 months 0.13 higher in hemiarthroplasty group (0.01 to 0.25, p = 0.03); 20 (18%) in internal fixation group experienced intra-operative problems; 9 changed to hemiarthroplasty because of irreducible fractures (8) or poor screw purchase (1). Hemiarthroplasty better functional results, but not all statistically significant. Harris hip scores at 24 months favored hemiarthroplasty (67.3±15.5 vs. 70.6±19.1, p = 0.26). Death rates same (34.8% vs. 35.5%).	"Hemiarthroplasty is associated with better functional outcome than internal fixation in treatment of displaced fractures of the femoral neck in elderly patients."	Trends favored hemiarthroplasty in functional measures. More transfusions with hemiarthroplasty. More mechanical failure of internal fixation or nonunion among fixation group.
Cornell 1998 (score = 7.5)	Hemiarthroplasty	RCT	No mention of sponsors hip or COI	N = 48 Displaced femoral neck fractures over 65 years	Mean age: 77 years; 12 Males, 36 Females	Group 1: Unipolar hemiarthroplasty (n = 15) vs. Group 2: bipolar hemiarthroplasty (n = 33)	6 weeks, 3 months, 6 months	Data at 6 months include one dislocation each group. Total rotation 36.6 uni vs. 50 bi. Abduction 22 vs. 38. Get up and go test 27.3±21 vs. 33.1±30 s. 6 minute walk test 1.93 ft/s vs. 2.67 (p <0.03).	"These early results suggest that use of the less expensive unip0olar prosthesis for hemiarthroplasty after femoral neck fracture may be justified in the elderly."	Unclear as to subjects enrolled; states 48 enrolled and completed 6 month follow-up. Data suggest better outcomes with bipolar group at 6 month follow-up.
Macaulay 2008 (score = 7.0)	Hemiarthroplasty	RCT	No mention of sponsors hip or COI	N = 40 Displaced femoral neck fracture	Mean age: 79 years; 19 Males, 21 Females	Group 1: Total hip arthroplasty (≥28mm femoral head implant) (n = 17) vs. Group 2:	6, 12, and 24 months	No differences at 6 months. Less pain THA group at 12 months (p = 0.02). At 24 months, pain on SF-36 subscale for THA (54.8±7.9) vs. hemiarthroplasty (44.7± 10.5), p = 0.04. WOMAC and Harris hip scores favored THA at 24 months.	"Significant differences in outcomes, without a significantly greater incidence of complications, suggest THA is a valuable treatment option for the active elderly hip fracture population."	Data suggest superiority of THA for active elderly with hip fractures at 2 years follow-up.

						hemi-arthroplasty (uni- or bi-polar) (n = 23)				
Keating 2006 (score = 7.0)	Hemiarthroplasty	RCT	Sponsored by National Health Service R&D Health Technology Assessment Programme. No COI.	N = 299 Displaced intra-capsular fractures	Mean age: 75 years; 66 Males, 233 Females	Group 1: Bipolar hemi-arthroplasty (n = 111) vs. Group 2: total hip arthroplasty (n = 69) vs. Group 3: Internal fixation (n = 118)	24 months	Over 24 months follow-up 44/118 (37.3%) fixation failed, additional hip surgery needed for 46/118 (39.0%) fixation vs. 6/111 (5.4%) for hemiarthroplasty (p <0.001). Patient-assessed outcomes 4 month EQ-5D assessed for worse general level of health 37/110 (33.6%) for fixation vs. 19/102 (18.6%) hemi-arthroplasty; OR = 0.45 (95% CI 0.23-0.86), p = 0.02. At 12 months hip rating questionnaire for patient-assessed outcomes for all patients 70.6 fixation vs. 77.1 hemiarthroplasty, adjusted difference -5.82, p = 0.01.	"Arthroplasty is more clinically effective and cost-effective than reduction and fixation in healthy older patients with a displaced intracapsular fracture of the hip. The long-term results of total hip replacement may be better than those of bipolar hemiarthroplasty."	Multiple arms with loose randomization schemes inducing addition of fixation as another treatment variable.
Parker 2002 (score = 6.5)	Hemiarthroplasty	RCT	No COI. No mention of sponsorship.	N = 455 Intra-capsular fractures	Mean age: 82 years; 209 Males, 246 Females	Group 1: Hemiarthroplasty with Austin Moore prosthesis (n = 229) vs. Group 2: internal fixation with 3 AO Stratec screws (n =226)	1 year, 2 years, 3 years	Trends towards worse survival for internal fixation for those 70-79, but better for internal fixation for those 80-89 or >90 years. Pain scores at 1 year hemi 2.41 vs. IF 2.22 (p = 0.91) and 3 years 1.79 vs. 1.92, p = 0.93.	"We recommend that displaced intracapsular fractures in the elderly should generally be treated by arthroplasty but that internal fixation may be appropriate for those who are very frail."	Large sample size.
Baker 2006 (score = 6.5)	Hemiarthroplasty	RCT	No COI or sponsorship.	N = 81 Displaced intra-capsular fractures	Mean age: 75 years; 17 Males, 64 Females	Group 1: Hemiarthroplasty (n = 41) Group 2: Total Hip Arthroplasty (n = 40)	Average follow up = 3 years	Patients reported significant decrease in walking distance (p <0.001) after hemi-arthroplasty vs. increase (p = 0.023) after total hip arthroplasty. No wear evidence in cemented polyethylene cup any hip. 21/32 (66%) acetabular erosion for hemiarthroplasty. Total hip arthroplasty group had significantly superior cementing technique (p =	"Findings suggest that total hip arthroplasty is superior to hemiarthroplasty. Total hip arthroplasty was associated with better functional outcomes, fewer complications, fewer revisions after	Study suggests THR had more advantages in this healthy younger population.

								0.028). Mean oxford hip score (points) at time of final follow up: 22.3 (12 to 48) hemiarthroplasty compared to 18.8 (12 to 47) total hip arthroplasty, p = 0.033. Mean walking distance (mi, km) at final follow-up 1.17 (0 to 4), 1.9 (0 to 6.4) hemiarthro-plasty vs. 2.23 (0 to 25), 3.6 (0 to 40.2) total hip arthro-plasty, p = 0.039. Borderline for overall rate of revision or planned revision with 14.6% (6/41) hemiarthroplasty vs. 2.5% (1/40) total hip arthroplasty, p = 0.058.	three years of follow-up."	
Sikorski 1981 (score = 5.0)	Hemiarthroplasty	RCT	No mention of sponsorship or COI.	N = 218 Displaced subcapital fracture	Mean age: 80.4 ± 6.2 years; 35 Males, 183 Females	Group 1: Internal fixation (n = 76) vs Group 2: Thompson hemi-arthroplasty through a McKee anterolateral approach (n = 57) vs Group 3: Thompson hemiarthroplasty through a Moore posterior approach (n = 57) *An additional 28 patients were initially allocated to internal fixation, but due to severity of the fracture, a hemiarthroplasty	Followed up for 2 years, or until death, at intervals of 3 months or less	Patients in irreducible group had highest mortality (21% vs. 1% internal fixation and 4% hemiarthroplasty, p <0.001). Crude mortality at 2 years also worse in these patients (70%), p <0.05. Pain after 1 month in 28% internal fixation vs. 11% anterior Thompson vs. 4% posterior Thompson. Revisions between 3-24 months in 32% vs. 7% vs. 1%. Technically unsatisfactory in 4. Pain after 1 month in 28% internal fixation vs. 11% anterior Thompson vs. 4% posterior Thompson. Revisions between 3-24 months in 32% vs. 7% vs. 1%. Technically unsatisfactory in 46% vs. 36% vs. 33%.	"Thompson hemiarthroplasty, using an anterolateral approach, is the safest operation in this group of patients."	Data support Thompson hemiarthroplasty for these fractures.

						was performed instead				
Dorr 1986 (score = 5.0)	Hemiarthroplasty	RCT	No mention of COI or sponsorship	N = 89 Femoral neck fractures	Mean age: 69 years; 31 Males, 58 Females	Group 1: Total Hip Rreplacement (n = 39) Vs Group 2: noncemented bipolar hemiarthroplasty (n = 13) Vs Group 3: cemented hemiarthroplasty (n = 37)	Range of follow up = 2-4 years	More pain, progressive pain with time and activity, decreased ambulation, increased need for assistive devices in uncemented hemiarthroplasty. Use of uncemented stem stopped after 13 complained of disabling pain and severely limited function. No difference in pain or aids required between cemented hemiarthroplasty and THR. THR had progressively improving ambulation and peak ambulation at 6 months vs. cemented hemiarthroplasty. No difference in gain velocity or single-limb stance between cemented hemiarthroplasty and THR.	"Consideration of patients' medical diseases must be a part of the decision of the surgical treatment to achieve optimal mortality rate. No deaths were recorded for patients younger than 60, even those with significant medical diseases. Fixation is a strong consideration for patients 60-70. Patients 70-90 years with medical diseases are optimal candidates for index replacement arthroplasty; rapid rehabilitation, low immediate mortality rate, and good pain relief with good functional status benefits these patients physically and mentally."	Study had lack of statistical data. Uncemented hemiarthroplasty arm was stopped due to disabling pain.
El-Abed 2005 (score = 4.5)	Hemiarthroplasty	Quasi-randomized RCT	No mention of sponsorship or COI	N = 122 Displaced subcapital hip fractures >70 years	Mean age: 73 years; 82 females, 40 males	Group A: Uncemented hemiarthroplasty (Austin Moore) (n = 62) vs Group 2: dynamic hip screw (AO Synthes) (n = 60)	36-54 months	Hemiarthroplasty results 42% excellent/good vs. 70% DHS (p <0.001). SF-36 hemi 50 percentile vs. 74, p = 0.002. Greater mortality with hemiarthroplasty (p <0.05).	"Both physician based and patient based outcome scores favour retention and internal fixation of the femoral head in this cohort of patients at a short term follow-up."	Mortality, overall results, SF-36 data support dynamic hip screw over hemiarthroplasty for these fractures.

Skinner 1989 (score = 4.5)	Hemiarthroplasty	RCT	No mention of sponsorship or COI	N =278 Displaced subcapital fractures	Mean age: 80.9 years; 28 males, 250 females	Group 1: Internal fixation vs Group 2: Moore hemi-arthroplasty vs Group 3: Howse II total hip replacement *specifications for number of patients allocated to each group not given	6 weeks, 3 months, annually	No differences between treatments for general medical complications or mortality 2 months or 1 year; 25% internally fixed fractures revised vs. 13% hemiarthro-plasties. Unfit patients more at risk for dislocation ($p < 0.05$). Infections different ($p < 0.01$). Total hip replacement patients had significantly less pain than other 2 groups.	"Internal fixation and particularly primary total hip replacement should be given serious consideration in the management of the elderly patient with a displaced subcapital fracture."	Hemiarthroplasty had lower revision but comparable mortality rates for displaced subcapital fractures. No control for physician experience was mentioned.
Santini 2005 (score= 4.5)	Hemiarthroplasty	RCT	No COI. No Sponsorship.	N = 106 Femoral neck fractures	Mean age: 81 years ; 24 Males, 82 Females	Group 1: Cemented (n = 53) vs Group 2: uncemented hemiarthroplasty (n = 53)	12 months	Significantly difference between the two groups for postoperative haemoglobin level, $p = 0.018$, though there was no difference in number of blood transfusions. Average hospital stay was 17.23 in cemented group and 17.46 in cementless group, NS. One year mortality rates were similar between groups.	"Delay of admission to operation, by 3 or more calendar days, almost doubled the risk of mortality within the first year after fractures. This association was not conditional on the number or severity of the medical conditions. Functional results of surviving patients: no significant difference 1 year after surgery."	Cost benefits analysis may not translate to U.S. health system. Treatment delays unlikely to apply to U.S.
Bong 1981 (score= 4.0)	Hip Screw/ Nail vs. Other Approaches	RCT	No mention of sponsorship or COI.	N = 150 Unstable inter-trochanteric fractures	Mean age: 69.3 years; 63 males, 87 females	Skeletal traction with tibial pin vs. medial displacement osteotomy vs. valgus osteotomy	1, 2, 3, 6 months, 1, 2 years	Percentages of cases with poor results: conservative 26.1% vs. medial displacement osteotomy 14.6% vs. valgus osteotomy 20.5%. 1 non-union in conservative group. 1 AVN in valgus osteotomy.27.2% of operative groups had mechanical failure.	"[S]howed no significant difference between those treated with the Dimon and Hughston osteotomy and those treated by the Sarmiento osteotomy. Conservative treatment of skeletal traction for unstable	Data suggest superior results with surgery.

									fracture was found to be well tolerated."	
Sonne-Holm 1982 (score = 3.5)										Author suggests patients and observers were blinded. Lack of methodology details.
Sadr 1977 (score = 2.5)										Variable length follow-ups of 3 to 17 months
Cemented vs. Uncemented										
Taylor 2012 (score = 7.0)	Hemiarthroplasty	RCT	Sponsored by New Zealand Orthopaedic Association, Wishbone Trust, & the Accident Compensation Corporation. CO: one or more of the authors have received or will receive benefits	N = 160 patients with an acute displaced femoral neck fracture	Mean age: 85 years; 50 Males, 110 Females	Group 1: Underwent hip hemiarthroplasty with a cemented femoral stem prosthesis (n = 801) vs Group 2: Underwent hip hemiarthroplasty with a cement-less femoral stem prosthesis (n = 80)	Follow up at 6 weeks, 6 months, 1 year, 2 years	Mean VAS pain score & mean SMFA score appeared better in cemented group compared to uncemented group. Mean Oxford hip score improved better in cemented group than uncemented group at 6 weeks post-op ($p < 0.05$). Patients in cemented group showed improved hip flexion at 6 months & 1 year post op compared with uncemented group ($p = 0.01$). At 6 weeks post-op cemented group was able to flex hip to 45 degrees without pain compared to uncemented group ($p = 0.007$).	"[U]se of a cemented Exeter implant and use of an uncemented Alloclassic implant provided a comparable outcome with regard to pain. However, implant-related complication rates were significantly lower in the group treated with a cemented implant."	Data suggest uncemented group had more complications (especially subsidence and intraoperative or postoperative fracture) and trended towards poorer mobility at 2 years post-op

			for personal or professional use.							
Figved et al. 2009 (score = 7.0)	Hemiarthroplasty	RCT	Sponsored by Eastern Norway Regional Health Authority. COI: one or more of the authors have received funding from Smith & Nephew, Inc., and OrtoMedic AS	N = 220 patients with intracapsular femoral neck fractures	Mean age: 83 years; 53 Males, 167 Females	Group 1: Underwent hip hemiarthroplasty with a cemented femoral stem prosthesis (n = 112) vs Group 2: Underwent hip hemiarthroplasty with a cement-less femoral stem prosthesis (n = 108)	Follow up at 1 week, 3 months, and 12 months	Outcome scales, HHS, BI, and EQ-5D showed no differences between cemented group and uncemented group. Mortality was similar between cemented and uncemented group (1 year p=0.11, 2 year p=0.56)	"The rates of complications and mortality were similar between groups. Both arthroplasties may be used with good results after displaced femoral neck fractures."	Data suggest comparable results in both groups at 12 months
Parker 2010 (score = 6.0)	Hemiarthroplasty	RCT	Sponsored by Peterborough Hospital Hip Fracture Fund. No COI.	N = 400 patients with displaced intracapsular fracture of the hip	Mean age: 83 years; 92 Males, 308 Females	Group 1: Underwent hip hemiarthroplasty with a cemented femoral stem prosthesis (n=200) vs Group 2: Underwent hip hemiarthroplasty with a cement-less femoral stem prosthesis	8 weeks, 3, 6 &9 months, 2-5 years; Mean time of follow up: 3.7 years	Residual pain for cemented group was less than uncemented group at 3 months (p<0.0001), 6 months (p=0.001), 9 months p=0.029), 1 year (p=0.006), and 2 years post-op (p=0.034). No difference in mortality at 1 year with cemented grou at 25% and uncemented group at 28% (p=0.776).	"The use of a cemented Thompson hemiarthroplasy resulted in less pain and less deterioration in mobility than an uncemented Austin-Moore prosthesis with no increase in complications."	Follow-up with many individuals not available for follow-up due to death. Data suggest cemented hemiarthroplasty group was associated with better outcomes (less pain and increased mobility) than uncemented group.

						(n=200)				
Nelissen 2005 (score= 5.5)	Cementation Types, Techniques, and Pressurization	RCT	Sponsored by Stryker, Howmedica, Kalamazoo, MI. COI: One or more of the authors have received or will receive benefits for personal or professional use.	N = 39 THA	No mention of mean age or sex.	Simplex P cement vs. Simplex AF cement; all Exeter prostheses	1 week, 6 weeks, 3 months, 6 months, 1 year, and 2 years postoperatively	No differences in translation or rotation migration. Subsidence of stem at 2-year follow-up was 1.1 +/- 0.56 mm for Simplex AF cement vs. 1.5 +/- 1.00 mm for Simplex P (NS). No significant correlation between minimum and maximum cement mantle thickness around components.	"2 acetabular cups in the Simplex AF group (almost 10%) were revised because of mechanical loosening. Because of these findings, we suggest caution before using this new high-viscosity bone cement for fixation of acetabular components."	Methods details sparse. Suggests very high viscosity may result in loosening, though results are not significant.
DeAngelis 2012 (score = 5.5)	Hemiarthroplasty	RCT	Sponsored by grant from Zimmer, Inc. No COI.	N = 130 patients with displaced femoral neck fracture	Mean age: 82 3± 8.3 years; 60 Males, 100 Females	Group 1: Underwent hip hemiarthroplasty with a cemented femoral stem prosthesis (n=66) vs. Group 2: Underwent hip hemiarthroplasty with a cement-less femoral stem prosthesis (n=64)	30 days, 60 days, and 1 year	Mean hemoglobin levels (g/dL) last in hospital were 10.3 in uncemented group and 10.5 in cemented group (p=0.306). Acute complication rates were 16.7% in cemented group and 18.8% in uncemented group (p=0.756). PADL scores at 1 year post-op were 5.7 for uncemented group and 4.4 for cemented group (p=0.168).	"[T]he use of cemented and uncemented femoral components is associated with similar functional outcome at 1 year"	At 1 month, 2 months, and one year post-op, data suggests comparable outcomes

Talsnes et al. 2013 (score= 5.0)	Hemiarthroplasty	RCT	Sponsored by Charnley Grand from Orthomedic AS, Centre of Medical Science, Education and Innovation, Innlandet Hospital Trust, & Elcerum, Norway. No COI.	N = 334 patients with dislocated cervical hip fracture	Mean age: 84 years; 83 Males, 251 Females	Group 1: Underwent hip hemiarthroplasty with a cement-less femoral stem prosthesis (n=172) vs. Group 2: Underwent hip hemiarthroplasty with a cemented femoral stem prosthesis (n=162)	1 year	One year mortality between cemented and uncemented group similar (p=0.233). Operation time in uncemented group was lower than cemented group (p=0.004). Volume of blood loss lower in uncemented group than cemented group (p=0.043).	"Installation of non-cemented hemiprostheses in elderly with hip fracture may have benefits periopertively regarding operation time and bleeding, and do not seem to influence 1 year mortality relative to cemented patients."	Data suggests at one year mortality rates are comparable between groups but although surgery time and bleeding are less in the non-cemented group, overall complications and reoperations are not addressed.
Emery 1991 (score= 4.5)	Hip Screw/ Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 53 Subcapital fracture	Mean age: 78.8 years; 7 males, 46 females	Cemented vs. uncemented Moore stems	17 months	No pain present in 13/19 (68.4%) cemented vs. 4/20 (25%) uncemented, p = 0.002. More dependency on walking aids after injury in 16 uncemented vs. 8 cemented, p = 0.015.	"After a mean follow-up of 17 months, significantly more of the uncemented group were experiencing pain in the hip and using more walking aids than the patients in the cemented group."	Details sparse. Data suggest cemented stem outperformed uncemented.
Kroon 2006 (score= 4.0)	Comparisons between Different Cement	RCT	Sponsored by A-One Medical B.V., Biomet, DePuy Internati	N = 103 Total hip surgery	No mention of mean age; 29 males, 74 females	Three intramedullary resorbable cement plugs in vitro and in vivo. (1) SEM II plus, (2) C-plug, (3) REX plug.	No mention of follow-up.	In vitro: C-plug unstable 4 of 5 times, SEM II once and minimal cement leakage 4 times. REX plug stable without leakage. In vivo: 17/37 (45.9%) SEM II migrations within 1cm margin. C plug unstable 23/31 (74.2%). REX plug unstable 16/35 (54.3%). Mean migrations	"We do not recommend the use of the C-plug in cemented hip arthroplasty. The REX plug is a promising design; however, insertion problems in vivo lead to	Most significant variables were type of plug (p = 0.02) and size of plug (p = 0.02). Medium-sized plugs were best.

	Restrictors		onal and Stryker. COI: MK was the main investigator for the clinical trial, CPJ co-wrote and supervised, RM co-wrote and investigated, and RB co-wrote and did stats.					corrected for size: C-plug 3.16±0.46 vs. SEM II 1.71±0.46 vs. REX 2.74±0.47.	disappointing results, so the insertion technique must be improved. The SEM II plug performs well in the case of a short stem and has a reproducible insertion technique."	
Vidovic et al. 2015 (score = 2.5)										Sparse methods. Data suggests less MBD reduction in lumbar spine and ipsilateral distal femur in patients with cemented hemiarthroplasty but the cementless group shows less BMD reduction in the contralateral hip and distal femur.
Hemiarthroplasty vs. Internal FixationStoen										
Stoen 2013 (score = 5.5)	hemiarthroplasty	RCT	Sponsored by South-Eastern Norway Regional	N=222 patients with femoral neck fractures	Mean age: 83 years; 57 Males, 165	Group 1: Randomized to be treated by internal fixation (n=122) vs.	4, 12, 24 months, 5-7 years	No difference patient survival at 6 years between Hemiarthroplasty (33.6%) and internal fixation (29.5%) (p=0.51). Reoperation rates were higher in the internal fixation	"Hemiarthroplasty has predicable and good long-term results after FNF and is the treatment of choice compared with internal fixation."	Data suggests survival was comparable between groups, but reoperation rates were higher in the internal fixation group.

			Health Authority. One or more of the authors have received or will receive benefits for personal or professional use.		Females	Group 2: Treated with standard hemiarthroplasty (n=110).		group (43%) than hemiarthroplasty group (10%) (p<0.001)		
Lu 2017 (score = 5.0)	hemiarthroplasty	RCT	No COI. No mention of sponsorship.	N=78 super-aged patients with undisplaced femoral neck fracture	Mean age: 86 years; 20 Males, 58 Females	Group 1: Treated with Multiple Cannulated Screws (MCS) internal fixation (n=41) vs. Group 2: Treated with standard Hemiarthroplasty (n=37)	5 years	Reoperation rates of Hemiarthroplasty group (HA) was lower than Internal Fixation group (IF) (p=0.000). No difference in survival time between HA group and IF group (p=0.682).	"Hemiarthroplasty with less postoperative complications, low reoperation rate and better function recovery in early stage provide a good choice for the treatment of super-aged patients with non-displaced femoral neck fracture.	Data suggests hemiarthroplasty better than internal fixation for non-displaced femoral fractures in the elderly due to less complications, fewer reoperations faster recovery time, and better functional outcomes.
Unipolar vs. Bipolar										
Kanto 2014 (score= 6.5)	hemiarthroplasty	RCT	No mention of sponsorship or COI.	N=175 displaced intracapsular femoral neck	Mean age: 81.7 years; 31 Males,	Group 1: Hemiarthroplasty with unipolar head prosthesis (n=88) vs.	30 days, 90 days, 12 months, 5 years, 8 years	Survivorship of unipolar group at 8-year follow up was 98% vs. 97% in bipolar group (p=0.71).Six patients had dislocations in the unipolar group vs. two patients in the bipolar group (p<0.01).	"Unipolar Hemiarthroplasty group had a significantly higher dislocation rate when compared with bipolar Hemiarthroplasty group.	Data suggests both types of hemiarthroplasty led to comparable ambulatory outcome but the unipolar group had a significantly higher dislocation rate

				fractures in patients over 65 years	144 Females	Group 2: Hemiarthroplasty with bipolar head prosthesis (n=87)			However, both provide elderly patients with equal ambulatory ability and low revision rate at medium-term follow-up.	
Calder 1996 (score= 6.5)	Hip Screw/ Nail vs. Other Approaches	RCT	No mention of sponsorship. No COI.	N = 250 Displaced intracapsular fractures	Mean age: 85 years; 35 males, 215 females	Unipolar uncemented vs. cemented bipolar prothesis	340-864 days	No difference in length of hospital stay. No difference in 1-year survival time. Cemented bipolar prothesis group appeared to enjoy higher levels of function although findings were not statistically significant (return to pre-injury level 39.8% vs. 28.8%, p = 0.07).	"Unipolar prosthesis may give better short-term results in octogenarians. Younger patients may benefit more from a bipolar implant due to more mobility. Regardless of mental state or mobility, we see no justification for the use of expensive bipolar hip prosthesis in patients 80 years or older."	Study lacked power due to high mortality rate at 1-year of 30%. Results showed trend to better functional results with bipolar prosthesis.
Raia 2003 (score= 5.5)	Hip Screw/ Nail vs. Other Approaches	RCT	No mention of sponsorship. COI: M.P Rosenwasser, MD, received funding as a consultant for Stryker Howmedica Osteonics.	N = 115 Displaced femoral neck fractures ages 65+	Mean age: 82.1 years; 32 males, 83 females	Uni- (Unitrax) vs. bi-polar (Centrax) hemi-arthroplasties	3, 12 months	EBL comparable (252 vs. 237mL). SF36 scores for physical function (baseline/3 months/1 year): uni (48.5/54.2/51.6) vs. bipolar (52.1/51/54.2) (NS). General health scores: uni (63.3/65.9/ 72.7) vs. bipolar (66.4/69.1/74.3) (NS).	"[T]he bipolar endoprosthesis provides no advantage in the treatment of displaced femoral neck fractures in elderly patients regarding quality of life and functional outcomes."	Data suggest unipolar prosthesis as bipolar not shown superior. High dropout rate; 24 known deceased at 1 year.

Hedbeck 2011 (score= 5.5)	hemiarthroplasty	RCT	Sponsored by Trygg-Hansa Insurance Company, the Regional Agreement on Medical Traning and Clinical Research between the Stockholm County Council and Karolinska Institute. No mention of COI.	N=120 patients with an acute displaced femoral neck fracture	Mean age: 86.1 years; 29 Males 91 Females	Group 1: Hemiarthroplasty with unipolar head prosthesis (n=60) Vs. Group 2: Hemiarthroplasty with bipolar head prosthesis (n=60)	4 months, 12 months	Man Harris Hip Score at 12 months was 78.2 for unipolar HA vs. 77.7 for bipolar HA (p=1.0). Rate of acetabular erosion with unipolar HA (20%) was higher than bipolar HA (5%) (p=0.03).	"[T]he significantly higher incidence of acetabular erosion in the unipolar HA group may imply that bipolar HA should be the preferred treatment."	Data suggests comparable efficacy at one year but significantly higher incidence of acetabular erosion in the unipolar HA group
Inngul 2013 (score= 5.5)	hemiarthroplasty	RCT	Sponsored by Trygg-Hansa Insurance Company, the Regional	N=120 patients with an acute displaced femoral neck fracture	Mean age: 86.1 years; 29 Males 91 Females	Group 1: Hemiarthroplasty with unipolar head prosthesis (n=60) Vs. Group 2:	4, 12, 24, & 48 months	Mean HRQoL was higher at 48 months in bipolar HA group (0.70) than unipolar HA group (0.59) (p=0.04). Rate of acetabular erosion at 12 months with unipolar HA (20%) was higher than bipolar HA (5%) (p=0.03).	"The bipolar Has seem to result in better HRQoL beyond the first two years after surgery compared to unipolar Has. Bipolar Has displayed a later onset of acetabular erosion	4 year follow up indicate similar efficacy but patients reported better QoL with bipolar device. The bipolar hemiarthroplasty resulted in late onset acetabular erosion

			Agreement on Medical Traning and Clinical Research between the Stockholm County Council and Karolinska Institute and Swedish Research Council. No mention of COI.			Hemiarthroplasty with bipolar head prosthesis (n=60)			compared to unipolar Has."	
Stoffel 2012 (score = 4.0)	hemiarthroplasty	RCT	No mention of sponsorship or COI.	N=261 displaced intracapsular femoral neck fractures	Mean age: 82 ± 7.9 years; 89 Males, 172 females	Group 1: Hemiarthroplasty with cemented prosthesis with unipolar head (n=133) vs. Group 2: Hemiarthroplasty with cemented prosthesis with bipolar head (n=128).	12 months	No difference in functional walking ability or endurance between groups (p=0.446). Self-selected pain ratings did not differ between groups (p=0.236).	"[S]hort term results suggest that unipolar implants share many of the advantages of the bipolar prosthesis but can be manufactured at substantially lower cost."	Data suggests comparable efficacy but unipolar implant are less costly
Jeffcote 2008										Data suggests bipolar hemiarthroplasty performed better than unipolar for

(score = 3.5)										clinical outcomes and acetabular cartilage preservation.
Surgical Approaches for Hemiarthroplasty										
Parker 2015 (score = 5.5)	Hemiarthroplasty	RCT	Sponsored by Peterborough Hospitals Hip Fracture Fund. No COI.	N=216 patients with an intracapsular hip fracture being treated with a cemented hemiarthroplasty	Mean age: 84 years; 18 Males, 198 females	Group 1: Hemiarthroplasty using Lateral Surgical Approach (n=108) vs. Group 2: Hemiarthroplasty using Posterior Surgical Approach (n=108).	1 year	No difference in mean pain scores at 1 year post-op (p=0.18). No difference in mean mobility scores at 1 year post-op (p=0.4).	"[N]o notable differences in the outcomes of pain and mobility between the lateral and posterior surgical approaches for inserting a hip Hemiarthroplasty."	Data suggests comparable results between groups with minimally invasive hemiarthroplasty vs. conventional approach
Field 2005 (score= 5.0)	Hemiathroplasty	RCT	No mention of sponsorship. No COI.	N = 50 Displaced subcapital fractures	Mean age: 81.8±6.4 years; 0 males, 50 females	All used Cambridge cup vs. Cambridge cup with hydroxyapatite coating removed. All Thompson hemiarthroplasties and Palacos-R cement.	6 weeks, 3, 6, 12, 18, 24 months	Mortality at 1, 2, 5 years was 16%, 28%, and 46%. Barthel index score recovered to pre-fracture levels at 2 years, then declined at 5 years to 17.8 in the HA-coated group vs. 17 in the non-coated group (p = 0.177). Charnley modified Merle d'Aubigne scores not different (p = 0.48).	"This trial shows good early results using a novel, hydroxyapatite-coated, physiological acetabular component… Although our retrieval data suggest that the HA-coated components remain well fixed to bone after resorption of the HA, a surface finish known to provide long-term osseointegration may be advantageous."	Experimental study. Data suggest hydroxyapatite coated acetabular cups may have less migration and require fewer revisions. However, functional scores not different.
Renken 2012 (score = 4.5)	Hemiarthroplasty	RCT	No COI. Sponsored by the University Lubeck.	N=60 patients with a femoral neck fracture treated with a	Mean age: 86 years; 10 Males, 50 Females	Group 1: Hemiarthroplasty using Direct anterior surgical approach (DAA) (n=30) vs. Group 2:	40 days	Mean measurement of mobility using Barthel index was 20 for DAA group and 10 for Watson-Jones group at 5 days post-op (p=0.009); 15 for DAA group and 20 for Watson-Jones group at 16 days post-op (p=0.05); 42.5 for DAA group and 30 for Watson-Jones	"[T]he mobilization process in the first 40 days is favourable if a minimal invasive approach is used."	Data suggests minimally invasive approach (DAA) resulted in improved mobilization vs. WJA and less pain. Complications and morality were not addressed

				bipolar hemiarthroplasty		Hemiarthroplasty using Watson-Jones surgical Approach (n=30).		group at 40 days post-op (p=0.013). VAS pain score was 1 for DAA group and 2 for Watson-Jones Group at 16 days post-op (p=0.035); 0 for DAA group and 1 for Watson-Jones at 40 days post-op (p=0.0004).		
Auffarth 2011 (score = 4.0)	Hemiarthroplasty	RCT	No sponsorship. No mention of COI.	N=48 patients treated by hemiarthroplasty of the hip	Mean age: 83.2 years; 10 Males, 38 Females	Group 1: Hemiarthroplasty using Minimally Invasive surgical approach (n=24) vs. Group 2: Hemiarthroplasty using Lateral surgical approach (n=24).	6 months	Median ASA score was 3.0 in lateral approach and 3.2 in the minimally invasive approach (p=0.76). Median change in Harris Hip Score was -8.0 in minimally invasive group and -10.0 in lateral approach (p=0.45). Post-operative pain rated as higher by patients in the minimally invasive group than the lateral approach within the first 4 days post-op (p=0.024).	"[P]ostoperative mobility does not seem to be greatly influenced by the choice of either an anterior modified Smith-Peterson or a lateral Hardinge approach for hip Hemiarthroplasty."	Data suggests comparable efficacy between surgical approaches.

Evidence for the Use of Antibiotics for Hip Surgery

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Antibiotics for surgery; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 56 articles in PubMed, 282 in Scopus, 6 in CINAHL, 8 in Cochrane Library, 18,000 in Google Scholar, and 6 from other sources. We considered for inclusion 15 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 21 articles considered for inclusion, 18 randomized trials and 3 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Bodoky 1993 (Score =10.0)	Antibiotics (Systemic and/or within Cement)	RCT	Sponsored by Ciba-Geigy in Switzerland. The authors declared no COI.	N = 239 Internal fixation with dynamic hip screw for hip fractures	Mean age: 76 years; 55 males, 184 females.	Antibiotic group: patients received cefotiam 2gm at anesthesia induction and 12 hours postoperatively (n=124) vs. placebo group: patients received 2 doses placebo 12 hours postoperatively (n=115).	No mention of follow-up.	Major wound infections: 5% placebo (n = 6) vs. 1% (n = 1) antibiotics (p <0.05). No differences in pulmonary infection (9% vs. 6%). Urinary infections: 31/115 (18%) vs. 15/124 (12%). Pre-op albumin and operation duration most predictive of minor wound infections.	"The most powerful predictors of major wound infection were the duration of the operation, the interval between the accident and admission to the hospital, and the duration of postoperative urinary catheterization. The preoperative level of serum albumin and the absolute lymphocyte count were significant predictors (p<0.05) of minor wound infection and systemic infection, respectively."	Data suggest peri-operative antibiotics effective for reducing risk of major wound infections in hip fracture patients.
Gatell 1984 (Score =8.0)	Antibiotics (Systemic and/or within Cement)	RCT	No mention of sponsorship or COI.	N = 284 any metal device inserted to be eligible (plates, screws, wires). No open fracture; no hip surgery; no joint replacements	Mean age: 55.4 years; 116 males, 168 females.	Group I: patients received cefamandole 2gm IV 30 minutes before, 2gm 2 hours after start of operation, 1gm IV or IM 8, 14, and 20 hours later (n=134) vs. Group II: patients received placebo with identical manner (n=150).	Follow-up at baseline, 12 and 24 months.	Superficial wound infections in 0/ 134 (0%) patients given cefamandole vs. 7/150 (4.7%), p <0.05. Two deep-wound infections developed in cefamandole group vs. four controls (p >0.05).	"Cefamandole (five doses) reduced the rate of wound infection in patients undergoing clean orthopaedic surgery that required an internal fixation device."	Varied diagnoses. Does not apply to hip. Cefamandole appears prevent superficial wounds, but not deep infections. Mortality was higher in Cefamandole group unrelated to infection, although did not reach statistical significance.
Wahlig 1984	Antibiotics (System	RCT	No mention of	N = 30 patients underwe	Mean age: 60 years; 8	Group A: patients received hip replacement using	No mention of follow-up.	Gentamicin concentrations in drainage fluid higher	"[A]pproximately twice as much gentamicin is detectable in the urine and from suction	Pharmacokinetic study without any clinical

(Score =7.0)	ic and/or within Cement)		sponsorsh ip or COI.	nt hip arthropla sty.	males, 22 females.	antibiotic-loaded acrylic cement containing 0.5g (n=15) vs. Group B: patients received 1.0g gentamicin base/ 40g polymer powder with no systemic antibiotics (n=15).		than minimal inhibitory concentrations or minimal bactericidal concentration values necessary for usual pathogens. Serum levels acceptably low.	drainage when one gram is added to 40g of powdered polymer… compared with the half gram used…While these pharmacokinetic results are conclusive, they do not prove whether or not one gram of half a gram of gentamicin added to the cement is more efficacious clinically."	outcomes to indicate reduced infections.
Sprow son 2016 (Score =7.0)	Antibiol otics for surgery	Quasi -RCT	The authors declared no sponsorsh ip or COI.	N=848 patients with intracaps ular hip fracture.	Mean age: 82.6 years; 216 males, 632 females.	Intervention group: patients received dual-antibioctic impregnated cement with high dose 1g of Gentamicin and 1g of Clindamycin (n=400) vs. Control group: patients received single-antibiotic impregnated cement with low dose 0.5g of Gentamicin and Palacos R +G (n=448).	Follow-up at baseline, 12 months.	The primary outcome deep surgical site infection (SSI) in intervention group was significantly lower (1.1%) than that in control group (3.5%) (Odds ratio=0.31; 95%CI=0.09 to 0.88; p=0.041).	"The use of high dose dual-antibiotic impregnated cement in these patients significantly reduces the rate of SSI compared with standard low dose single antibiotic loaded bone cement."	Data suggest statistically significant reduction in deep SSI's in the high dose dual impregnated cement group versus the control group (1.1% vs. 3.5%).
Westb erg 2015 (Score =7.0)	Antibiol otics for surgery	RCT	No mention of sponsorsh ip. The authors declared no COI.	N=684 patients with femoral neck fracture.	Mean age: 82.5 years; 177 males, 507 females.	Gentamicin group: patients received bipolar hemiarthroplasty with 10 x 10 x 0.5 cm gentamicin collagen sponges (n=329) vs. Control group: patients received no placebo sponge (n=355).	Follow-up at baseline, 4 weeks and 6 months.	The primary outcome postoperative surgical site infection score (SSIs) in gentamicin group (16/329, 4.9%) indicated no significant difference with that in control group (19/355, 5.4%) (p=0.77). Also, the superficial SSI in gentamicin group (2/329, 0.6%) showed no significant difference with that in control group (3/355, 0.8%) (p=0.99).	"Locally administered gentamicin-collagen sponges did not reduce the incidence of SSI in elderly patients treated with a hemiarthroplasty because of femoral neck fracture."	Data suggest no additive benefit of gentamicin-containing sponges for the prevention of SSI after hip arthroplasty for femoral neck fracture.

Hedström 1987 (Score =6.5)	Antibiotics for surgery	RCT	No mention of sponsorship or COI.	N=121 patients with trochanteric fracture.	Mean age: 75.9 years; 34 males, 87 females.	Group A: patients received 0.75 gram cefuroxime thrice intravenously per day (n=56) vs. Group B: patients received cefuroxime and then placebo for 6 days (n=65).	Follow-up at baseline, 6 weeks and 4 months.	56 patients in group A completed the treatment of 1 day cefuroxime and 6 days cephalexin regimen; 65 patients in group B completed 1 day cefuroxime regimen.	"There were no differences between the groups. We concluded that the prophylaxis time need not be longer than 3 days."	Data suggest antibiotic prophylaxis should not exceed 3 days.
Nungu 1995 (Score =4.5)	Antibiotics for surgery	RCT	No mention of sponsorship or COI.	N=559 patients with intracapsular / subtrochanteric femoral fracture.	Mean age: 81.5 years; 147 males, 412 females.	Group A: patients received 1 g oral cefadroxil concentrations with 100 ml water 2 hours preoperatively (n=242) vs. Group B: patients received 1.5g intravenous cefuroxime would concentrations with anesthesia injection (n=210).	Follow-up at baseline, 4 weeks and 4 months.	87% patients in group A obtained 4µg/ml cefadroxil and 97% patients in group B has increased minimum inhibitory concentrations (MIC-90). Total infection rate in group A and that in group B showed non-significant significance (P=0.07).	"In conclusion, the oral route for antibiotic prophylaxis in trochanteric femoral fracture surgery with two doses of cefadroxil seems to be practical and as effective as intravenously administered cefuroxime."	No placebo group. Data suggest comparable efficacy between groups.
Kadar 2015 (Score =4.5)	Antibiotics for surgery	RCT	No mention of sponsorship or COI.	N=55 patients with extracapsular or intracapsular hip fracture.	Mean age: 79.6 ± 12.37 years; 18 males, 37 females.	Silver group: patients received Silver Guard dressing with porous adhesive tapes (n=31) vs. Regular group: patients received regular dressing with transparent moisture vapor adhesive permeable film (n=24).	Follow-up at baseline, 5 to 7 days.	Surgical technique in the two groups indicated no significant difference (p=1.0), and skin colonization in both groups showed no significant difference. The regular dressing group showed less cumulative cost than the silver dressing group during postoperative 5th and 7th days: $ 1775 vs. $ 2475.	"The use of SD was associated with higher costs than RD, but not superior in preventing SSIs in elderly patients undergoing hemiarthroplasty or fixation of hip fractures. SD was also not effective in reducing bacterial skin colonisation following hip fracture and surgery."	Data suggest silvery impregnated dressings were not superior to standard dressings in preventing SSIs in elderly hip fracture patients lout bacterial colonization was decreased.
McQueen 1987	Antibiotics (Systemic	RCT	No mention of	N = 295 patients with hip or knee	Mean age: 68 years; 89 males,	Bone cement group: patients received cefuroxime in bone cement (1.5g mixed in	No mention of follow-up.	21 infections in 3 month period (6.8%), 11 (7.5%) in cement vs. 6.7% parenteral (NS).	"Both methods of administering Cefuroxime appear to be satisfactory in the	Data suggest equivalent efficacy for IV vs. antibiotic in the cement

(Score =4.5)	and/or within Cement)		sponsorship or COI.	arthroplasties.	185 females.	40gm CMW cement powder) (n=146) vs. Systematic cefuroxime group: patients received cefuroxime 1.5gm IV at induction and 750mg Q6 hour x 2 (n=149).		Three deep infections, 1 in cement (0.7%) vs. 2 in parenteral (1.3%), (NS).	prevention of early infection after total joint replacement."	for prevention of infections.
Josefsson 1993 (Score =4.0)	Antibiotics (Systemic and/or within Cement)	Ten-Year Survey RCT	No mention of sponsorship or COI.	N = 1688 patients underwent total hip arthroplasties.	Mean age: 69 years; 783 males, 816 females.	SA group: patients received 1 g prophylaxis with systematic antibiotics (SA) 4 time per day in 7-14 days (n=835) vs. GBC group: patients received 1 g gentamicin bone cement (GBC) 4 times per day in 9-11 days (n=853).	Follow-up at baseline, 8.4, 10.3, and 12.6 years.	During 10-year period, 585 hips developed signs of aseptic loosening of 1 or both components: 301 hips (55%) SA; 284 (50%) GBC. Christiansen prosthesis showed high (80%) loosening rate in both groups.	"[T]he differences between the SA and GBC groups found at both the two- and five-year reviews are no longer significant at ten years after surgery."	Methodology details sparse. Systemic antibiotics not standardized at start. Higher rates of aseptic loosening among systemic antibiotic group.
Josefsson 1981 (Score =4.0)	Antibiotics (Systemic and/or within Cement)	RCT	Sponsored by Swedish medical research council. No mention of COI.	N = 1685 patients underwent total hip arthroplasties.	Mean age: 69 years; 783 males, 816 females.	Antibiotics group: patients received 1 g prophylaxis with systematic antibiotics (SA) 4 time per day in 7-14 days (n=835) vs. Gentamicin group: patients received 1 g gentamicin bone cement (GBC) 4 times per day in 9-11 days (n=853).	Follow-up at baseline, 5 years.	Systemic antibiotic: 49 (5.9%) vs. 71(8.3%) gentamicin cement with superficial infections. Difference statistically significant ($p < 0.05$). Deep infections favored gentamicin cement (0.4% vs. 1.6%, $p < 0.01$).	"The difference in deep infection frequency between the antibiotic and gentamicin group was statistically significant."	First of 3 publications on same group. Sparse methodological description weakens score. Systemic antibiotics not standardized. More superficial infections in cement group, but fewer deep infections.
Josefsson 1990 (Score =4.0)	Antibiotics (Systemic and/or within Cement)	Five-Year Survey RCT	No mention of sponsorship or COI.	N = 1,688 patients underwent total hip arthroplasties.	Mean age: 69 years; 783 males, 816 females.	SA group: patients received 1 g prophylaxis with systematic antibiotics (SA) 4 time per day in 7-14 days (n=835) vs. GBC group: patients received 1 g gentamicin bone cement (GBC) 4 times	Follow-up at baseline, 1, 2, and 5 years.	After 1-2 years follow-up, infection rates favored gentamicin cement. After 5 years, difference unaltered. Total 16 deep infections SA group (1.9%), 7 (0.8%) in gentamicin ($p < 0.05$).	"The results of this five-year review clearly showed the prophylactic value of gentamicin cement against deep infection after THA but did not support the hypothesis that this effect was prolonged over one year."	2nd of 3 publications of this population. Participants increased from original. Methodology details sparse. Study demonstrated poor results of Christensen prothesis, which was

						per day in 9-11 days (n=853).		Roentgenographically, aseptic loosening 29% vs. 24% respectively, suggesting admixture of antibiotic did not weaken cement.		"obsolete:" at time of this follow-up.
Buckley 1990 (Score =3.5)										Data suggest empirical use of perioperative cefazolin prophylaxis appears to decrease surgical wound infection rates in hip fracture surgery patients although not statistically significant.
Nungu 1995 (Score =3.5)										Data suggest oral cefadroxil was adequate in most patients for bone and wound concentration but parenteral cefuroxime was better.
McQueen 1990 (Score =3.5)										Data shows lack of efficacy in administration of a single dose of antibiotic prophylaxis to reduce wound infection.
Burnett 1980 (Score =3.5)										Sparse methods. Data suggest prophylactic antibiotics may reduce infections in surgical patients but colonization with antibiotic resistant organisms increased making the argument for storying the antibiotics before colonization occurs.
Kaukonen 1995										Single dose antibiotic upon induction to surgery. Sparse methods. Data suggest lack of efficacy for

(Score =2.5)										cefuroxime group as both groups had similar infection rates.
Hjortrup 1990 (Score =2.0)										Sparse methods and minimal details. Data suggest lack of efficacy of antibiotic prophylaxis but sterile operating environment is essential.

Evidence for the Use of Acupuncture for Hip Arthroplasty

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Acupuncture; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 article in PubMed, 1 in Scopus, 1 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 2 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 2 articles considered for inclusion, 2 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Usichenko 2005 (score= 8.0)	Acupuncture	RCT	No mention of sponsorship or COI.	N = 61 THA	Mean age: 67 years; 24 males, 30 females.	Auricular acupuncture (hip joint, shenmen, lung, thalamus) vs. sham (4 helix points) up to 3 post-op days	Follow-up at baseline and 3 days.	Auricular acupuncture 32% less piritramide vs. control 1st 36 post-op hours (37 vs. 54mg, p = 0.004). Total dose 36% lower (0.54 vs. 0.84 mg/kg, p = 0.002). Time to 1st request lower (40 vs. 25 minutes, p = 0.04).	"(Auricular acupuncture) could be used to reduce postoperative analgesic requirement."	No differences in rates of belief of receipt of real acupuncture.
Usichenko 2006 (score= 7.5)	Acupuncture	RCT	Sponsored by the International College of Acupuncture & Electro-Therapeutics and the New York Academy of Medicine. No mention of COI.	N = 64 THA	Mean age: 67 years; 28 males, 29 females.	Auricular acupuncture (lung, shenmen, forehead, hip) vs. sham (4 helix points)	Follow-up at baseline and 24 hours.	21% less fentanyl (3.9±1.4 vs. 4.9±1.2, p = 0.005) in acupuncture group vs. sham. 6 in acupuncture group required intraoperative atropine vs. 3 (NS).	"Auricular acupuncture reduced fentanyl requirement compared to sham procedure during hip arthroplasty."	Data suggest mild reduction in fentanyl. No other differences. Considering quality evidence, traditional acupuncture not superior to sham for LBP, arthritis. Study requires replication.

Evidence for the Use of Compression Stockings

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Compression Stockings; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized

controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 43 in Scopus, 3 in CINAHL, 1 in Cochrane Library, 1040 in Google Scholar, and 4 from other sources. We considered for inclusion 3 from PubMed, 1 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 6 from other sources. Of the 13 articles considered for inclusion, 13 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Robinson 1997 (score=9.0)	Compression Devices vs. Other Treatment	RCT	Sponsored by the Medical Research Council of Canada. Dr. Anderson is a Research Scholar of the Canadian Heart and Stroke Foundation.	N = 1,024 Total hip or knee replacement	Mean age: 67.3 years; 400 males, 624 females.	Bilateral screening compression ultrasonography (n=518) - using a high-resolution color duplex-doppler scanner with an electronically focused linear array transducer and either 5- or 7.5-MHz probes. vs. sham ultrasonography (n=506) – designed to mimic the technique of the genuine compression ultrasonography.	3 months.	518 screening compression ultrasonography; 19 (3.7%) positive result; 6/19 proximal DVT excluded by venography; 4 (0.8%) developed symptomatic proximal DVT. All 4 normal results on screening compression ultrasonography. Of 506 randomly assigned to sham ultrasonography, 3 developed symptomatic DVT, 2 non-fatal symptomatic PE. Total primary outcome cluster event rate 1% (CI, 0.3-2.2%).	"Our results suggest that continuing warfarin prophylaxis beyond an average of 9 days after total hip or knee arthroplasty would be of little value, given the low rate of symptomatic venous thromboembolic complications."	Unusual blinding: techs had blank screen during sham so not to affect results. Followed all excluded patients who gave informed consent. Co-interventions mentioned but not accounted for.
Kalodiki 1996 (score=7.0)	Compression Devices vs. Other Treatment	RCT	Sponsored by Rhone-Poulenc-Rorer. No mention of COI.	N=93 patients having unilateral total hip replacement	Mean age: 69 years; 43 males, 50 females.	Group A Placebo (n=14) Vs. Group B Low weight molecular heparin (enoxaparin 40 mg once daily) (n=32) Vs. Group C Enoxaparin (40 mg once daily) plus graduated elastic compression (TEDR) (n=32). All treatments lasted 8-12 days.	No follow up.	Controls discontinued as 93% developed DVT vs. 23% in enoxaparin and 20% in enoxaparin plus stockings (p <0.001). Patients then randomized to enoxaparin vs. enoxaparin plus stockings. Enoxaparin plus stockings reduced proximal DVT (p<0.01). PE in 42% controls, 10% of enoxaparin vs. 6% of enoxaparin plus stockings, (p <0.01).	"[O]ne subcutaneous daily dose of enoxaparin 40 mg was at least as effective and well tolerated as standard LDH. The effect of the combined use of LMWH with GEC stockings in the prevention of DVT in patients having total hip replacement has not been evaluated."	Placebo for meds blinded, but 1 group had stockings, not blinded. Meds after discharge unclear. Data suggest efficacy compared with placebo, and that enoxaparin plus stockings superior to medication alone as well as placebo.

Bailey 1991 (score=6.5)	Compression Devices vs. Other Treatment	RCT	Sponsored by Kendall Corporation. No mention of COI.	N= 95 patients with deep vein thrombosis (DVT) after total hip arthroplasty (THA)	Mean age: 64.9 years; 46 males, 49 females.	Low-dose warfarin (LDW) (n=45) vs. sequential compression devices (SCD) (n=50) after total hip arthroplasty.	No follow up.	DVT in 12/45 (26.6%) on LDW vs. 3/50 (6%) with SCDs, p <0.006.Venous thrombi in 12/46 (26%) primary THAs and 3/42 (7.1%) revision cases.	"[L]DW was found to be more protective than SCDs against thigh thrombi…SCDs were found to be significantly better then LDW at reducing the overall thrombi rate. However, the thrombi, when present, typically occurred in clinically serious locations."	SCD better at reducing total rate.
Pitto 2004 (score=6.5)	Compression Devices vs. Other Treatment	RCT	No mention of sponsorship. The author or one or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of	N = 200 patients with venous thromboembolic disease (DVT) after total hip replacement (THR)	Mean age: 57.7 years; 62 males, 138 females.	Foot-pump group: received A-V impulse system foot pump (compression cycle of 20 seconds at 13. mmHg for 1 second) and patients wore bilateral thigh-high anti-thromboembolic stockings (n=100) vs. LMWH Group: received subcutaneous low molecular weight heparin (dose weight dependent 0.2-0.6 mL=950 IU of anti-Xa) 12 hours before operation (Fraxiparin) (n=100). All treated with stockings.	3, 10 and 45 days.	DVT in 3/100 pump vs. 6/100 LMWH (p <0.05). Greater post-op draining in LMWH (p <0.05).	"The foot pump was associated with greater effectiveness than LMWH and lacked the side effects of chemical intervention"	Used hose, no mention of meds. Notes some patients do not tolerate pump; suggests efficacy.

			this article. In addition, benefits have been or will be directed to a research fund, foundation, educational institution, or other nonprofit organisation with which one or more of the authors are associated.							
Hull 1990 (score=6.5)	Compression Devices vs. None	RCT	Sponsored by Ontario Ministry of Health, Toronto, Canada; the Heart and Stroke Foundation of	N = 310 THR	Mean age: 65 years; 128 males, 182 females.	Sequential intermittent calf and thigh compression (n=152) vs placebo for 14 days (n=158). Total hip arthroplasties	3 months.	DVT in 77/158 (49%) in controls vs. 36/152 (24%) of compression group (p = 0.0001).	"[S]equential intermittent leg compression is effective for reducing the frequency of calf vein and proximal vein thrombosis following total hip replacement. Intermittent compression also reduced the extent of deep vein thrombosis as	Data suggest efficacy.

			Ontario, Toronto, Canada; and the Canadian Heart Foundation, Ottawa. No mention of COI.						measured impedance plethysmography."	
Bradley 1993 (score=6.0)	Compression Devices vs. None	RCT	No mention of sponsorship or COI.	N = 74 THA	Mean age: 70 years; no mention of gender ratios.	Compression foot pump (n=30) vs. no foot pump post-operatively until discharge (n=44). All thigh-length compression stockings, heparin 5000 IU SC BID, hydroxychloroquine sulphate 40mg BID.	No follow up.	12 (27.3%) thromboses in non-pumped vs. 2 (6.6%), p <0.025.	"[T]he combination of chemical prophylaxis, graded compression stockings, and the arteriovenous impulse system reduces the incidence of deep venous thrombosis further than when chemical prophylaxis is used alone."	DOB used to randomize. One group larger than other by chance. Data suggest pump helpful adjunctive treatment.
Gallus 1983 (score=6.0)	Compression Devices vs. None	RCT	No mention of sponsorship or COI.	N = 98 THR	Mean age: 68 years; 35 males, 55 females.	Intermittent foot/calf compression 1 week (n=43) vs. untreated (n=47). Compression continuous day/night other than walk, PT, etc.	No follow up.	15/43 (35%) compression vs. 25/47 (53%) controls with DVT (NS).Incidence of calf vein thrombosis lower among treated patients 45 vs. 16 %, p <0.005.	"Intermittent calf compression significantly reduced the postoperative calf vein thrombosis rate by 64 percent."	Data suggest efficacy.
Woolson 1991 (score=5.0)	Compression Devices vs. Other Treatment	RCT	No sponsorship. No mention of COI.	N = 239 THA	Mean age: 65.4 years; 95 males, 112 females.	Group I - Thigh-high stocking with graduated elasticity, thigh-high 6 chambered boot for sequential intermittent compression (n=76)	3 months.	196 patients included. DVT in 12% of intermittent compression vs. 10% of intermittent compression plus aspirin vs. 9% of compression plus warfarin group (p = 0.8).	"Intermittent compression during and after the operation effectively reduces the rate of proximal-vein thrombosis after total hip replacement."	Blinding of radiologist unclear. Small amount of variation in timing to check for DVT. No mention of co-interventions. Conclusion regarding efficacy of compression unclear as no placebo/ control for that

						vs. Group II - elastic stockings, intermittent pneumatic-compression boots, 650mg aspirin orally BID beginning evening before operation (n=72) vs. Group III - elastic stockings, compression boots, 7.5 or 10mg warfarin orally evening before operation (n=69).				treatment. Study suggests addition of ASA or warfarin not significant.
Hui 1996 4.0 (score=5.0 for TKA patients)	Compression Stockings vs. No Stockings	RCT	Sponsored by Brevet Hospital Products. No COI.	N = 177 Total hip or knee arthroplasties	Mean age: 68.9 years; 55 males, 88 females.	Above vs. below-knee graded compression stocking (n=84) vs. controls (n=54).	No follow up.	DVT on venograms in 27% controls vs. 22% above-knee vs. 50% below-knee stockings of THR patients. Knee rates 78% vs. 65% vs. 68%. THR patients wearing below-knee stocking had a higher rates of proximal or major calf DVT (p = 0.03).	"[W]ith the exception of below-knee stockings in knee replacement patients, graded compression stockings were ineffective in preventing DVT after hip or knee replacement surgery."	Two studies done together analyzed differently. Included lower risk patients. THA groups less comparable.
Kaempffe 1991 (score=5.0)	Compression Devices vs. Other Treatment	RCT	No mention of sponsorship or COI.	N = 149 Total hip or knee arthroplasty	Mean age: 64 years; 98 males, 2 females.	Coumadin group - Coumadin 10mg night before surgery, 5mg night after, then dose keeping PT = 15s (n=52) vs. IPC group - thigh-length intermittent pneumatic compression (IPC). Treatment duration unclear, appears to be during	No follow up.	13/52 (25%) had roentgenographic DVT evidence 5/21 (24%) total hip arthroplasty patients developed DVT. Overall DVT incidence with IPC 12/48 (25%) vs. 13/52 (25%) on coumadin. Following total hip arthroplasty, the IPC group was more effective at preventing DVT (16% vs 24% in coumadin).	"36% of patients (5/14) who were treated with revision surgery developed DVT despite prophylaxis (4/10 in the Coumadin group and ¼ in the IPC group). These figures may indicate that neither Coumadin nor IPC are effective in the prevention of thrombi in this group of patients."	Relatively small numbers of subjects. Different clotting risk in revision THA. Data suggest equivalency.

						hospitalization (n=48).				
Santori 1994 (score=5.0)	Compression Devices vs. Other Treatment	RCT	No sponsorship. No mention of COI.	N = 132 THR	Mean age: 71 years; 34 males; 98 females.	Heparin group - Calcium heparin 5000 IU TID (n=65) vs. A-V- Impulse system group - intermittent plantar pump for 10 days. Pump used except when walking or PT (n=67).	No follow up.	23/65 (35.4%) DVT in heparin group vs. 9/67 (13.4%) in plantar foot pump (p <0.005). "The differences for all thromboses and for major thromboses were highly significant at P<0.005."	"Because of the potential complication of pharmacological prophylaxis, it seems that impulse pumping may become the treatment of choice for the prophylaxis of DVT and PE."	Blinding unknown for assessor. Mentions only some co-interventions.
Cohen, 2006 (score=4.5)	Compression Stockings for Prevention of Venous Thromboembolic Disease/Factor XA Inhibitors	RCT	No mention of sponsorship. COI: one, or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of	N = 795 patients undergoing primary or revision total hip replacement or surgery for fracture of the proximal third of the femur.	Mean age: 65 years; 343 males, 452 females.	Fondaparinux – patients received fondaparinux (2.5 mg daily) for 5-9 days (N = 400) vs Fondaparinux and GCS – patients received fondaparinux (2.5 mg daily) for five to nine days plus graduated compression stockings for 35 to 49 days (N = 395)	At end of Fondaparinux and GCS treatment arm.	The venous thromboembolism or sudden death by day 42 outcome measure in Fondaparinux group (%) was 22, Fondaparinux plus GCS (%) was 19, adjusted odds ratio (95% CI) was 0.88 (0.46 to 1.65), p = 0.69.	"The addition of graduated compression stockings does not appear to improve the effectiveness of prophylactic anticoagulation with fondaparinux. As graduated compression stockings are time-consuming to measure and fit, inconvenient, and expensive, we recommend that their use in hip surgery be reconsidered. In future, their use may be replaced by a more extended period of anticoagulation."	Study terminated early. Data suggest compressive stockings do not add benefit to fondaparinux (low molecular heparin)

			this article.							
Kennedy, 2000 (score=3.5)	Compression Stockings for Prevention of Venous Thromboembolic Disease									Data suggest comparable efficacy between pumps and aspirin.

Evidence for the Use of Lower Extremity Pumps

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Lower extremity pumps, Intermittent Pneumatic Compression Device, Lymphedema, Lymphedema Pump, Compression devices, foot pump, Leg Compression Machine, Bio Compression Systems, Sequential Compression Device, arteriovenous impulse system, mechanical prophylaxis; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 articles in PubMed, 8 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 8440 in Google Scholar, and 7 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 7 articles considered for inclusion, 4 randomized trials and 0 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Pitto 2004 (score= 6.5)	Compression Devices vs. Other Treatment	RCT	No mention of sponsorship. The author or one or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article. In addition, benefits have been or will be directed to a research fund, foundation, educational institution, or other nonprofit organisation with which one or more of the authors are associated.	N = 200 patients with venous thromboembolic disease (DVT) after total hip replacement (THR)	Mean age: 57.7 years; 62 males, 138 females.	Foot-pump group: received A-V impulse system foot pump (compression cycle of 20 seconds at 13. mmHg for 1 second) and patients wore bilateral thigh-high anti-thromboembolic stockings (n=100) vs. LMWH Group: received subcutaneous low molecular weight heparin (dose weight dependent 0.2-0.6 mL=950 IU of anti-Xa) 12 hours before operation (Fraxiparin) (n=100). All treated with stockings.	3, 10 and 45 days.	DVT in 3/100 pump vs. 6/100 LMWH ($p < 0.05$). Greater post-op draining in LMWH ($p < 0.05$).	"The foot pump was associated with greater effectiveness than LMWH and lacked the side effects of chemical intervention"	Used hose, no mention of meds. Notes some patients do not tolerate pump; suggests efficacy.
Bradley 1993 (score= 6.0)	Compression Devices vs. None	RCT	No mention of sponsorship or COI.	N = 74 THA	Mean age: 70 years; no mention of gender ratios.	Compression foot pump (n=30) vs. no foot pump post-operatively until discharge (n=44). All thigh-length compression stockings, heparin 5000 IU SC BID, hydroxychloroquine sulphate 40mg BID.	No follow up.	12 (27.3%) thromboses in non-pumped vs. 2 (6.6%), $p < 0.025$.	"[T]he combination of chemical prophylaxis, graded compression stockings, and the arteriovenous impulse system reduces the	DOB used to randomize. One group larger than other by chance. Data suggest pump helpful adjunctive treatment.

									incidence of deep venous thrombosis further than when chemical prophylaxis is used alone."	
Gallus 1983 (score= 6.0)	Compression Devices vs. None	RCT	No mention of sponsorship or COI.	N = 98 THR	Mean age: 68 years; 35 males, 55 females.	Intermittent foot/calf compression 1 week (n=43) vs. untreated (n=47). Compression continuous day/night other than walk, PT, etc.	No follow up.	15/43 (35%) compression vs. 25/47 (53%) controls with DVT (NS).Incidence of calf vein thrombosis lower among treated patients 45 vs. 16 %, p <0.005.	"Intermittent calf compression significantly reduced the postoperative calf vein thrombosis rate by 64 percent."	Data suggest efficacy.
Santori 1994 (score= 5.0)	Compression Devices vs. Other Treatment	RCT	No sponsorship. No mention of COI.	N = 132 THR	Mean age: 71 years; 34 males; 98 females.	Heparin group - Calcium heparin 5000 IU TID (n=65) vs. A-V- Impulse system group - intermittent plantar pump for 10 days. Pump used except when walking or PT (n=67).	No follow up.	23/65 (35.4%) DVT in heparin group vs. 9/67 (13.4%) in plantar foot pump (p <0.005). "The differences for all thromboses and for major thromboses were highly significant at P<0.005."	"Because of the potential complication of pharmacological prophylaxis, it seems that impulse pumping may become the treatment of choice for the prophylaxis of DVT and PE."	Blinding unknown for assessor. Mentions only some co-interventions.

Evidence for the Use of Low-Molecular Weight Heparin

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Low-Molecular-Weight Heparin; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 45 articles in PubMed, 168 in Scopus, 18 in CINAHL, 24 in Cochrane Library, 6400 in Google Scholar, and 48 from other sources. We considered for inclusion 5 from PubMed, 0 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 46 from other sources. Of the 52 articles considered for inclusion, 48 randomized trials and 5 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Heit 2000 (score =11.0)	Low Molecular Weight Heparin vs. Placebo	RCT	Grant support by Wyeth-Ayerst Research, Philadelphia, Pennsylvania. No mention of COI.	N = 1195 Total hip or knee arthroplasty	Mean age: 65.5 years; 540 males, 655 females.	All received open label treatment for 4 to 10 days. Then randomized to extended treatment with daily subcutaneous ardeparin (100 anti-X_a IU/kg (n=607) vs placebo for total hip or knee replacement from hospital discharge to 6 weeks after surgery. (n=588)	Follow up at 10-12 weeks.	Incidence of 9 (1.5%) with extended treatment vs. 12 (2.0%) for placebo, OR = 0.7 (0.3-1.7), p >0.2.	"The low rate of symptomatic venous thromboembolism in the part B placebo is consistent with the hypothesis that most cases of asymptomatic deep venous thrombosis that occur despite in-hospital low-molecular-weight heparin prophylaxis are not clinically important. Our findings call into question the need for extended out-of-hospital prophylaxis in all patients undergoing elective hip replacement."	Low number of higher risk patients, thus article primarily addresses low risk. Study primarily addresses benefit of extended treatment as all initially were actively treated.
Beisaw 1988 (score =11.0)	Heparin vs. Placebo	RCT	Funded by the Sandoz Research Institute. No COI.	N = 148 THA	Mean age: 65.2 years; 52 males, 76 females.	Dihydro-ergotamine 0.5mg and heparin sodium 5,000 units (n=63) vs. placebo of lidocaine hydrochloride for 7-9 days (n=65)	Follow up on day 3 and 7.	128 patients completed the study; 52.3% placebo vs. 25.4% dihydroergotamine mesylate/heparin sodium developed DVT, p = 0.0021. No PEs.	"[T]he combination agent dihydroergotamine mesylate/heparin sodium was effective and safe prophylaxis against deep-vein thrombosis for the patients who underwent total hip replacement in this study."	Heparin appears more effective for reducing proximal thrombi; thought more clinically useful. Intent to treat done on efficacy study, not safety.
Eriksson 2006 (score =10.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other	RCT	This study was supported by Bayer HealthCare AG	N = 722 THR	Mean age: 65.0 years; 284 males, 420 females.	Oral BAY 59-7939 2.5, 5, 10, 20, or 30mg BID (n=572) vs. enoxaparin 40mg QD for 5-9 days after surgery (n=132)	Follow up 30-60 days after receiving last dose of drug.	VTE in 15%, 14%, 12%, 18%, and 7% of patients (2.5, 5, 10, 20, and 30mg) vs. 17% enoxaparin. Comparable major VTEs. Major, postoperative bleeding not different (NS).	"[I]n patients at high risk for developing thrombosis and bleeding, direct FXa inhibition with BAY-59-7939 was effective across the dose range studied, and compared favorably with enoxaparin; safety was similar between BAY 59-7939 2.5-10mg twice daily and enoxaparin."	Data suggest comparable efficacy.

	Treatments									
Eriksson 2006 (score =10.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	Study was sponsored by Bayer HealthCare. No mention of COI.	N = 873 THR	Mean age: 64.9 years; 347 males, 498 females.	Phase 2 study. Oral rivaroxaban 5, 10, 20, 30, or 40mg once daily (n=713) vs subcutaneous enoxaparin 40mg once daily for 5-9 days after totally hip replacement. (n=160)	Follow up 30-60 days after receiving last dose of drug.	Major postoperative bleeding in 2.3%, 0.7%, 4.3%, 4.9%, and 5.1% (5, 10, 20, 30, and 40mg rivaroxaban) vs. 1.9% with enoxaparin (NS). DVT incidence was 14.9%, 10.6%, 8.5%, 13.5%, 6.4% for rivaroxaban vs. 25.2% for enoxaparin.	"[A]n 8-fold dose of rivaroxaban (to 40 mg) given once daily postoperatively showed similar efficacy to enoxaparin (40mg once daily) for the prevention of VTE after elective total hip replacement surgery, without the need for routine coagulation monitoring. Major bleeding rates observed in the 5- and 10-mg rivaroxaban once daily dose groups were similar to those with enoxaparin."	Suggests rivaroxaban has lower risk of DVT.
Kakkar 2000 (score =10.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	Financially supported by Knoll AG. No mention of COI.	N = 298 Hip arthro-plasties	Mean age: 59.6 years; 630 males, 721 females.	Bemiparin 3,500 IU SC once daily plus placebo injection (saline) (n=655) vs. 5,000 IU Unfractionated heparin 5,000 IU BID 2 hours before surgery continued for at least 8 days post surgery (n=677)	Follow up on day 12.	DVT in 9/101 (8.9%) of bemiparin vs. 24/116 (20.7%) UFH (p = 0.03). Total VTE: 9 (7.2%) bemiparin vs. 25 (18.7%) UFH, p = 0.01. 37 patients adverse events either during in patient stay or during follow up, 22 adverse events bemiparin vs. 15 UFH, p = 0.20. One bemiparin patient died on 3rd post-op day and 3 died during follow-up. S major bleeds, but not different (NS).	"[B]emiparin, a second generation LMWH, administered subcutaneously once daily, at a dose of 3,500 IU in high risk patients undergoing hip arthroplasty is more effective but equally safe in preventing post-operative DVT than standard UFH administered twice daily at a dose of 5,000 IU."	Not clear ITT used. Strongly supports LMWH to prevent DVT.
Bara 1999 (score =10.5)	Low Molecular Weight Heparin vs.	RCT	No mention of sponsorship or COI.	N = 440 THR	No mention of age or sex.	4,500IU anti-Xa tinzaparin vs. 4000IU anti-Xa (40mg) enoxaparin for 8-14 days	Follow up with clinical examination daily from day 1 to days 8–14 and bilateral	DVT rate was similar in both groups 21.7% and 20.1%. Mean plasma anti-Xa activity was significantly higher in the enoxaparin group.	"A significant correlation was observed between anti-IIa activity and anti-Xa activity and the dose of each LMWH injected. The anti-Xa activity was significantly higher with enoxaparin and the anti-IIa	Actual study of DVT published (Planes, et al 1999). Used much of same scoring. Most details are left out of this report.

	Other LMWH Doses or Other Treatments						venography on days 8–14.		activity was significantly higher with tinzaparin. No clear relationship between these two activities and the clinical outcomes was observed."	
Planes 1996 (score =10.5)	Low Molecular Weight Heparin vs. Placebo	RCT	No mention of sponsorship or COI.	N = 179 THR	Mean age: 69.0 years; 102 males, 77 females	Enoxaparin 40mg SC QD (n=90) vs. placebo 12 hrs preop, 12 hours post-op then QD for 21±2 days (n=89)	Follow up 21 days after discharge	Six patients rejected because of unsuccessful second bilateral phlebography with 18 more rejected from study, leaving 155 fully compliant patients. 7.1% vs. 19.3% enoxaparin with DVT (p=0.018). Trend towards enoxaparin for proximal DVT (p = 0.064). No deaths.	"[I]n patients who have undergone THR, who do not have venogram-proven DVT at hospital discharge, and who do not receive antithrombotic prophylaxis after discharge, the risk for late-onset DVT remains high for 35 days after surgery. Continued prophylaxis with enoxaparin is an effective and safe way to reduce the rate of DVT in such patients."	Data demonstrate efficacy among usual THR patients. Both efficacy & safety ITT analyses. Data may suggest longer treatment.
Comp 2001 (score =10.0)	Low Molecular Weight Heparin vs. Placebo	RCT	Funded by Aventis Pharmaceuticals, Incorporated, Bridgewater, New Jersey, and Aventis Pharma, S.A., Antony, France, formerly Rhône-Poulenc	N = 873 Total hip or knee replacement	Mean age: 65.1 years; 469 males, 404 females.	Enoxaparin 40mg QD (n=441) vs. placebo for 12 weeks (n=432)	Follow up at day 90.	Prevalence of venous thromboembolism in enoxaparin 8% (18/224) vs. 23.2% (49/211) for placebo (p <0.001). OR = 3.62 (95% CI 2.00- 6.55), Relative risk reduction 65.5%.	"[T]he recommended seven to ten-day postoperative thromboprophylactic regimen of 30mg of enoxaparin twice daily for patients treated with total hip replacement is suboptimal and that a substantial therapeutic benefit is gained, without compromising safety, by prolonging the enoxaparin treatment (at a dose of 40mg once daily) for an additional three weeks postoperatively (resulting in a total of four weeks of enoxaparin treatment)"	Suggests efficacy. Includes younger patients. Stratified analyses suggest no effect in males with knee replacement. Suggests treatment for 4 weeks.

			Rorer Pharma, S.A., Collegeville, Pennsylvania, and Antony, France. COI: One or more of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article							
Adolf 1999 (score =9.5)	Low Molecular Weight Heparin vs.	RCT	No mention of sponsorship or COI.	N = 172 THR	Mean age: 68 years; 134 males, 207 females.	Certoparin 3,000 IU aXa (n=172) vs. 5,000 IU aXa low molecular weight heparin daily 12-14 days (n=169)	Follow up on the 12th and the 14th postoperative day.	DVTs in 8.7 (3,000) vs. 7.1% (5,000 IU) (NS). Bleeding rates not different except cell saver volumes (770±136 vs. 475±186ml; p <0.001).	"[C]onventional dosage (3,000 IU aXa/day) of certoparin ensures maximal antithrombotic activity."	No physical. Concealment unclear. Suggests 3,000 dose sufficient.

	Other LMWH Doses or Other Treatments									
Levine 1991 (score =9.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	Grant support from the Heart and Stroke Foundation of Ontario and the Medical Research Council of Canada. No mention of COI.	N = 669 Hip replacement	Mean age: 66.5 years; 305 males, 360 females.	Low molecular weight heparin 30mg (n= 333) vs. standard calcium heparin 7,500U SC BID. First dose 12-24 hours after surgery continued for 14 days or until discharge. (n=263)	Follow up on day 10 and 14, or sooner if pt ready for discharge.	Thrombi in 57/333 (17.1%) LMWH vs. 63/332 (19.0%) standard. Total bleeding events in 5.1% vs. 9.3%, p = 0.035.5.7% standard heparin vs. 3.3% LMW heparin with major bleeding, p = 0.13. No differences in transfusions (NS).	"Low molecular weight heparin is significantly less hemorrhagic than standard unfractionated heparin; the difference in the rate of deep vein thrombosis, although not statistically significant (p>0.2), favors the use of LMW heparin."	Data suggest LMWH not superior, although trend towards more thrombi in standard heparin group and less hemorrhage.
Eriksson 1991 (score =9.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	Funding sources were grants from the Swedish Medical Research Council, Project 00660 & The Medical Society of	N = 136 THR	Mean age: 68.7 years; 56 males, 79 females.	Low molecular weight heparin 5000 IU SC QD (n=67) vs. unfractionated heparin 5000U TID for 10 days (n=69)	Follow up at 6-8 weeks postoperative.	DVT in 30.2% LMWH vs. 42.4% unfractionated heparin (NS). PE in 12.3% LMWH vs. 30.6% (p = 0.016).Total blood loss and total blood transfused higher with standard heparin.	"The efficacy of low-molecular-weight heparin was superior to that of standard heparin in the prevention of femoral thrombosis and pulmonary embolism, although the over-all incidence of deep-vein thrombosis was not statistically different. Safety was also improved, since the over-all volumes of blood loss and transfused blood were significantly less in the	Medications not mentioned. Data suggest LMWH superior.

			Gothenburg; and Gothenburg University. No COI.						patients who received low-molecular-weight heparin."	
Lassen 1998 (score =9.5)	Low Molecular Weight Heparin vs. Placebo	RCT	No mention of sponsorship. COI: The authors comprise the DaPP Study Group; principal investigators and writing committee members are M.R. Lassen and L.C. Borris.	N = 281 THR	Mean age: 69.0 years; 128 males, 152 females.	Dalteparin 40mg (n=140) vs. placebo QD for 35 days (n=141)	Follow up at day 35	17 (8%) patients developed DVT. Risk of postoperative DVT reduced 63%. Serious adverse events less frequent in the dalteparin group 4/140 (2.9%) vs. placebo 9/141 (6.4%).	"[P]rolongation of prevention with dalteparin for 35 days is effective and safe, but further new studies with prolonged prophylaxis using clinical endpoints, such as survival with an observation period of at least 2-3 years, are warranted."	Suggests efficacy.
Agnelli 1992 (score =9.5)	Dermatan Sulphate vs. Placebo	RCT	No mention of sponsorship or COI.	Phase 1: N = 80 Phase 2: N = 126 Hip fracture	Mean age: 75.2 years; 27 males, 99 females	2-ml ampules of MF 701 dermatan sulphate 100 or 200 mg vs. placebo (saline solution) for 14 days in non-operated patients or 10 days post-operative	Post-operatively, 1 day, 10 days, 14 days	MF 701 had no protective effect against total or proximal DVT. DVT incidence 64.9% in MF 701 vs. 51.4% in placebo (NS) (proximal DVTs 40.5% vs. 29.7%). No difference in bleeding; 6 patients died, 3 in-hospital, 3 during follow up. In Phase 2, 37.8% of MF	"[O]ur study provides the first clinical demonstration that dermatan sulphate is an effective and remarkably safe antithrombotic agent. This result was obtained in a patient population that tends to be resistant to conventional measures for DVT prophylaxis, often	Some co-interventions. Phase 1 and 2 studies. Trend towards more DVT in active treatment group in one study and towards placebo in other.

								701 group, 63.9% of placebo group developed DVT (p = 0.01). 3 patients died, 2 in hospital, 1 during follow-up.	resulting in side effects. Our study also provides evidence of the biological role of HC II."	
Westrich 2005 (score =9.0)	Heparin vs. Placebo	RCT	Benefits or funds were received in partial or total support of the research material described in this article from the Orthopaedic Research and Education Foundation. No mention of COI.	N = 165 THA	Mean age: 73 years; 62 males, 72 females.	Unfractionated heparin 1 IV dose intra-operative before femoral preparation (n=69) vs. IV saline. Both treated with elastic stockings and 325mg aspirin BID 1 month. (n=60)	Follow up at 3 months.	Evaluated with MR venograms. No increased blood loss, bleeding, units transfused hemoglobin/ hematocrit with heparin. No clinical PE or symptomatic thrombo-emboli observed. No demonstrated reduction of thrombosis with heparin (13% vs. 10.8%, p >0.05).	"[P]elvic thrombi may form following THA and that a single dose of intraoperative heparin does not prevent their formation, but may be effective at preventing ipsilateral femoral thrombi."	Single-dose heparin. Included those usually excluded. Minimal post-surgical prophylaxis. No efficacy of single dose heparin for DVTs.
Turpie 1986 (score =9.0)	Low Molecular Weight Heparin vs. Placebo	RCT	Supported by grants from The Heart and Stroke Foundation of Ontario and the	N = 100 Elective hip surgery	Mean age: 67.1 years; 48 males, 52 females.	PK10169 low-molecular-weight heparin (n=50) vs placebo for 14 days (n=50)	Follow up at days 5, 7, 9, 11, and 13.	Thromboses in 6/50 (12%) on low-molecular-weight heparin vs. 21/50 (42%) on placebo (p = 0.0007). Hemorrhagic complications in 2/50 on LMWH vs. 2/50 on placebo (NS).	"The marked reduction in proximal-vein thrombosis indicates that prophylaxis with PK10169 heparin is effective in reducing the risk of clinically important thromboembolic events in patients undergoing elective hip replacement."	Data support efficacy vs. placebo. Appear to be lower risk patients. Concealment implied. Physical examination not mentioned.

			Medical Research Council of Canada. No mention of COI.							
Arnesen 2003 (score =9.0)	Low Molecular Weight Heparin vs. Placebo	RCT	No mention of sponsorship or COI.	N = 265 THR	Mean age: 71 years; 77 males, 188 females.	Dalteparin 5000IU vs. placebo for 35 days	Follow up at days 1, 6, and 35.	Differences at day 35 significant for F1+2 (p = 0.02), TAT (p = 0.01) and D-dimer (p <0.001) with highest values in placebo group, and also for PA1-1act (p = 0.04) with highest values with dalteparin. 32/104 (33%) on placebo had venographically proven DVT vs. 22/114 (19%) on dalteparin at day 35.	"[D]emonstrated that the well known initial activation of coagulation after HRS is sustained at least for 35 days postoperatively, and that this activation is significantly reduced by the subcutaneous administration of dalteparin 5000 IU od."	Thrust of study mechanistic. Suggests efficacy. D-dimer decreased in placebo group that does not have DVT. Score relies on Dahl 1997 for methods.
Jorgensen 1992 (score =9.0)	Low Molecular Weight Heparin vs. Placebo	RCT	No mention of sponsorship or COI	N = 82 Hip fracture surgery	Mean Age: 79.5 years; 16 males, 52 females	Low molecular weight heparin (Fragmin) 2,500 IU for first 2 injections then 5000 IU antifactor Xa SC vs. placebo for 6 days	Follow up at baseline, 6 weeks, and 12 weeks	Fourteen (14) excluded. DVTs in 30% Fragmin vs. 58% placebo (p <0.03). Blood drainage (NS); higher need for blood transfusions in Fragmin (p <0.005); 7 died during trial. No DVTs/ PEs suspected at follow-up exam in any patients.	"Fragmin given once daily offers an effective and safe thromboprophylaxis in hip fracture surgery."	Short term study of 6 days. Unknown if co-interventions. Suggests efficacy.
Detournay 1998 (score =8.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or	RCT	Sponsored by grant from Rhône-Poulenc Rorer Company. No mention of COI.	N = 498 THA	Mean age: 73.7 years; no mention of sex.	Low-molecular weight heparin reviparin-sodium (Clivarine®) 4200IU anti-Xa activity vs. enoxaparin 40mg SC QD for 10-14 days. Treatment 12 hours pre-op.	3 weeks	Total DVTs in 22/230 (10%) enoxaparin vs. 27/230 (12%) reviparin (NS). 6% each group with proximal DVTs. 2 vs. 1 major bleeds.	"The clinical tolerance was statistically unequivalent in favor of reviparin-sodium with regard to haemoglobulin and wound haematoma. Biologically we had great discrepancy between the anti-Xa activity of the two groups."	No differences in DVT. More hematomae with enoxaparin.

	Other Treatments									
Spiro 1994 (score =8.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	Sponsorship and COI: Study was conducted by Rhone-Poulenc Pharmaceuticals Inc. and Rhone-Poulenc Rorer Pharmaceuticals.	N = 572 Hip replacements	Mean age: 64.7 years; 358 males, 210 females.	10mg enoxaparin QD (n=161) vs. 40mg enoxaparin QD (n=199) vs. 30mg enoxaparin every 12 hours (n=208), all subcutaneous injections with 1st dose within 24 hours before surgery and continued up to 7 days	Follow up on day 7 of treatment.	16% of 568 developed DVT. 36/161 (31%) 10mg vs. 21/149 (14%) 40mg vs. 16/143 (11%) 30mg BID (p <0.001 comparing 10mg, but p> 0.2 for 40 vs 30mg). Use of graduated compression stocking reduced DVT incidence DVT 12% vs. 26%, p <0.001.Incidence of hemorrhagic complications similar in 40 and 30mg groups.	"[E]noxaparin is an effective agent to prevent deep venous thrombosis in patients having elective hip replacement surgery. Administered after surgery of 30 mg of enoxaparin every 12 hours or 40 mg once daily substantially reduces the incidence of deep venous thrombosis compared with an ineffective dose (10 mg given once daily)."	10mg stopped due to higher risk than 30mg, and 40mg. Graduated compression stockings decreased DVT's (p <0.001), however not randomized on this factor.
Dahl 1997 (score =8.5)	Low Molecular Weight Heparin vs. Placebo	RCT	No mention of sponsorship or COI.	N = 308 THR	Mean age: 71.2 years; 66 males, 161 females	Dalteparin 5000 IU vs. placebo QD for 4 weeks	7 days, 35 days	DVT at Day 35 in 11/93 (11.8%) of dalteparin vs. 23/89 (25.8%) of placebo. (RR = 0.46, 95% CI 0.24-0.88, p = 0.017).	"[T]he occurrence of DVT increased significantly from 1 to 5 weeks after hip replacement surgery in patients without prolonged thromboprophylaxis. One daily self-administered dose of dalteparin (Fragmin), 5000 IU, significantly counteracted the progression of DVT."	VQ scan also used. Incidence & prevalence. Reported. Population reported in Arnesen. Data suggest efficacy.
Hoek 1992 (score =8.5)	Low Molecular Weight Heparin vs. Placebo	RCT	No mention of sponsorship or COI.	N = 218 Hip arthroplasties	Mean age: 68.7 years; 47 males, 149 females	Org 10172 (Lomoparan) anti-factor Xa 750U vs. placebo SC BID for 10 days	10 days, 8 weeks	DVT in 15.5% Lomoparan vs. 56.6% of placebo (p <0.001). No major bleeding. No differences in drain fluid or transfusions.	"[T]he low molecular weight heparinoid (Org 10172) is a highly effective antithrombotic agent in reducing the occurrence of both proximal- and isolated calf-vein thrombosis in the post operative hospitalisation period following elective total hip replacement surgery."	Only 1st phase study randomized. Blinding mentioned in abstract only. Data suggest efficacy.

Hull 1993 (score =8.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	No mention of sponsorship or COI.	N = 795 Hip surgery patients N = 641 Knee arthroplasty patients	Mean Age: 66 years; 592 males, 844 females	Warfarin sodium initial dose 10mg post-operatively on evening of surgery and QD with dose adjusted to INR 2.0-3.0 vs. low molecular weight heparin fixed dose of 75 IU/kg body weight SC QD. Treatments until 14th post-operative day or hospital discharge.	Follow up at baseline and 3 months	37.4% warfarin vs. 31.4% of the low molecular weight heparin group developed DVT, p = 0.03. 1.2% of warfarin group vs. 2.8% low molecular weight heparin group with major bleeding, p = 0.04.	"[L]ow-molecular-weight heparin given in a single subcutaneous injection per day is effective, as compared with warfarin sodium prophylaxis, and that it avoids the need to monitor the level of anticoagulation. The reduction in the rate of venous thrombosis with low-molecular-weight heparin, as compared with warfarin, is offset by an increase in the number of bleeding complications and wound hematomas."	Dropouts unclear. Appears to be ITT. Data suggest modest reduced risk for DVT with LMWH.
Eriksson 2007 (score =8.0)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	No mention of sponsorship or COI.	N = 641 THA	Mean age: 65.0 years; 260 males, 365 females	Dose escalation study. Rivaroxaban 2.5, 5, 10, 20 or 30mg vs. enoxaparin. Rivaroxaban 6-8 hours after wound closure and every 12±1 hour after vs. rivaroxaban 30mg beginning 6-8 hours after wound closure, every 24±1 hour after for 5-9 days after surgery vs. enoxaparin 40mg SC evening before surgery then 6-8 hours after wound closure and QD evenings for 5-9 days after surgery.	3, 5, 6, 9 days, and 30-60 days	Major VTE incidence inverse with rivaroxaban dose (total DVT, non-fatal, PE, all cause mortality: 22.2%, 23.8%, 20.0%, 15.1%, 10.2%, 17.4% vs. enoxaparin 16.8%) (p = 0.0108). Rivaroxaban vs. enoxaparin (NS). Major post operative bleeding more frequently with rivaroxaban vs. enoxaparin (0%, 2.5%, 2.9%, 4.5%, 6.5%, 10.8% vs. 0%), p = 0.0008.	"This study demonstrated proof-of-principle for rivaroxaban to reduce the incidence of VTE."	Some co-interventions. Data suggest rivaroxaban equivalent efficacy to enoxaparin. Dose-response relationship for rivaroxaban. Higher bleeding rates in rivaroxaban.
Samama 2002 (score =7.0)	Low Molecular Weight Hepari	RCT	Supported by Knoll-France, Lavalois-Parret,	N = 1,279 total hip replacement patients.	Mean age: 65.5 years; 1188 males,	Fixed-dose subcutaneous low-molecular-weight heparin administered once daily for 6 weeks (n = 644) vs	Follow-up at preclusion, randomization, discharge, and the end of the treatment	Failure rate reviparin (4.2%) lower than acenocoumarol (10.3%). Low-molecular-weight heparin with fewer	"[T]he extended use of low-molecular-weight heparin given in a single subcutaneous injection per day is superior to acenocoumarol prophylaxis in	Clinically significant events – more "real world." Sufficient power to find differences. Suggests LMWH superior.

	n vs. Other LMWH Doses or Other Treatments		France. Local investigators received $400 per patient in the study and the investigator-in-chief, Dr Samama, received a $4000 final grant.		101 females.	Adjusted-dose oral anticoagulant (acenocoumaro) administered once daily for 6 weeks (n = 645)	period (6-9 weeks).	bleeding complications (p = 0.0001).	patients undergoing elective hip surgery and that it avoids the need to monitor the level of anticoagulation."	
Perhoniemi 1996 (score =7.0)	Defibrinating Enzyme vs. Placebo	RCT	Sponsored by Rhône-Poulenc Rorer-Rinland. No mention of COI.	N = 165 hip or knee replacement or remural fractures.	Mean age: 72.9 years; 43 males, 118 females	Enoxaparin 40mg SC QD vs. dihydroergotamine 0.5mg and heparin 5,000 IU SC for 7 days. First dose of enoxaparin 12 hours before operation and heparin-dihydroergotamine (HDHE) 2 hours before heparin.	0, 1, 2, 3, 5, 6 days	One case of DVT in enoxaparin vs. 0 in HDHE group. 2 cases of PE in HDHE group and 0 in enoxaparin (NS). No differences in blood loss.	"[E]noxaparin is as effective as HDHE in thromboprophylaxis of patients undergoing othopaedic surgery."	Higher risk patients. Dropouts not mentioned. Appears underpowered. Suggests comparable efficacy.
Eriksson 1996 (score =7.0)	Heparin	RCT	No mention of sponsorship or COI.	N = 1,119 total hip replacement patients.	Mean age: 66.4 years; 422 males, 697 females.	10, 15, or 20mg CGP 39393 twice daily (n = 842) vs 5,000 IU unfractionated porcine heparin TID right before surgery and for 8-11 days (n = 277)	Follow-up at 6 weeks.	837 patients actually in study. DVTs in 23.9% vs. 18.4% vs. 17.7% vs. 34.2% (p <0.001 comparing hirudin doses with heparin). Fewer proximal DVT in 3 doses of CGP 39393 compared to heparin (CGP 10mg, p <0.001; 15mg, p <0.001; 20mg, p <0.001). CGP 39393 dose response not	"[S]pecific inhibition of thrombin by prophylactic CGP 39393 significantly reduces thromboembolic complications in patients undergoing total hip replacement."	Co-interventions not mentioned. Data suggest hirudin superior to unfractionated heparin.

								significant. No differences in blood loss.		
Hayes 1996 (score =7.0)	Aprotinin vs. Placebo	RCT	Supported by Cappagh Hospital Trust, Dublin, Ireland. No mention of COI.	N = 40 total hip replacement patients.	Mean age: 71.45 years; 25 males, 15 females.	Group A: Aprotinin 2M KIU intravenously (n = 20) Vs Group C: Placebo (n = 20) (both groups received enoxaparin and stockings).	No mention of follow-up.	No differences in total blood loss, intraoperative blood loss, or postoperative blood loss between groups. No differences in DVT between groups, with 0 below DVT in the aprotinin group vs. 1 placebo.	"A single bolus dose of 2 million KIU of aprotinin did not reduce blood loss or transfusion requirements in patients undergoing total hip replacement surgery."	Single administration; provider blinding unclear. Data suggest no differences in complications. Very low DVT rate due to enoxaparin and stockings for all.
Dechavanne 1989 (score =6.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	No mention of sponsorship or COI.	N = 124 Elective hip surgery	Mean age: 63.6 years; 57 males, 67 females.	Kabi 2165 2,500 anti-Xa U every 12 hours vs. 2,500 anti-Xa U Kabi 2165 every 12 hours for 48 hours post-operatively, then 5,000 anti-Xa U QAM vs. 5,000 IU subcutaneous Calciparine® 5,000 U SC BID for 2 days, then heparin dose adjusted by APTT	10-13 days	DVTs in 2/38 BID dose vs. 3/39 QD dose vs. 4/40 standard heparin (NS). On day 7 there was significant decrease in antithrombin-III in patients without DVT treated with standard heparin vs. anti-thrombin-III activity before surgery ($p<0.001$). No difference among 3 groups for blood loss as well as transfusion requirements.	"[K]abi 2165 treatment provides convenient and effective prophylaxis of postoperative thrombosis in patients undergoing elective hip surgery."	Heterogenous patients. Blinding of assessor unknown. No physical. Pre-op NSAIDS accounted for. Appears under-powered.
Sørensen 1990 (score =6.5)	Low Molecular Weight Heparin	RCT	No mention of sponsorship or COi.	N = 70 THR	Mean age: 69.0 years; 24 males, 43 females.	LMWH Logiparin 50 anti-Xa U/kg SC QD vs. placebo for 7 days. Both groups with and without DVT.	1,3, 5, 7 days	Factor VIII clotting activity differed ($p = 0.039$) Day 7 due to high levels in those with DVT. Day-to-day variation of Thrombin-antithrombin-III complex also different ($p <0.001$) due to high levels Days 1 and 3. Day-to-day variation of factor VIII significant ($p <0.001$) due to high levels Days 3, 5, 7 vs. Days -1 and 1.	"[S]eems likely that the post-operative hypercoagulable condition is a result of an enhanced activation of coagulation factors and reduced fibrinolytic capacity."	Some details sparse. Mentions only some co-interventions. Limited description of population and unable to assess baseline comparability.

Manganelli 1998 (score =6.5)	Low Molecular Weight Heparin	RCT	Supported by the National research Council, Cardiorespiratory group and the Italian Ministry of University and Scientific and Technologic Research. No mention of COI.	N = 61 total hip replacement patients.	Mean age: 65.6 years; males, females.	Short-term prophylaxis (subcutaneous UH 15,000 IU/24 hours for 15 days) (n = 28) vs Long-term prophylaxis (subcutaneous UH 15,000 IU/24 hours for 30 days) (n = 33).	Follow-up at 45 days.	DVT in 21.4% (6/28) short-term vs 12.1% (4/33) long-term UH-treated patients, (p = 0.48).	"[T]he risk for delayed proximal DVT in patients treated with THR remains high for at least 45 days after surgery. Continuation of prophylaxis with UH appears an effective and safe method to reduce the rate of delayed DVT after THR."	Underpowered. Trends towards fewer DVT in longer treatment group.
Hamulyak 1995 (score =6.5)	Low Molecular Weight Heparin	RCT	Sponsored by Sanofi Winthrop, Maaddlus, The Netherlands. No mention of COI.	N = 672 total hip or knee replacement patients.	Mean age: 67 years; 190 males, 482 females.	Oral anticoagulant (OAC, acenocoumarol) 4mg day before surgery, 2mg evening of surgery day, then adjusted to maintain INR 2.0-3.0 for 10 days (n = 342) vs Low molecular weight heparin (LMWH, nadroparine) SC Q24 hour (about 60 IU of antifactor Xa (AXa)/kg), 0.3ml for patients weighing <60kg, 0.4ml for those 60-80kg, 0.6ml	No mention of follow-up.	50/257 (20%) OAC vs. 43/260 (17%) nadroparine with DVTs (p = 0.45). No differences in bleeding, transfusions.	"[F]ixed-dose subcutaneous nadroparine is at least as effective and safe as adjusted-dose OAC for prophylaxis against DVT after hip or knee implantation, but more convenient to administer."	Blinded assessor mentioned only in abstract. Stockings not meds mentioned as co-interventions. Data suggest comparable efficacy.

						for patients weighing >80kg, for 10 days (n = 330)				
Schmidt 2003 (score =6.0)	Defibrinating Enzyme vs. Placebo	RCT	No mention of sponsorship or COi.	N = 346 1º or 2º THR and TKR	Mean age: 66.9 years; 113 males, 222 females.	Prolonged prophylaxis nadroparine 2500-4,000 IU between Day 11 and Day 35 vs. sonographic screening for DVT before Day 10	1, 3, 12 months	36.8% of patients in ultrasound group had asymptomatic thrombosis. Combined endpoint of proximal DVT, symptomatic PE or death by PE diagnosed in 15 (8.7%) U/S screening group vs. 7 patients (4.3%) under prolonged prophylaxis (p = 0.12). Any symptomatic event of VTE in 4 (2.3%) in U/S screening (1 PE, 3 thrombosis) vs. 7 (4.3%) under prolonged prophylaxis (2 PE, 5 thrombosis; p = 0.37).	"[U]ltrasound screening for distal thrombosis after hip or knee replacement surgery with termination of heparin prophylaxis after exclusion of in-hospital thrombosis does not reduce the incidence of proximal DVT or symptomatic PE over five weeks postoperatively when compared to prolonged prophylaxis with LMWH. [Study indicates] efficacy of nadroparin calcium in preventing post-operative DVT in patients undergoing elective total hip replacement."	Study terminated early because of higher DVTs in ultrasound group, though not statistically significant. Co-interventions not mentioned.
Planes 1991 (score =6.0)	Defibrinating Enzyme vs. Placebo	RCT	No mention of sponsorship or COI.	N = 188 total hip replacement patients.	Mean age: 69 years; 102 males, 77 females.	Placebo Group: spinal anesthesia and no injection of enoxaparin (n = 89) vs Enoxaparin Group: spinal anesthesia and enoxaparin 20mg (n = 90).	Follow-up at 3 months.	Total and proximal DVTs not different. Distal DVT differed among 3 groups, p = 0.007) and comparing groups I and II I respectively (Fisher's exact test, p = 0.013). Confidence intervals for total DVT increased from group II to group I: group I, 7.8% to 26.1%; group II, 3.6% to 19.8%; group III, 0.3% to 12.6%).	"[T]he administration of enoxaparin at the dose of 40mg started 12 hours before operation performed under general anesthesia, or at the dose of 20/40 mg started one hour after spinal anesthesia, achieves a safe and effective prophylaxis against DVT in elective hip surgery."	Comparable efficacy.
Leyvraz 1988 (score =6.0)	Defibrinating Enzyme vs. Placebo	RCT	Sponsored by Sandoz Products, Ltd. And	N = 102 total hip replacement patients.	No mention of mean age or sex.	Group 1: received heparin subcutaneously three times daily in doses adjusted as a function of activated	16 days	11 patients in the heparin sodium group developed DVT vs. 10 in DHE (p >0.5). More transfusions in heparin group (p = 0.004).	"[T]he best preventive regimen for thromboembolism after total hip arthroplasty is subcutaneous heparin in APTT-adjusted doses."	Different criteria for diagnosis of DVT than many articles.

			Hoffman-LaRoche. No mention of COI.			partial thromboplastin time (n = 50) vs Group 2: received a fixed dose of 5,000 IU heparin plus 0.5 mg dihydroergotamine twice daily (n = 52)				
Flicoteaux 1977 (score =6.0)	Defibrinating Enzyme vs. Placebo	RCT	No mention of sponsorship or COI.	N = 40 total hip replacement patients.	Mean age: 63.5 years; 13 males, 27 females.	ASA vs. no ASA in addition to Calcium heparin 5,000 IU SC 2 hours before, 12 hours after operation and Q8 hours for 10 days	24 hours, 10 days	No difference in rate of DVT. 77 limbs examined using 125 I fibrinogen test and venography. Both tests positive in 12 legs and negative in 60. In 3 radioactive fibrinogen test positive, while phlebograms failed to show thrombi. In 2 limbs 125 I fibrinogen test negative, but venograms showed a filling defect. No difference in rate of DVT.	"[T]here is a good agreement between the results of 125 I fibrinogen test and venography in the detection of DVT. Moreover a combination of low dose heparin and aspirin does not improve the results obtained with low dose heparin alone in the prevention of DVT. Finally, a significant tendency towards increased bleeding is observed with such a combination."	Appears to control other methods of DVT prophylaxis. At odds with other literature on ultrasound vs venography for usefulness. Suggests ASA not helpful as adjunct to heparin.
Colwell 1994 (score =6.0)	Heparin	RCT	Sponsored by Rhône-Poulenc Rorer Pharmaceuticals, Incorporated, Collegeville, Pennsylvania. COI: One or more of the	N = 610 total hip replacement patients.	Mean age: 65.4±10.96 years; 298 males, 309 females.	Group 1: 30mg of enoxaparin every 12 hours (n = 194) vs Group 2: 40mg enoxaparin once daily (n = 203) vs Group 3: 5000 units of unfractioned heparin every 8 hours (n = 207)	Follow-up at 8, 12 hours.	Rate of DVT lower with enoxaparin 30mg vs. unfractionated heparin (p = 0.014) and enoxaparin 40mg QD (p = 0.0002).	"The efficacy and safety profile of enoxaparin supports consideration of enoxaparin as a therapeutic option for the prevention of deep venous thrombosis in this specific population of patients. Administered postoperatively, enoxaparin was more effective than heparin and was as safe as heparin in this study."	Small numbers to show efficacy. Blinding of assessor unclear.

			authors have received or will receive benefits for personal or professional use.							
Yoo 1997 (score =5.5)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	Sponsored by Sanofi Ltd. No COI.	N = 100 total hip replacement patients.	No mention of mean age; 83 males, 17 females.	Treatment group: low molecular weight heparin, nadroparin calcium 41 IU/kg initial dose through 3rd day then 65 IU/kg (n = 50) vs Control Group: no prophylaxis pre-operatively, 10 days post-op (n = 50)	No mention of follow-up.	In control group 16 % (8/50; p = 0.015) developed DVT vs. 2% (1/50) for treatment group (p = 0.015).	"[Study indicates] efficacy of nadroparin calcium in preventing post-operative DVT in patients undergoing elective total hip replacement."	Suggests nadroparin effective.
Eriksson 1988 (score =5.5)	Defibrinating Enzyme vs. Placebo	RCT	Supported by the Swedish Medical Research Council, the Medical Society of Gotebor g, the University of Gotebor	N = 113 total hip replacement patients.	Mean age: 67.15 years; 47 males, 51 females.	Fragmin (LMWH) 0.2mL 12,500 anti-factor Xa units/mL SC BID subcutaneously twice a day for 7 days with first injection 2 hours before operation (n = 49) vs Dextran 70, 500ml during operation, 500ml within 6 hours post-operatively, then 500ml 1st and 3rd post-op days (n = 49).	Follow-up at 6 weeks.	More with previous DVT in dextran group. DVT in 20% of LMWH vs. 45% dextran, p <0.01.	"In conclusion, this randomized prospective comparison of LMWH and dextran 70 in patients undergoing total hip replacement showed a statistically significantly better effect of LMWH in preventing DVT in the legs."	Allowed higher risk patients. Some baseline differences. Suggests efficacy of LMWH.

			g and KabiVitrum, AB, Stockholm. No mention of COI.							
Leyvraz 1983 (score =5.5)	Heparin	RCT	No mention of sponsorship or COI.	N = 96 total hip replacement patients.	Mean age: 68.6 years; 38 males, 40 females.	Group 1: Heparin 3,500 IU SC Q 8 hour (n = 41) vs Group 2: Adjusted dose by PTT for 8 days (n = 38).	No mention of follow-up.	DVT in 16/41 (39%) of fixed dose vs. 5/38 (13%) in adjusted dose, p<0.01. Proximal DVTs in 16 vs. 5. No differences in blood transfusions.	"Adjusted low-dose heparin prophylaxis appears to be a safe and efficacious method to reduce the frequency of deep-vein thrombosis in patients undergoing total hip replacement."	Data suggest adjusted dose superior to fixed dose. No placebo group.
Kakkar 1979 (score =5.0)	Heparin vs. Other Treatments	RCT	Supported by the Medical Research Council of the United Kingdom program grant 973/756, and King's College Hospital Medical School Voluntary Research	N = 300 major abdominal surgeries, 100 total hip replacement patients.	Mean age: 62.3 years; 127 males, 173 females.	Abdominal surgery trial: Group 1: dihydroergot-amine mesylate vs. heparin 5000 IU SC (n = 100) vs Group 2: 5,000 IU heparin calcium vs 5,000 IU heparin calcium plus 0.5mg (n = 97) vs Group 3: dihydroergotamine mesylate 2 hours before surgery and Q8 hours 7 post-op days or longer if confined to bed (n = 100).	No mention of follow-up.	Abdominal surgery trial: 10/50 dihydroergotamine vs. 2/50 (4%) heparin (p <0.05). THR study: DVTs on heparin 26/50 (52%) vs. heparin plus dihydroergotamine 10/50 (20%), p <0.01. Blood loss and hematoma not different. THR patients significant different DVT incidence (p <0.01) in favor of combination group.	"[T]he combination of dihydroergotamine and heparin represents an effective form of prophylaxis in patients undergoing total hip replacement."	Suggests heparin superior to dihydroergotamine in abdominal surgery and combination better than heparin alone for THR.

			Trust. Dihydroergotamine was supplied by Sandoz AG, Nuremberg, West Germany. Consultant surgeons of King's College Hospital allowed us to study their patients.							
Avikainen 1995 (score =5.0)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	No mention of sponsorship or COI.	N = 167 THR	Mean age: 65.5 years; 55 males, 112 females.	Enoxaparin 40mg SC QD, 12 hours pre-operatively vs. unfractionated heparin 5,000 IU SC BID starting 2 hours pre-op, 2nd dose 12 hours post-op for 10 days	2, 7 days	Four in unfractionated heparin group vs. 1 enoxaparin developed DVT, (p >0.05). No differences in hematomas, transfusions, blood loss.	"[E]noxaparin is an effective and safe form of DVT prophylaxis in patients undergoing elective hip replacement …The regimen was well tolerated and there was no evidence of increased bleeding."	Underpowered. Trend but no p-values given. Unclear whether accounted for ASA or physical.
Senaran	Low Molec	RCT	Sponsored by	N = 100 THA	Mean age: 53.8	Enoxaparin 40mg SC QD 12 hours pre-op vs.	6 weeks	DVT in 2 enoxaparin vs. 0 heparin (NS), 0 late DVT in	"[L]ow molecular weight heparin (Enoxaparin) was	Some details sparse. Blinding unknown.

2006 (score =5.0)	ular Weigh t Hepari n vs. Other LMWH Doses or Other Treat ments		Eczacıba ş¸I-Rhone Poulenc co. No mention of COI.		years; 29 males, 71 females.	standard heparin 5,000 IU SC 8 hours pre-op and continued to 15,000 per day in 3 equal doses every 8 hours for 7-10 days		enoxaparin vs. 2 heparin (NS). No differences in complications and blood loss.	found to be as safe and as effective as standard heparin in the prophylaxis of DVT in patients undergoing elective hip arthroplasty."	Compliance and dropouts unclear. Underpowered.
Borris 1991 (score =5.0)	Low Molec ular Weigh t Hepari n vs. Other LMWH Doses or Other Treat ments	RCT	No mention of sponsors hip or COI.	N = 246 THR	Mean age: 69 years; no mention of sex.	Enoxaparin 40mg SC QD for 8 days starting 12 hours after surgery vs. dextran 70 (60mg) IV starting during anesthetic induction, 2nd dose 6 hours later, and 3rd and 4th on Days 1 and 3 post-op	7 days	Heptest increased from baseline with Enoxaparin ($p < 0.001$) vs. decrease in Dextran ($p<0.01$).TAT increased from pre-operative level. On Day 7, Dextran group had higher levels of TAT than Enoxaparin group. Significant difference in DVTs in favor of enoxaparin ($p < 0.01$).	"Postoperative levels of TAT [thrombin-antithrombin complexes], D-dimer, and t-PA:ag were significantly increased in both groups, however, TAT was significantly higher in patients in the Dextran group than in the Enoxaparin patients.D-dimer was significantly higher in Dextran patients with DVT postoperatively compared with patients without DVT. No differences concerning TAT or t-PA:ag were observed between patients with and without DVT in any of the groups."	Lack of power in enoxaparin - no decision on usefulness of D-dimer. Article mainly on association between blood tests and DVT for mechanism hypothesis generation.
Huo 1992 (score =5.0)	Defibri nating Enzym e vs. Placeb o	RCT	No mention of sponsors hip or COI.	N = 286 total hip replacem ent patients.	Mean age: 64.7 years; 101 males, 145 females.	Intraoperative heparin 30 minute interval dose (1,000U at beginning surgery and 500U Q 30 minutes) vs. continuous adjusted dose (30-50% PTT elevation) vs. fixed dose (1,000U before hip dislocation plus 500U before femoral canal	30 minutes	Proximal femoral DVT in 9.1% controls vs. 1.7%, 1.6% and 1.7%, $p < 0.02$ compared with control. Overall DVT rate reduced 24.3% to 10%, $p < 0.01$.	"[I]n conjunction with hypotensive epidural anesthesia and postoperative aspirin, is effective in reducing proximal DVT to less than 2% in primary THA.	Only some co-interventions mentioned. Suggests intraoperative heparin reduces risk.

						prep) during surgery. All ASA 325mg BID post-op.				
Kim 1998 (score =5.0)	Defibrinating Enzyme vs. Placebo	RCT	Sponsored by National Institute of Diabetes and Digestive and Kidney Diseases grant, Veterans Affairs Central Office Merit Review, and a grant from the Margaret Duffy and Robert Camercon Troup Memorial Fund for Cancer Research of the Buffalo General Hospital and by National	N = 150 THR; some trauma	Mean age: 48.2 years; 38 males, 10 females.	Aspirin EC 400mg TID starting 48 hours before surgery, finish 14 days after vs. low molecular weight dextran 50mL/hour infused intravenously perioperatively and continued for 2 days vs. controls	6 weeks, 3, 6 months, 1 year, then yearly thereafter	Incidence of DVT was 10/50 (20%) controls vs. 6/50 (12%) ASA vs. 3/50 (6%) LMW dextran ($p<0.05$ for LMW dextran vs. control). No differences in major bleeds.	"[L]MW dextran proved to be an effective and well tolerated prophylactic treatment."	Starts with premise of lower prevalence in Koreans. Compliance unknown. Data suggest dextran effective.

			Eye Institute grants and Veterans Affairs Central Office Merit Review. No mention of COI.							
Menzin 1994 (score =4.0)	Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments	RCT	No mention of sponsorship. COI: One or more of the authors have received or will receive benefits for personal or professional use.	N = 607 THR	Mean age: 65 years; 297 males, 306 females.	Enoxaparin 30mg q12 hour vs. enoxaparin 40mg QD vs. unfractionated heparin 5,000 U q8hour for 7 post-operative days	4, 7, 14 days	Confirmed DVT rates enoxaparin 30mg 4.7% vs. enoxaparin 40mg 14.9% vs. heparin 11.6%. Enoxaparin 30mg superior to heparin, p <0.05. No difference between enoxaparin 40mg and unfractionated heparin (p = 0.33). Fewer major bleeds in enoxaparin 40mg than heparin. No difference between heparin and enoxaparin 30mg (p = 0.72). Unfractionated heparin group in hospital longer than enoxaparin groups, 11.3 days heparin, 9.9 days enoxaparin 40mg, 9.5 days enoxaparin 30mg.	"Compared with unfractionated heparin, use of enoxaparin following total hip replacement may decrease the risk of DVT and length of hospital stay."	Blinding not mentioned. Co-interventions unclear. Unknown if ITT applicable. Data suggest enoxaparin superior.
Kew 1999 (score =3.5)										Sparse information. No demographics. No dose of medicine.
Horbach 1996										Some baseline differences with more obesity in UFH should bias against

(score =3.5)										UFH. No difference between LMWH and unfractionated heparin.

Evidence for the Use of Factor Xa Inhibitors

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Factor Xa Inhibitors, Anticoagulants; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 59 articles in PubMed, 16 in Scopus, 28 in CINAHL, 2 in Cochrane Library, 2830 in Google Scholar, and 5 from other sources. We considered for inclusion 8 from PubMed, 2 from Scopus, 4 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 5 from other sources. Of the 23 articles considered for inclusion, 10 randomized trials and 8 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Agnelli 2007 (score= 10.5)	Factor Xa Inhibitor vs. Other Treatments	RCT	No mention of sponsorship. No COI.	N = 511 Total hip or knee replacements	Mean age: 62.6 years; 230 males, 277 females	Dose escalation study. Oral LY517717 (Difumarate) 25, 50, or 75mg or later doses of 100, 125, or 150mg 6-8 hours after wound closure then every morning after overnight fasting at 7am±1 hour vs. enoxaparin 40mg SC evening before surgery, then every evening at 8pm±2 hours; both treatments continued for 6 to 10 doses.	23-37 days	Difumarate resulted in dose-dependent decrease in the incidence of thromboembolic events (p = 0.0001). Doses between 25-75 mg ineffective. Incidences of VTE with 100, 125 and 150mg of 19%, 19% and 16% vs. 21% enoxaparin (NS).	"In conclusion, this phase II proof-of-concept study demonstrated the safety and efficacy of LY517717 for the prevention of VTE following THR or TKR in comparison to enoxaparin."	Suggests comparable efficacy with enoxaparin.
Eriksson 1997 (score= 10.0)	Factor Xa Inhibitor vs. Other Treatments	RCT	Sponsored by Novartis. No mention of COI.	N = 2079 THR	Mean age: 66.5 years; 876 males, 1212 females	Desirudin 15mg SC BID, first injection 30 minutes before surgery vs. enoxaparin 40mg QD, first injection evening before surgery. Both 8-12 days treatment.	12 hours, 8-12 days	6.2% of all patients had a major thromboembolic event (proximal DVT, pulmonary embolism, or unexplained death). Major TE event in 4.9% desirudin vs. 7.6% enoxaparin, p = 0.02. Relative reduction 36.4%. Proximal DVT in 36/802 (4.5%) desirudin vs. 59/785 (7.5%) enoxaparin, p = 0.01. Overall DVT rate lower, p = 0.001.During follow up, 4 patients died. Total blood loss was not significantly different between the groups.	"[S]pecific inhibition of thrombin is effective in preventing postoperative thromboembolism in high-risk patients who have undergone hip-replacement surgery. The patients who received desirudin twice daily for at least eight days had a 40 percent lower risk of proximal deep-vein thrombosis than those given enoxaparin, a low-molecular-weight heparin. The treatment regimens were equally safe and did not require specific laboratory monitoring."	No physical allowed, ASA ok. Suggests desirudin superior to enoxaparin. Post hoc analyses support age, general anesthesia, obesity, cement as risks.
Eriksson 2003 (score= 10.0)	Factor Xa Inhibitors vs. Placebo	RCT	Sponsored by grant from Sanofi-	N = 656 Hip fracture surgery	Mean age: 79 years;	Fondaparinux sodium: received 2.5mg SC (n=327) vs. Placebo: (n=329) for 19-23 days	11, 49 days	Venous thromboembolic incidence of 35% (77/220) on placebo vs. 1.4% (3/208) with fondaparinux. Relative	"[E]xtended prophylaxis with fondaparinux for 3 weeks after hip fracture surgery reduced	Suggests efficacy. Few exclusions except for drug safety. Physical exam not allowed.

			Synthelabo, Paris, France, and NV Organon, Oss, the Netherlands. No mention of COI.		190 males, 466 females	after total hip replacement		risk reduction 95.9% (95% CI 87.2%-99.7%, p = 0.001). Significant reductions in total, proximal as well as distal-only deep vein thrombosis (p <0.001).	the risk of VTE by 96% and was well tolerated."	Appears to include ITT, but not labeled such in report.
Eriksson 2001 (score= 7.0)	Factor Xa Inhibitor vs. Other Treatments	RCT	Sponsored by NV Organon and Sanofi-Synthelabo. COI: All authors have served as consultants to NV Organon and Sanofi-Synthelabo.	N = 1711 Hip fracture surgery	Mean age: 77.1 years; 411 males, 1262 females	Fondaparinux 2.5mg QD vs. enoxaparin 40mg QD for at least 5 days after surgery	5, 11, 35, 49 days, 6 weeks	Venous thromboembolism incidence by Day 11 52/626 (8.3%) with fondaparinux vs. 119/624 (19.1%) with enoxaparin. Major bleeding by Day 11 in 18/831 fondaparinux vs. 19/842 enoxaparin (p = 1.00).	"[P]rophylactic fondaparinux is more effective than enoxaparin in preventing venous thromboembolism in patients undergoing hip-fracture surgery and does not increase the risk of clinically relevant bleeding."	Data suggest fondaparinux superior to enoxaparin
Tang, 2017 (score= 5.5)	Factor Xa Inhibitors	RCT	No sponsorship or COI.	N = 287 patients with hip fractures.	Mean age: 69.7 years; 110 males, 177 females	The Rivaroxaban group (treated with oral dosage of 10 mg/d 6 h after operation for 28 d) (n = 96) vs The low-molecular-weight heparin group (administered with subcutaneously Enoxaparin at 400 IU/d	Follow-up at 7 d, 14 d, 21 d, and 30 d following surgery based on postoperative time.	The incidence of VTE was 10.10% (29/287) in the control group of the study. The incidences of VTE were altered in the Rivaroxaban group to 5.21%, low-molecular-weight heparin group to 14.74%, and the sequential therapy group to 10.42% (P = 0.091), respectively. Significant differences	"[T]he sequential therapy of low-molecular-weight heparin and Rivaroxaban can achieve the prevention of VTE. The effects were not significantly different from the treatment of Rivaroxaban alone. However, sequential therapy significantly reduced postoperative drainage, improved the incidence of	Data suggests low molecular weight heparin and rivaroxaban can reduce VTE but results of this sequential therapy group not substantially different than rivaroxaban group alone

						for 12 h following operation) (n = 95) vs The sequential therapy group (treated with Enoxaparin at a dose of 4000 IU/d 12 h for 1 w, then oral Rivaroxaban at 10 mg 1 time/d for 28 d) (n = 96)		between the Rivaroxaban and the low-molecular-weight heparin groups (P = 0.028). Incidence of VTE in the Rivaroxaban group was significantly lower than that in the other two groups, and the highest in low-molecular-weight heparin group. Compliance rates of the three groups were 82.3%, 71.6%, and 88.5% although significant difference was not seen between the three groups (P > 0.05).	adverse incisions, and reduced the treatment cost.	
Li, 2017 (score= 5.0)	Factor Xa Inhibitors	RCT	Supported by the Projects of International Cooperation and Exchanges NSFC, National Key Technology Program, Excellent Young Scholars NSFC, Jiangsu Provincial Key	N = 80 patients with femoral neck fracture.	Mean age: 76.05 years; 28 males, 52 females	Oral rivaroxaban (10 mg one daily) (n=39) vs Conservative Treatment (stay in bed with mobilization without ingesting any thromboprophylaxis drugs) (n=41)	Follow-up at 6 months.	Rivaroxaban reduced the incidence of DVT from 19.5% to 2.6% (P=.016) compared to the conservative treatment. After including the incidences of DVT that occurred preoperatively, there was a significant reduction in the incidence of DVT with rivaroxaban compared with the conservative treatment (29.3% vs 10.3%, P=.034). If preoperative DVT were to be excluded, there were no significant differences between the 2 groups (7.7% vs 9.8%, P=.744).	"Thromboprophylaxis with rivaroxaban prior to surgery can effectively reduce the risk of DVT for patients with femoral neck fracture without increasing the bleeding rates. We recommend routine thromboprophylaxis with rivaroxaban on the first day of the patients' admission."	Data suggest preoperative rivaroxaban can effectively decrease DVT rush in femoral neck fracture surgery patients

			Research and Development Fundation, Jiangsu Provincial Key Medical Center Foundation, Jiangsu Provincial Medical Talent Foundation, and Jiangsu Provincial Medical Outstanding Talent Foundation. No COI.							
Cohen, 2006 (score= 4.5)	Compression Stockings for Prevention of Venous Thromboembolic Disease/ Factor XA Inhibitors	RCT	No mention of sponsorship. COI: one, or more of the authors have received or will receive benefits for personal	N = 795 patients undergoing primary or revision total hip replacement or surgery for fracture of the	Mean age: 65 years; 343 males, 452 females.	Fondaparinux – patients received fondaparinux (2.5 mg daily) for 5-9 days (N = 400) vs Fondaparinux and GCS – patients received fondaparinux (2.5 mg daily) for five to nine days plus graduated compression stockings for 35 to 49 days (N = 395)	At end of Fondaparinux and GCS treatment arm.	The venous thromboembolism or sudden death by day 42 outcome measure in Fondaparinux group (%) was 22, Fondaparinux plus GCS (%) was 19, adjusted odds ratio (95% CI) was 0.88 (0.46 to 1.65), p = 0.69.	"The addition of graduated compression stockings does not appear to improve the effectiveness of prophylactic anticoagulation with fondaparinux. As graduated compression stockings are time-consuming to measure and fit, inconvenient, and expensive, we recommend that their use in hip surgery be reconsidered. In future, their use may be replaced by a more extended period of anticoagulation."	Study terminated early. Data suggest compressive stockings do not add benefit to fondaparinux (low molecular heparin)

			or professional use from a commercial party related directly or indirectly to the subject of this article.	proximal third of the femur.						
De Valk, 1995 (score= 4.0)	Factor Xa Inhibitors	RCT	Supported by the Scientific Development Group. No mention of COI.	N = 209 patients suspected to have venous thromboembolism.	Mean age: 57.8 years; 83 males, 105 females	Danaparoid (1250 unfractionated dose/2 d every 12 h) (n=71) vs Danaparoid (2000 unfractionated dose/2 d every 12 h) (n=68) vs Intravenous Heparin (2300 unfractionated dose followed by 30000 unfractionated dose/24 hours) (n=70)	Follow-up assessment 2 months after initiation of treatment.	patients with deep venous thrombosis, high-dose danaparoid reduced The frequency of recurrence or extension (3 of 58 patients) compared with heparin; relative risk, 0.47 [CI, 0.12 to 1.77]). Patients receiving high-dose of danaparoid had reduced incidence of new defects (4 of 61 patients) compared with patients receiving heparin (14 of 58 patients); relative risk, 0.27 [CI, 0.09 to 0.78]), but patients receiving low-dose (relative risk, 0.76 [CI, 0.38 to 1.53]) did not. Incidence of overall recurrence was reduced in patients receiving	"[R]esults suggest that high-dose danaparoid is safer and more effective than unfractionated heparin for the treatment of venous thromboembolism."	Open Label Study. Baseline comparatively differences between groups (age is younger on IV herparin group). Data suggest danaparoid more effective than unfractionated heparin.

								high-dose danaparoid (8 of 63 patients) compared with patients receiving heparin (17 of 60 patients; relative risk, 0.45 [CI, 0.21 to 0.96]) but not in patients receiving low-dose danaparoid (18 of 65 patients); relative risk, 0.98 [CI, 0.56 to 1.72]) compared with those receiving heparin.		
Fuji, 2014 (score= 3.5)										Open Label Comparator Study. Data suggest oral 30 mg edoxaban tablets taken once daily has comparable efficacy to 2000 IU edoxaban subcutaneously given twice daily.
Sasaki, 2009 (score= 3.0)										Sparse methods data suggest FPX prevents VTE post hip fracture but FPX group reported major post-operative bleeding in 7.9% of the patients.

Evidence for the Use of Warfarin and Heparin

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Warfarin, Heparin; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and

prospective studies. We found and reviewed 71 articles in PubMed, 160 in Scopus, 15 in CINAHL, 1281 in Cochrane Library, 3380 in Google Scholar, and 19 from other sources. We considered for inclusion 7 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 19 from other sources. Of the 30 articles considered for inclusion, 25 randomized trials and 1 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Eriksson 2003 (score= 9.0)	Aprotinin vs. Placebo	RCT	Supported by a research grant from AstraZeneca. COI: Some members of the steering committee received travel grants or honoraria from AstraZeneca; Some members are AstraZeneca employees.	N = 2,835 Total hip or knee replacement	Mean age: 67 years; 1,051 males, 1,713 females.	Melagatran/ ximelagatran 2mg SC immediately before surgery and 3mg melagatran evening after surgery followed by 24mg ximelagatran orally (n=1377) vs. enoxaparin 40mg SC QD 12 hours before surgery. Both treatments 8-11 days (n=1387)	Follow up at 4-6 weeks after surgery	2316 patients assessed for first stage and 2326 for second stage. VTE in 2.3% of ximelagatran vs. 6.3% enoxaparin (p = 0.0000018). Relative risk reduction 23.7%. Rate in THR group lower (1.8% vs. 5.5% enoxaparin, 0.6% of ximelagatran and 0.9% enoxaparin had confirmed symptomatic VTE. More transfusions (66.8% vs. 61.7%) and somewhat higher blood loss (geometric mean 1,014mL vs. 913mL) with ximelagatran.	"In patients undergoing total hip or knee replacement, preoperatively initiated s.c. melagatran followed by oral ximelagatran was significantly more effective in preventing VTE than preoperatively initiated s.c. enoxaparin."	Data suggest melagatran/ximelagatran superior.
Colwell 2003 (score= 7.5)	Miscellaneous	RCT	No mention of sponsorship or COI.	N = 1,557 THR	Mean age: 64.3 years; 749 males, 808 females.	Ximelagatran 24mg (n=782) vs. enoxaparin 30mg SC BID for 7-12 days (n=775)	Follow up at 6 weeks after surgery.	[O]verall incidence of VTE 62/782 (7.9%) in ximelagatran vs. 36/775 (4.6%) with enoxaparin	"[A]lthough both patients populations had a low incidence of VTE, enoxaparin-treated patients had a significantly lower incidence than did ximelagatran-treated patients."	Details absent, including possible blinded assessors. Suggests enoxaparin superior.
RD Hepari	Low Molec	RCT	Sponsored by grant	N = 1173 Total hip	Mean age: 66.3	Anti-factor-X_a 50U of RD	6 hours, 12 hours	VT disease among 8% (14 patients). RD bid heparin 3% (n =	"For patients who had a total hip arthroplasty, a	Accounted for medications & physical

n Arthroplasty Group 1994 (score= 7.5)	ular Weight Heparin vs. Placebo		from Wyeth-Ayerst Research, Philadelphia, Pennsylvania. No COI.	or knee arthroplasty	years; 558 males, 615 females	heparin/kg SC BID vs. anti-factor-X_a ()U of RD heparin/kg body weight SC QD vs. warfarin 5mg QD and adjustments to PTT 1.2-1.5 for total hip replacement		5/178) had proximal DVT vs. 14% (24/171) QD heparin vs. 14% (24/174) on warfarin. No difference between heparin BID and warfarin efficacy – p = 0.07 for BID vs. warfarin and p = 0.82 for QD vs. warfarin.	fixed dose of anti-factor-Xa units of RD heparin per kilogram of body weight, administered unmonitored twice daily, beginning postoperatively, and low-dose warfarin were equally effective and safe."	exams. Suggests comparable efficacy, although trend towards BID heparin dosing.
Schulman 1995 (score= 7.5)	Durations and Doses of Warfarin	RCT	No mention of sponsorship or COI.	N = 897 First episode of venous thrombo-embolism	Mean age: 60.8 years; 504 males, 393 females.	Warfarin 6 weeks (n=443) vs. 6 months oral anticoagulant targeting INR 2.0-2.85 (n=454)	Follow up at 2 years.	No significant difference in mortality or major hemorrhage. Distal thromboses in 79 patients 6-weeks vs. 81 6-month group patients (NS). Significant difference in recurrent venous thromboembolism between 6-week group (18.1%) and 6-month group (9.1%, p <0.001).	"[T]he long-term outcome for patients with venous thromboembolism was discouraging, since there was no difference in the incidence of recurrent events in the two groups from 6 to 24 months after the initial episode. There was a linear increase in the cumulative risk, corresponding to 5 to 6 percent annually."	Included multiple risk factors. Longer follow-up of 2 years. ASA not allowed. Data suggest longer anticoagulation not necessary.
Francis 1992 (score= 7.0)	Defibrinating Enzyme vs. Placebo	RCT	Supported in part by grant HL-30616 from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md. No mention COI.	N = 232 THR	Mean age: 64 years; 95 males, 106 females	Warfarin 10-14 days before operation on 2-step regimen with dose adjustments for 6-8 days (n=103) vs. EPC (external pneumatic compression) with 11 second inflation cycle and 60 second deflation cycle. Treatment until venography 6-8 days (n=98)	Follow up at 6-8 days postoperatively.	Total VT incidence 32/103 (31%) with warfarin vs. 26/98 (27%) EPC (NS). Proximal thromboses in 3% warfarin vs. 12% EPC, p = 0.012.	"Warfarin therapy is significantly more effective than EPC in preventing serious proximal vein thrombosis after total hip replacement."	Unclear length of follow-up and uneven time of assessments. Data suggest increased proximal thromboses with pneumatic compression.

Hull 1979 (score= 7.0)	Durations and Doses of Warfarin	RCT	Supported by grants from the Province of Ontario and from the Ontario and Canadian Heart Foundations. No mention of COI.	N = 68 THR	No mention of mean age; 29 males, 39 females.	Adjusted-dose warfarin sodium 10mg (1.5-2x) (n=33) vs. low-dose subcutaneous heparin 5,000IU (PTT to 1.5-2 times) after surgery for 14 days with 12 week follow up (n=35)	Follow up at 3, 6, and 12 weeks.	Recurrence in 19 (47%) with proximal DVT vs. none of 17 on warfarin (p <0.001). Hemorrhagic complications in7/33 4 major) on warfarin and 0 on low-dose heparin (p <0.005).	"Although adjusted-dose warfarin sodium prevented recurrence, its effectiveness was counterbalanced to some degree by the frequency of bleeding associated with its use. It is possible that subcutaneous heparin in higher doses or oral anticoagulants in lower doses than those used in this trial might also be effective in preventing venous thromboembolism without producing the same high risk of bleeding."	Recommended that possibly higher dose heparin or lower dose warfarin be studied. Data suggest warfarin better for preventing recurrence, but more bleeding.
Agnelli 2001 (score= 7.0)	Durations and Doses of Warfarin	RCT	No mention of sponsorship or COI.	N = 290 Idiopathic DVT patients	Mean age: 67.2 years; No mention of sex.	Warfarin 3 months (n=133) vs. 1 year. INR 2.0-3.0. (n=134)	Follow up at 3, 6, and 12 months.	Twenty-three excluded; 15.7% of continuation group vs. 15.8% discontinuation with recurrent venous thromboembolism, RR = 0.99. 18/115 (15.7%) of continuation vs. 21/126 (16.7%) discontinuation with recurrence, p = 0.94. 14 patients died.	"In patients with idiopathic deep venous thrombosis, the clinical benefit associated with extending the duration of anticoagulant therapy to one year is not maintained after the therapy is discontinued."	Most recurrences within 2 years; no statistically significant differences between early vs. late dis-continuation.
Powers 1989 (Score= 7.0)	Warfarin vs. Aspirin vs. Placebo	RCT	Sponsored by a grant from the Heart and Stroke Foundation of Ontario. No mention of COI.	N = 194 patients with hip fracture who developed deep vein thrombosis (DVT).	Mean Age: 74.7 years; 54 males, 140 females	Warfarin group: patients received orally 10mg warfarin right after surgery then daily doses adjusted on basis of prothrombin time for 21 days after surgery or dis-charge (n=65) vs. Aspirin group: patients received 650mg enteric-	Follow up at baseline, 3 months.	DVT and/or PE in 20.0% warfarin, 40.9% aspirin, 46.0% placebo (p = 0.005). "[W]arfarin was clearly much more effective than aspirin or placebo, and there was little difference between aspirin and placebo." Bleeding outcomes not statistically significant; 6 patients died during 21-day period, 7 during follow up. None lost to follow up after 3 months; 1 thromboembolic event in that time span.	"[S]odium warfarin therapy is safe and effective in preventing thromboembolic complications in patients undergoing surgery for fractured hip, and that aspirin therapy is an equally safe and effective method for preventing proximal vein thrombosis or pulmonary embolism."	No mention of ambulation or stockings. Bias not discussed. Patients blinded to some interventions (pills). Suggests warfarin superior to ASA and placebo. Short flu time. Blinding of ASA and placebo groups but warfarin group does not appear to be blinded. Data suggest warfarin and aspirin produced

						coated aspirin at 8am and 8pm daily after surgery, lasted 21 days (n=66) vs. Placebo group: patients received inert tablets at 8am and 8pm daily, after surgery, lasted 21 days (n=63).				similar efficacy compared to placebo.
Bern 2002 (score= 7.0)	Durations and Doses of Warfarin	RCT	This study was supported by donations to the Foundation for Hematology Research offered by patients and by residual funds from a previously given grant by the Dupont Pharmaceuticals Company. No mention of COI.	N = 98 Unilateral hip replace-ment or degenerative joint disease	Mean age: 63.6 years; 55 males, 43 females.	Warfarin 1mg QD (n=49) vs. variable dose warfarin 7 days pre-operatively continued until discharge (n=49)	Follow up at the time of discharge or after 7 days postoperatively, after 6 weeks postoperatively, or at time of clinical suspicion of DVT or PE	No patients with DVT or PE. Median PT for patients receiving 1mg warfarin was 13.8 sec and 17.3 sec for variable dosage group ($p < 0.05$). No statistically difference between groups. Null hypothesis accepted.	"This fixed very low dose warfarin therapy, when begun preoperatively, appears to be a useful method for prophylaxis against DVT in these selected patients. This technique appears to be equal to variable dose warfarin in its efficacy, while being less complicated to administer and less expensive to monitor."	Patients with low DVT risk. Some baseline differences. Ultrasound might have missed some DVTs. LMWD but no p-value.

Gerhart 1991 (Score= 6.5)	Defibrinating Enzyme vs. Placebo	RCT	Sponsored by National Institutes of Health Grant and G. H. Besselaar Associates, Princeton, New Jersey, acting as an agent for Organon International, Oss, The Netherlands. No mention of COI.	N = 263 patients with multiple trauma or deep vein thrombosis.	Mean Age: 82.5 years; 47 males, 216 females	Org 10172 group: patients received Lomoparan for 750 units before surgery subcutaneously every 12 hour for 9 days, and received warfarin from day 7 until discharge (n=12) vs. Warfarin group: patients received warfarin orally until hospital discharge (n=131).	No mention of follow-up.	DVT in 7% Org 10172 vs. 21% of warfarin group, p <0.001. Eight patients in Org 10172 group vs. 5 on warfarin had major complications (NS). Blood loss or transfusions not different. 1 patient in Org 10172 group died vs. 7 on warfarin, p <0.04.	"[T]he low-molecular-weight heparinoid Org 10172 is a safe, convenient, effective antithrombotic agent for the prevention of venous thrombosis after an operation for fracture of the hip."	Broad range of risk factors allowed (not exclusion criteria). ITT term not used, but appears to have been done. Data suggest Lomoparan superior to warfarin,including deaths. Low mw heparin versus warfarin. Data suggest low mw heparin better than warfarin for DVT prophylaxis.
Pinede 2001 (score= 6.5)	Durations and Doses of Warfarin	RCT	Supported by the French Ministry of Health. No mention of COI.	N = 736 DVT or PE	Mean age: 58.5 years; 348 males, 388 females.	Warfarin 6 weeks for isolated calf deep vein thrombosis (C-DVT) (n=197) vs. 3 to 6 month warfarin for proximal DVT (P-DVT) or for pulmonary embolism (PE), INR 2.0-3.0 (n=539)	Follow up at 1.5, 3, 6, and 15 months	Twenty withdrew, 24 died, 22 dropped out (3%), and 25 developed cancer; 82 received shorter course than scheduled. No difference in bleeding complications. Lower recurrence rate for patients with C-DVT 2.6%, than P-DVT or PE, 8.4%. Permanent risk factors including cancers associated with higher risk of recurrence.	"After isolated C-DVT, 6 weeks of oral anticoagulation is sufficient. For P-DVT or PE, we demonstrated an equivalence between 3 and 6 months of anticoagulant therapy. For patients with temporary risk factors who have a low risk of recurrence, 3 months of treatment seems to be sufficient. For patients with idiopathic venous thromboembolism or permanent risk factors who have a high risk for	Open label RCT; timing of assessments and variety of interventions. Many community physicians and centers involved, but reflects more real life comparison. Data suggest 6 weeks for calf DVT and 3 months for proximal DVT or PE.

									recurrence, other trials are necessary to assess prolonged therapy beyond 6 months."	
Barsotti 1990 (Score= 6.0)	Low molecular weight Heparin	RCT	No mention of sponsorship or COI.	N=103 patients with recent femur neck fracture.	Mean age: 82.2 years; 21 males, 82 females.	Group A: patients received Enoxaparin 20 mg twice per day (n=54) vs. Group B: patients received Enoxaparin 40 mg once per day (n=49).	Follow-up at baseline, 12 hours.	18.3% patients received 20mg Enoxaparin and 10.4% patients received 40mg Enoxaparin got the diagnosis of thrombosis. No significant difference in red cell transfusion was found between both groups (group A: 217±132 ml vs. group B: 226±212 ml; p>0.05).	"[A] total daily dose of 40mg of Enoxaparin can be effective in the prevention of deep vein thrombosis in elderly surgically treated patients and does not involve a major risk of bleeding."	Low molecular weight heparin (Lovenox). Short term follow-up (12 hours) comparative study. Data suggest Enoxaparin may prevent DVT in the elderly post fractured femur surgery without excessive bleeding.
Comp 1998 (score= 6.0)	Defibrinating Enzyme vs. Placebo	RCT	Sponsored by a grant from Organon Inc. No mention of COI.	N = 488 THR	Mean age: 66.5 years; 192 males, 204 females	Danaparoid 750 anti-Xa units SC vs. Warfarin 10mg until hospital discharge	1, 2, 3 months	DVT rates 14.6% (29/199) danaparoid vs. 26.9% (53/197) warfarin. Absolute risk reduction 12.3% danaparoid (95% CI: 4.4%-20.2%, p = 0.003). Overall bleeding rates not different.	"Danaparoid is significantly more effective than warfarin in preventing combined proximal and distal lower extremity DVT following THR and at least as effective as warfarin in preventing DVT."	Data suggest danaparoid superior to warfarin.
Francis 1997 (score= 6.0)	Defibrinating Enzyme vs. Placebo	RCT	The funding sources were Grant HL-30616 from the National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland, and a	N = 580 THA	Mean age: 63 years; 259 males, 291 females.	Dalteparin sodium 1st dose 2,500 IU SC 2 hours before operation then 5,000 IU QD 1st post-op day until venography (about 7th post-op day) (n=271) vs. warfarin sodium 1st dose orally evening before operation, patients weighing ≤57kg received 5mg, patients weighing >57kgs	No mention of follow up.	Thirty (30) patients excluded from ITT and 168 excluded from per-protocol analysis. DVT in 15% of dalteparin vs. 26% of warfarin, p = 0.006. No difference in blood loss.	"[P]reoperative prophylaxis with dalteparin is significantly more effective than that with warfarin in preventing deep-vein thrombosis after total hip arthroplasty. The greater effectiveness of dalteparin must be considered, however, in light of an increased need for postoperative transfusions and an increase in the prevalence of wound-related bleeding complications."	Some baseline differences. Co-interventions unknown. Suggests pre- and early post-operative dalteparin superior to warfarin.

			grant from Pharmacia-Upjohn, Kalamazoo, Michigan. COI: benefits have been or will be received but are directed solely to a research fund, foundation, educational institution, or other non-profit organization with which one or more of the authors are associated.			7.5mg, daily doses adjusted to maintain INR 2.5. (n=279)				
Colwell 1999 (score= 5.0)	Low Molecular Weight Heparin vs. Other	RCT	Sponsored by Rhône-Poulenc Rorer Pharmaceuticals. No COI.	N = 3,011 THR	Mean age: 64.0±13.19 years; 1337 males, 1674 females	Enoxaparin 30mg SC vs. warfarin dose adjusted to INR 2.0-3.0 for 14 days after surgery; 3-month follow-up	Weekly for 12 weeks	2,229 patients completed; 782 discontinued prematurely. VT disease in 111 (3.7%), 55 in enoxaparin group (3%) and 56 in warfarin group (3.7%); 19 patients died. Adverse events occurred in 1,921 (63.8%) of 3,011 patients. Serious adverse events in 301	"[T]he data-collection tool designed to capture overall bleeding events was neither sensitive or specific enough to delineate bleeding events induced by the study medication from those caused by concurrent	Warfarin allowed. Blinding unknown. Some differences at baseline. Variable dosing intervals results in questions regarding conclusions of relative efficacy.

	LMWH Doses or Other Treatments							patients (10%). DVT was found in 0.1% of enoxaparin group and 1% of the warfarin group.	illness or operative procedure… The timing of the dose of the enoxaparin had a notable effect on the occurrence of major bleeding in association with enoxaparin therapy were administered the medication from zero to twelve hours postoperatively."	
Vives 2001 (score= 5.5)	Durations and Doses of Warfarin	RCT	No sponsorship or COI.	N = 245 Total hip or knee arthroplasties	Mean age: 63.6 years; 111 males, 111 females.	Fixed minidose warfarin 2mg a day (n=109) vs. adjusted higher dose warfarin with target PT range of 14 to 16 seconds (INR 1.4 - 1.8) (n=113); both taken for 6 weeks	Follow up at 6 weeks.	Twenty-three patients eliminated; 7.1% of adjusted low-dose group vs..4.6% fixed minidose group developed symptomatic DVT, p = 0.02; 8.0% of THA patients and 6.0% TKA patients in adjusted dose group developed symptomatic DVT, p = 0.03; 6.0% THA patients vs. 4.0% TKA patients on fixed dose developed symptomatic DVT, p = 0.01. No major bleeds.	"We found no difference in efficacy between the fixed 2-mg dose and the adjusted higher dose warfarin groups. The rates of symptomatic DVT were not significantly different with the numbers available. [W]arfarin has a low rate of major and minor complications when maintained properly on an adjusted low-dose or a fixed minidose regimen. Fixed minidose warfarin holds promise as a streamlined approach to outpatient thromboembolic prophylaxis after total joint arthroplasty. The efficacy of the fixed minidose regimen appears similar to that of adjusted-dose warfarin."	Study thrust to reduce warfarin to oviate need for testing. Conclude that need to monitor on low dose as well.
Campbell 2007 (score= 5.0)	Durations and Doses	RCT	No sponsorship or COI.	N = 810 DVT and/or PE	Mean age: 58.7 years; 398	Three months warfarin (n=369) vs. 6 months warfarin with an	Follow up at 1 year	61 patients excluded. 4 patients died of DVT or PE. 28 died for other reasons. 23 DVT or PE recurrences in 3 month vs. 16 in 6	"For patients in the UK with deep vein thrombosis or pulmonary embolism and no known risk factors for	Uneven follow-up and treating physicians. Bias not discussed. No blinding. No clear

	of Warfarin				males, 351 females.	INR between 2.0 and 3.5 (n=380)		month. Fatal and non-fatal failures during treatment plus recurrences after treatment overall in 31 (8.4%) in three month vs. 29 (7.6%) in 6 month groups (p = 0.80).	recurrence, there seems to be little, if any, advantage in increasing the duration of anticoagulation from three to six months. Any possible advantage would be small and would need to be judged against the increased risk of haemorrhage associated with the longer duration of treatment with warfarin."	advantage of 6 vs. 3 months. May have excluded many orthopedic patients.
Bergqvist 1979 (Score= 5.0)	Heparin	RCT	No mention of sponsorship or COI.	N = 290 patients with hip fracture experienced hip arthroplasty.	Mean Age: 77 years; 22 males, 55 females	Heparin group: patients received heparin 5,000 international unit (IU) 1 hour before surgery and 5,000 IU every 12 hour for 5 days (n=110) vs. Dextran group: patients received dextran 500ml during operation, 500ml right after operation; 500ml on 1st and 3rd post-op days (n=70) vs. Control group: patients received no treatment (n=110).	Follow up at baseline and 2 years	DVT in hip fracture patient controls 90.9% vs. dextran 48.1% vs. heparin 63.0% (p <0.05 comparing no treatment controls). Thigh thromboses in 50.0% vs. 22.2% vs. 37.0%. thromboses among elective hip surgery patients were 62.7% vs. 57.4% vs. 48.0%.	"[D]extran 70 is to be preferred for DVT prophylaxis after hip fractures."	No treatment controls. Data suggest heparin superior to no treatment for hip fracture, but dextran superior to low dose heparin. Results less strong for arthroplasty patients.
Oertli 1992 (Score= 4.5)	Heparin / Dextran	RCT	Sponsored by Sandoz Wander in Berne, Switzerlan	N=216 patients with proximal femoral	Mean age: 79.3 years; 37 males,	Sandoparin group: patients received 36 mg low molecular weight heparin (LMWH) for 10	Follow-up at baseline, 14 and 17 days.	33% patients received low molecular weight heparin (LMWH) and 48.4% patients received dextran 70 indicated increasing fibrinogen in calf and popliteal. Significant difference in deep vein	"[T]he LMWH we used is safe, was well tolerated, and has a significantly better thromboprophy lactic effect than dextran 70."	Randomized open-label trial with short follow-up. Data suggest low mw heparin better than dextran for DVT prophylaxis.

			d. No mention of COI.	fractures.	179 females.	days (n=113) vs. Dextran group: patients received 500 ml dextran 70 on 5th day after surgery (n=103).		thrombosis (DVT) was found between LMWH (23%) and dextran (37,9%) groups (p=0.017).		
Haentjens 1996 (Score= 4.5)	Heparin	RCT	No mention of sponsorship or COI.	N=283 patients with pelvic / spinal fracture / lower limb injury.	Mean age: 61.1 years; 117 males, 160 females.	Group A: patients received fixed low 3075 international units (IU) molecular weight heparin (n= 142) vs. Group B: patients received adjusted dose with 40 IU in 3rd day to 60IU in 4th day (n=141).	Follow-up at baseline, 6 weeks.	Thrombosis rate in group A at 6th week postoperatively was 1.3%, and 5.4% in group B. No significant difference of deep vein thrombosis (DVT) was found in both groups (1.9% vs. 2.7%; p>0.05). The platelet in group A decreased to 50 x 10^9/l, and that in group B decreased to 39 x 10^9/l.	"[B]oth regiments were equally safe following a spinal fracture, a pelvic fracture or a lower limb injury. The risk of DVT and PE was similar with both regimens."	Data suggest comparable efficacy between groups.
Zanasi 1988 (score= 4.0)	Defibrinating Enzyme vs. Placebo	RCT	No mention of sponsorship or COI.	N = 63 Most hip surgery; some trauma	Mean age: 71.2 years; 14 males, 49 females	Defibrotide vs. calcium heparin and ASA for 8 days	No mention of follow up.	"Although the size of the sample was inadequate for statistical comparison of the three treatment regimens with respect to the incidence of symptomatic DVT and of PE, a trend in favor of defibrotide was apparent."	"[T]he effectiveness of defibrotide in preventing DVT in patients recovering for orthopedic surgery is approximately equal to that of established treatments such as calcium heparin and ASA."	Sparse methods and details. Heterogeneous patients. Little baseline data. Underpowered.
Barber 1977 (score= 4.0)	Defibrinating Enzyme vs. Placebo	RCT	No mention of sponsorship or COI.	N = 128 THR	Mean age: 65.5 years; 50 males, 78 females	Dextran 70 1gm start of anaesthesia, 1,000ml QD 3 days, then 500ml alternate days for 10 days vs. warfarin 36 hours before surgery, 15mg loading dose followed by none next day,	2 weeks	DVT in 54.7% of all (dextran 26/51 (51%) vs. warfarin 34/58 (58.6%) vs. heparin 10/19 (52.6%), p >0.05. 1 patient each died from PE in heparin and dextran groups.	"[T]he use of warfarin as a safe method for the prophylaxis of pulmonary embolism, following total hip replacement, in preference to dextran 70 or twice-daily subcutaneous heparin. Its effects might be increased by commencing administration before operation."	Minimal comparative information between groups. Data suggest no differences between the treatments.

						5mg day after that, dosage adjusted for PT of "10-20%" continued 3 weeks vs. heparin 5,000 U SC Q12 hour evening before surgery and for 3 weeks.				
Tabern er 1989 (Score= 3.5)										Adjusted versus low dose heparin prophylaxis. Data suggest best DVT prophylaxis is adjusted group.
Pini 1985 (Score= 3.5)										Dextran vs. Heparin. Data suggest dextran / aspirin group was associated with more hemorrhage than heparin.
Moskov itz 1978 (Score= 3.5)										Low dose heparin vs. placebo. Data suggest heparin better than placebo for DVT prevention for THA but no difference in hip fractures.

Evidence for the Use of Aspirin

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Aspirin, Acetylsalicylic Acid; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 9 articles in PubMed, 111 in Scopus, 22 in CINAHL, 17 in Cochrane Library, 6590 in Google Scholar, and 2 from other sources. We considered for inclusion 2 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 2 from other sources. Of the 8 articles considered for inclusion, 2 randomized trials and 3 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Powers 1989 (score =8.5)	Warfarin vs. Aspirin vs. Placebo	RCT	Sponsored by grant from the Heart and Stroke Foundation of Ontario. No mention of COI.	N = 194 Hip fracture	Mean age: 74.7 years; 54 males, 140 females	Warfarin orally 10mg right after surgery then daily doses adjusted on basis of prothrombin time for 21 days after surgery or dis-charge vs. 650mg enteric-coated aspirin at 8am and 8pm daily starting post-op, continuing 21 days or dis-charge vs. placebo	3 months	DVT and/or PE in 20.0% warfarin, 40.9% aspirin, 46.0% placebo (p = 0.005). "[W]arfarin was clearly much more effective than aspirin or placebo, and there was little difference between aspirin and placebo." Bleeding outcomes not statistically significant; 6 patients died during 21-day period, 7 during follow up. None lost to follow up after 3 months; 1 thromboembolic event in that time span.	"[S]odium warfarin therapy is safe and effective in preventing thromboembolic complications in patients undergoing surgery for fractured hip, and that aspirin therapy is an equally safe and effective method for preventing proximal vein thrombosis or pulmonary embolism."	No mention of ambulation or stockings. Bias not discussed. Patients blinded to some interventions (pills). Suggests warfarin superior to ASA and placebo.
Lancet 2000 (score =7.0)	Aspirin	RCT	Sponsored by Health Research Council of New Zealand, the National Heart Foundation of New Zealand, the	N = 13,356 hip fracture surgeries plus	Mean age: 79 years; 2805 males, 10551 females	ASA 160mg QD vs. placebo for 35 days	35 days	DVT HR 0.71 (0.52-0.97). Death from PE HR 0.42 (0.24-0.73)	"[A]spirin reduces the risk of pulmonary embolism and deep-vein thrombosis by at least a third throughout a period of increased risk."	Large study, some details sparse. Data suggest ASA effective for preventing both

			Wishbone Trust of New Zealand, the Auckland Orthopaedic Society, the National Health and Medical Research Council of Australia, and the British Heart Foundation. No mention of COI.	4,088 arthroplasty patients						venous and arterial events.

Evidence for the Use of Post-Operative Exercise and Rehabilitation

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Activities of daily living, rehabilitation, home physical therapy;Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 149 articles in PubMed, 178 in Scopus, 8 in CINAHL, 109 in Cochrane Library, 22900 in Google Scholar, and 21 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 21 from other sources. Of the 26 articles considered for inclusion, 14 randomized trials and 4 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Lamb 2002 (score=9.5)	Post-operative exercise and rehab	RCT	No COI. Sponsored by the Research into Ageing and the PPP Healthcare Charitable Trust.	N = 26 Females over 75 years with hip fractures	Mean age: 83.7±3.7 years; 0 males, 26 females.	Patterned neuromuscular stimulation (PNMS) (n=12) vs. placebo of quadriceps muscle (n=12)	Follow-up at 6 or 7 days, 7 and 13 weeks	Nine PNMS women recovered mobility vs. 3 placebo (p = 0.046). 8 PNMS women could tandem stand vs 3 in placebo group after 7 weeks (p = 0.03). Near equal number of participants able to stand tandem at 13 weeks. No differences in recovery of leg extensor power during or after stimulation. PNMS group participants had more even distribution of power between injured and non-injured legs and difference significant at 6 weeks but not at 13 weeks. No statistically or clinically significant differences in pain scores at any assessment intervals.	"Neuromuscular stimulation at home is feasible and may be effective in speeding recovery of mobility after surgical fixation of hip fracture."	Wide range in response outcomes. Suggests PNMS may be beneficial. Major outcomes benefits not generally shown, but sample size small.
Hauer 2003 (score=7.0)	Post-operative exercise and rehab	RCT	No COI. Sponsored by the Ministerium für Wissenschaft, Forschung und Kunst Baden-Wuerttemberg and the University of Heidelberg.	N = 57 Geriatric females with history of severe falls	Mean age: 84.3±4.4 years; 0 males, 57 females	Ambulatory training of strength, functional performance, and balance 3 times a week for 3 months (n=31) vs. placebo (n=26)	Follow-up at 2 years	At 2 years, differences between groups were significant in most functional performances, despite decline from significantly improved motor performance levels achieved in the initial training intervention. Persons institutionalized or being cared for by family members showed greater functional decline. Physical activity returned to low baseline levels.	"Improved functional performance in the training group did not lead to an increased level of physical activity after training, which might have preserved the functional improvements."	Short term results suggest efficacy, however, long term improvements less strong, likely due to fewer differences in physical activity.

Hauer 2001 (score=7.0)	Post-operative activity limitations and rehab programs	RCT	Sponsored by Ministerium für Wissenschaft, Forschung und Kunst Baden-Wuerttemberg and the University of Heidelberg. No COI.	N = 57 Geriatric females with history of severe falls	Mean age: 82±4.8 years; 0 males, 57 females	Ambulatory training of strength, functional performance, and balance 3 times a week for 3 months (n=31) vs. placebo (n=26)	3 months	Increased strength, functional motor performance, and balance significant in intervention group. Significant reduction also found for fall-related behavioral and emotional restriction for intervention group. Moderate loss of improvement during 3-month follow up. No change in strength, functional performance, or emotional status during intervention and follow up for control group.	"Progressive resistance training and progressive functional training are safe and effective methods of increasing strength and functional performance and reducing fall-related behavioral and emotional restrictions during ambulant rehabilitation in frail, high-risk geriatric patients with a history of injurious falls."	Suggests benefits of a progressive resistance training program.
Binder 2004 (score=6.5)	Post-operative activity limitations and rehab programs	RCT	Sponsored by National Institute of Aging grant, the Washington University General Clinical Research Center grant, the Washington University Clinical Nutrition Research Center grant, and the Barnes Jewish Hospital Foundation. COI: One or more of the authors	N = 100 All had hip fracture from a fall not over 16 weeks previously, treated either ORIF or hemiarthro-plasty and all had had "standard" PT	Mean age: 80.5 years; 23 males, 67 females	Supervised physical therapy (3 times a week, 36 sessions), exercise training (n=46) vs. home exercise (n=44) (emphasizing flexibility) for 6 months. Supervised PT at indoor exercise facility, 2x3-month phases. Initial phase with small group including	3, 6 months	Physical performance test results (baseline/3 months/6 months): physical therapy (22.2±5.9/26.5±6.3/29.0± 6.1) vs. controls (20.7±6.2/ 23.7±8.2/23.3±7.4) (p <0.05). Instrumental activities of daily living: physical therapy (10.4±2.2/ 11.7±2.3/11.9±2.6) vs. controls (10.0±2.6/11.0± 2.6/11.3±2.5).	"In community-dwelling frail elderly patients with hip fracture, 6 months of extended outpatient rehabilitation that includes progressive resistance training can improve physical function and quality of life and reduce disability compared with low-intensity home exercise."	Entry criteria required frailty, limiting generalizability to similar patients. Home program focused primarily on flexibility, suggesting exercise regimen may be inferior, but no non-exercise control to address that question. Suggests frail patients may benefit from extended exercise with emphasis on active components such as resistance.

			have received or will receive benefits for personal or professional use.			flexibility, balance, coordination, movement speed and some strengthening. Second phase progressive strengthening.				
Ruchlin 2001 (score=6.0)	Post-operative activity limitations and rehab programs	RCT	Sponsored by a grant from Arthritis Foundation and a grant from NIH. No mention of COI.	N = 114 Hip fracture	Mean age: 79.1 years; 23 males, 91 females	Routine post-op care vs. patient education and high intensity strengthening	18 months	Control group total cost was $17,139 compared to intervention group total cost of $13,842. Baseline and 6-month follow up among individuals in physical role limitation component of SF-36 favored intervention (66.1 vs. 38.9, p = 0.002).	"The results indicate that the benefits of the intervention exceeded its costs."	Cost savings study. Intervention group less costly.

Mangione 2005 (score=6.0)	Post-operative activity limitations and rehab programs	RCT	Sponsored by Foundation for Physical Therapy Research Grant. COI: One or more of the authors have received or will receive benefits for personal or professional use.	N = 33 Elderly who completed physical therapy following hip fracture	Mean age: 78.6±6.8 years; 9 males, 24 females	Resistance vs. aerobic training vs. controls; 20 visits, twice a week 2 months, then once a week 1 month. Resistance training (hip extensor/ abductors/knee extensors, plantar flexors with latex band machine). Aerobic 20-minutes walking at 65-75% HR max. Education controls.	12 weeks	Six-minute walk distances: Resistance (197.1±104.2/ 278.9±114.6m) vs. Aerobic (232.4±122/321.1±101.7m) vs. controls (180.6±104.3/ 266.2±82.4m), NS. MVC Resistance (48.5±12.6/ 59.6±18.2kg) vs. Aerobic (55.6±17.4/67.1±22.3) vs. controls (64.1±24.6/67.7 ±22.2kg), p = 0.04	"High-intensity exercise performed in the home is feasible for people with hip fracture."	Higher dropouts in resistance training. All groups improved walking distances considerably. Suggests either exercise beneficial.

Mitchell 2001 (score=5.0)	Post-operative activity limitations and rehab programs	RCT	No mention of sponsorship. No COI.	N = 80 Patients rehabili-tating after proximal femoral fracture	Mean age: 80.1 years; 13 males, 67 females	Six weeks quadriceps training vs. standard physiotherapy after proximal femoral fracture. Quadriceps training: 3 sets of 12 repetitions of knee extension for 2 weeks at 50% of maximum strength. Then 2 weeks at 70% of new maximum and then 80% at new maximum for another 2 weeks.	16 weeks	Quadriceps training group: baseline; week 6; week 16. Leg extensor power fractured leg (W): 10.1 (0.8); 25.7 (2.1) $p \leq 0.01$; 33.0 (3.9) $p \leq 0.001$. Leg extensor power non-fractured leg (W): 20.5 (1.6); 34.9 (3.0) $p \leq 0.01$; 40.1 (4.3) $p \leq 0.05$. Elderly Mobility scale (median IQR): 10 (7, 12); 17.5 (16, 20) $p \leq 0.001$; 18 (16, 20) $p \leq 0.05$. Control group: baseline; Week 6; Week 16. Leg extensor power fractured leg (W): 11.4 (1.2); 17.7 (1.6); 21.2 (2.3). Leg extensor power non fractured leg (W): 20.8 (2.3); 24.8 (2.5); 25.4 (2.2). Elderly mobility scale (median IQR): 11 (8, 12.75); 16 (14.75, 18); 17 (15.25, 19.5).	"Progressive high-intensity quadriceps training resulted in large increases in leg extensor power and reduced disability after proximal femoral fracture."	Gains were retained at 16 weeks.
Sherrington 1997 (score=4.0)	Post-operative activity limitations and rehab programs	RCT	No mention of sponsorship. No COI.	N = 42 All hip fracture mean 7 months earlier	Mean age: 78.6 years; no mention of sex.	Home exercise program (step exercises) vs. no exercise controls; 1 follow-up visit at 1 week	7 months	Quadriceps strength improved (baseline/post-test): exercise (7.7±4.6kg/10.4±4.9, $p < 0.01$) vs. no exercise (6.6±2.7kg/7.3±3.7, NS). Gait velocity: exercise (0.46±0.28/0.51±0.34 m/s, $p < 0.05$) vs. no exercise (0.52±0.33/0.50±0.35, NS).	"This exercise program improved strength and mobility following hip fracture. Further research is needed to ascertain whether the extent of this improvement in these fall risk factors is sufficient to prevent falls."	Baseline differences of uncertain effect. Suggests home exercise program of step exercises is effective.

Evidence for the Use of Geriatric Unit Treatment

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Health Services for the Aged, Geriatric Assessment, Geriatrics, Rehabilitation Centers, Rehabilitation Programs; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 24 articles in PubMed, 151 in Scopus, 29 in CINAHL, 3 in Cochrane Library, 9660 in Google Scholar, and 21 from other sources. We considered for inclusion 11 from PubMed, 7 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 15 from Google Scholar, and 21 from other sources. Of the 54 articles considered for inclusion, 36 randomized trials and 14 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Edgren 2015 (Score= 6.5)	Physical rehab	RCT	No mention of sponsorship. The authors declared no COI.	N=81 elder community dwelling patients with hip fracture.	Mean age: 79.4 years; 18 males, 63 females.	Intervention group: patients received promoting mobility after hip fracture (ProMo) and standard care with 5 to 7 home exercises without additional resistance (n=40) vs. Control group: patients received standard care with 5 to 7 home exercises without additional resistance (n=41).	No mention of specific follow-up.	The primary outcome of this study was physical disability self-reported walking difficulty, and it was assessed by activities of daily living (ADL) and instrumental activities of daily living (IADL). The mean score of ADL in intervention group was 4.7±3.2, and 3.9±3.0 in control group (p=0.19). IDAL value score in intervention group was 9.4±7.7, and 7.8±6.5 in control group (p=0.651).	"The current analyses suggest that home-based rehabilitation may reduce disability among older people after hip fracture. The present results need to be confirmed in a study with larger sample size. Potentially a more task-oriented rehabilitation approach might gain more benefits."	Data suggest reduced disability post hip fracture with home based rehab.
Turunen 2017 (Score= N/A)	Home-based rehab	Secondary analysis of Edgren	Sponsored by the social insurance institution of	N=81 elder community dwelling patients with hip fracture.	Mean age: 79.4 years; 18 males, 63 females.	Intervention group: patients received promoting mobility after hip fracture (ProMo) and standard care with 5 to 7 home exercises without additional resistance	Follow-up at baseline, 1 year.	Physical activity (PA) level in intervention group patients was higher that control group, but the difference was not statistically significant (p=0.262). Short physical performance battery (SPPB) was used to assess physical	"The 12-month individualized multicomponent rehabilitation program increased PA among older patients with hip fracture. The increase was found to be	Data suggest a 12 month individualized multifaceted rehab program did increase physical activity in elderly hip fracture patients with gains maintained at 1 year.

		2015	Finland-Kela, and the ministry of education and culture.			(n=40) vs. Control group: patients received standard care with 5 to 7 home exercises without additional resistance (n=41).		function. Patients with SPSS score lower than 7 indicated physical disability (p=0.033) and mobility limitation (p=0.05).	maintained at the 1-year follow-up."	
Huusko 2000 (score= 6.5)	Rehab Programs for Geriatric Unit	RCT	No mention of COI. Sponsored by the Central Finland Health Care District, Kuopio University Hospital, Emil Aaltonen Foundation, Uulo Arhio Foundation and Novartis Finland Ltd.	N = 243 Community dwelling hip fracture patients over 64 years (same as Huusko 2002; this report on mild dementia)	Mean age: 80 years; 69 males, 174 females	Geriatric ward for team rehabilitation for 2 weeks (early ambulation, self-motivation and function) then 10 home PT visits over 2 months (n=120) vs. local ward for standard care (n=123)	Follow-up at 3 months and 1 year	Among those with mild dementia, 91% of geriatric unit treated patients lived independently vs. 67% of controls. For those with moderate dementia, 63% vs. 17% lived independently.	"Hip fracture patients with mild or moderate dementia can often return to the community if they are provided with active geriatric rehabilitation."	Usual care bias. Data suggest that even in mild to moderate dementia patients with hip fracture, they can return to community life if given active rehabilitation.

Huusko 2002 (score= 6.5)	Rehab Programs for Geriatric Unit	RCT	No mention of COI. Sponsored by the Central Finland Health Care District, Kuopio University Hospital, Emil Aaltonen Foundation, Uulo Arhio Foundation and Novartis Finland Ltd.	N = 243 Community dwelling hip fracture patients over 64 years	Mean age: 87.04 years; 69 males, 174 females	Geriatric ward for team rehabilitation for 2 weeks (early ambulation, self-motivation and function) then 10 home PT visits over 2 months (n=120) vs. local ward for standard care (n=123)	Follow-up at 2 weeks, 3 and 12 months	Hospital stay averaged 34 in the geriatric ward group vs. 42 in controls (p = 0.05). Mortality and complication rates not statistically different. Interventions recovered instrumental activities of daily living faster (p = 0.05). Total costs €17,900 vs. €15,900 controls.	"…the length of hospital stay of community dwelling hip fracture patients can be diminished significantly by intensive geriatric rehabilitation, which continues in the patients' homes after their discharge from hospital."	Baseline geriatric ward group less likely functionally independent (34% vs. 54%) presumably favoring controls. Data suggest intervention group rehired to the activities of daily living faster than the standard care group.

Botella-Carretero 2008 (Score= 6.0)	Geriatric	RCT	No mention of sponsorship or COI.	N=90 patients with hip fracture.	Mean age: 83.8 years; 19 males, 71 females.	Control group: patients received no oral nutritional supplements (ONS) (n=30) vs. Protein group: patients received 10 g of packets of Vegenat with 9 g protein, and 38 kcal, with 4 packets of 36 g protein daily (n=30) vs. Energy group: patients received 18.8 g protein and 250 kcal with 200 ml 2 bricks daily (n=30).	Follow-up at baseline, 1 week.	The change of primary outcome serum albumin was significant ($p<0.001$), but the decrease in three groups was similar ($p=0.251$). The change of Serum prealbumin was significant ($p=0.005$), and the change of retinol-blinding globulin (RBG) was significant ($p<0.001$). No difference was found in body mass index ($p>0.05$).	"Oral nutritional supplements in normally nourished or only mildly undernourished geriatric patients with hip fracture submitted to surgery may be of interest for patients with postoperative complications and long hospital stays."	Data suggest lack of efficacy.
Naglie 2002 (Score= 5.5)	Rehabilitation/ geriatrics	RCT	Sponsored by the Ontario ministry of health. The authors declared no COI.	N=279 patients with hip fracture and underwent surgery.	Mean age: 84.2 years; 57 males, 223 females.	Interdisciplinary group: patient received daily care and routine surgical care after surgery which was supervised by internist geriatrician and senior internal resident (n=141) vs. Usual group: patients received only routine care after surgery with geriatric consultation (n=138).	Follow-up at baseline, 6 months and 1 year.	The difference of proportion of patients alive without ambulation decline in two groups was not significant at 3rd month after surgery ($p=0.44$), same at 6th month ($p=0.67$). The short mental status questionnaire (SMSQ) scores indicated statistical significance to predict better clinical results ($p<0.05$).	"[W]e did not observe any significant longterm benefits of inpatient interdisciplinary geriatric care for a heterogeneous group of elderly patients with hip fracture, but the statistical power of our study was limited."	Usual care bias. Data suggest comparable efficacy between interventional group and usual care group.

Crotty 2003 (Score= 5.5)	Home based rehabilitation	RCT	Sponsored by the south Australian department of human services. The authors declared no COI.	N=66 patients with hip fracture and received acute care.	Mean age: 81.8±7.2 years; 25 males, 41 females.	Conventional group: patients received routine hospital rehabilitation (n=32) vs. home rehab group: patients received 48 hours postoperative therapy includes nursing care, light domestic tasks, and podiatry with occupational therapists, physiotherapists, social workers, and speech pathologists (n=34).	Follow-up at baseline, 4 and 12 months.	The conventional group patients indicated significant improvement on their measure of daily activities performance - Modified Barthel Index (MBI) (p=0.036), physical component summary score of medical outcomes study with 36 items short form health survey (SF-36) (P=0.012), and the measure of mobility- timed up and go (TUG) (p=0.001) scores. Meanwhile, the home rehab group patients also indicated significant improvement on their MBI (P=0.001), SF-36 (p=0.23), and TUG (p=0.003) scores. No significant differences were found between the two groups on MBI (P=0.25), SF-36 (P=0.386), and TUG (p=0.314) scores.	"For patients who were previously functionally independent and living in the community, early return home with increased involvement of caregivers after hip fracture resulted in similar patient outcomes (home vs hospital) and less caregiver burden at 12 months."	Data suggest at 12 months, early return to home followed up with caregiver visits resulted in increased independence and less caregiver burden.
Kennie 1988 (score= 5.5)	Rehab Programs for Geriatric Unit	RCT	No mention of COI. Sponsored by the Forth Valley Health Board.	N = 106 All females with proximal femoral fractures	No mean age specified. Median age for intervention group: 79 years, median age for control group: 84 years; 0 males,	Rehabilitation ward (general practitioner care, geriatric consultant with 2 ward rounds and 1 weekly multidisciplinary team conference) (n=54) vs. orthopaedic ward care (n=54). Both groups received PT, OT, and orthotics.	Follow-up at 1 and 3 months	Inpatient hospital stays favored rehabilitation ward with less than 4 weeks stays among 32/54 rehabilitation ward care patients vs. 18/54 orthopaedic ward care. More discharges (31 vs. 19) to patients' homes occurred in rehabilitation group (p = 0.03).	"Both hospital and patient benefited when postoperative rehabilitation was provided in a setting specialising in such care for elderly patients with trauma."	Supports rehabilitation ward treatment.

					108 females					
Reid 1989 (score= 5.5)	Rehab Programs for Geriatric Unit	RCT	No mention of COI or sponsorship.	N = 106 All females with proximal femoral fractures	No mean age specified. Median age for intervention group: 79 years, median age for control group: 84 years; 0 males, 108 females	Same study as Kennie, except 1-year follow-up	Follow-up at 1 year	At 1-year, 67% controls vs. 81% rehabilitation ward treated patients survived. Living location was same as pre-fracture for 69% of rehabilitation ward treated patients vs. 39% of controls.	"These outcomes challenge the conventional practice of keeping elderly patients with femoral fractures in orthopaedic wards for their postoperative rehabilitation."	Supports rehabilitation ward for both return to the same living environment as well as survival.
Sherrington 2003 (score= 5.5)	Rehab Programs for Geriatric Unit	RCT	Sponsored by the Health Research Foundation Sydney South West and the Arthritis Foundation. No mention of COI.	N = 80 All had hip fracture from a fall and in inpatient rehabilitation	Mean age: 81 years; 26 males, 54 females	Two week programs of daily weight-bearing exercise program (n=41) vs. non-weight-bearing (n=39) (exercises same as Sherrington 2004 above). All received practice with walking and advancement with walking aids.	No long term follow-up.	Physical performance and mobility examination scores (pre/post): weight bearing (5.4/7.5) vs. non-weight bearing (4.5/6.8) NS. Gait (m/s): weight bearing (0.12/0.25) vs. non-weight-bearing (0.09/0.19), NS. Strength measures not different between groups. Ability to walk with either 1 stick or no aid 20% vs. 5%, p <0.05.	"Weight-bearing and non-weight-bearing exercise programs produce similar effects on strength, balance, gait and functional performance among inpatients soon after hip fracture."	Trial length of only 2 weeks and co-interventions of exercises with both weight-bearing appear likely to have reduced possible differences. Walking ability favored weight bearing exercise group.
Stenvall, 2007 (score= 5.0)	Post-operative activi	RCT	Supported by the "Vårdal Foundati	N = 199 patients with femoral	Mean age: 82.15 years; 51	Intervention group: geriatric ward with special intervention program received;	No follow-up.	Fall incidence rate was 6.29 per 1,000 days for the intervention group compared to 16.28 per 1,000 days in the	"A team applying comprehensive geriatric assessment and	Baseline differences between groups for anti-depressants and depression. Data

	ty limitations and rehab programs		on," the Joint Committee of the Northern Health Region of Sweden (Visare Norr), the JC Kempe Memorial Foundation, the Dementia Fund, the Foundation of the Medical Faculty, the Borgerskapet of Umeå Research Foundation, University of Umeå, the County Council of Västerbotten,	neck fracture.	males, 148 females	comprehensive geriatric assessments, management, and rehabilitation (staffing was 1.07 nurses/aids per bed) (n=102) Vs Control Group: received conventional postoperative care in orthopedic geriatric ward with no rehabilitation (staffing 1.01 nurses/aids per bed) (n=97)		control group (IRR=0.38; 95% CI 0.2-0.76). Fall rate was reduced in intervention group compared to control group (p=0.008). Fall risk was lower for intervention group (HRR=0.41; 95% CI 0.2-0.82; p=0.012). Intervention group did not have any fractures compared to control group with 4 new fractures.	rehabilitation, including prevention, detection, and treatment of fall risk factors, can successfully prevent inpatient falls and injuries, even in patients with dementia."	suggest a comprehensive multidisciplinary program can prevent excess falls even in those with dementia.

			and the Swedish Research Council, Grants. No COI.							
Taraldsen 2013 (Score= 5.0)	Geriatrics	RCT	Sponsored by the central Norway health authority, Norwegian research council, St. Olav hospital trust, department of neuroscience Norwegian university of science and technology, Norwegian women's health association. One of the	N=317 patients with hip fracture and can walk 10 meters before fracture.	Mean age: 83.1 years; 81 males, 236 females.	Intervention group: patients received comprehensive geriatric care (CGC) includes interdisciplinary function, health, social, disease assessment and meetings (n=175) vs. Control group: patients received orthopedic care (OC) includes traditional in hospital physiotherapy (n=142).	No mention of follow-up.	The primary outcome total time spent in upright in intervention group (average 57.6 minutes) was significantly higher than that in control group (average 45.1 minutes) (p=0.016). The number of upright events in intervention group was also significantly higher than that in control group (p=0.005).	"When treated with CGC, compared with OC, older persons suffering a hip fracture spent more time in upright, had more upright events, and had better lower limb function early after surgery despite no difference in their need for assistance during ambulation."	Data suggest CGC group experienced increased lower limb function and spent more time in upright events compared OC group.

			authors has received or will receive benefits for personal or professional use.							
Hagsten 2004 (Score= 5.0)	Occupational therapy training	RCT	Sponsored by the King Gustaf V and Queen Victoria foundation, the Swedish foundation for healthcare sciences and allergy research, the Swedish foundation of occupational therapists, Huddinge universit	N=100 Swedish patients with hip fracture.	Mean age: 80 years; 20 males, 80 females.	Occupational group: patients received occupational therapy (OT) training with 45 to 60 minutes every weekday morning (n=50) vs. Control group: patients received conventional care with nursing staff supervision (n=50).	Follow-up at baseline, 2 months.	Compared with control group, the occupational group indicated better activities of daily life (ADL) includes dressing (p=0.0001), toilet visits (p=0.02), and bathing (p=0.0001). The disability rating index (DRI) in the two groups did not showed significant difference (p>0.05). At follow-up, the occupational group indicated worse outdoor instrumental activities of daily living (IADL) than that in control group.	"We conclude that individualized OT training can speed up a patient's abilities to perform ADL on discharge from hospital, which enhances the possibility of the patient returning to independent living at home."	Data suggest early and individualized post-operative OT training increased ADL and could likely cause a return to independent living earlier as well as decreasing home care requirements.

			y hospital (Stockholm), and the research committee for caring sciences at Karolinska institutet. The authors declared no COI.							
Prestmo 2015 (Score= 5.5)	Geriatrics	RCT	Sponsored by St. Olav hospital trust and fund for research and innovation, Norwegian university of science and technology, Norwegian research council,	N=397 Norwegian patients with hip fractures.	Mean age: 83.3 years; 104 males, 293 females.	Geriatric group: patients received comprehensive geriatric care (n=198) vs. orthopaedic group: patients received orthopaedic care (n=199). Both groups analyzed progress using measurements from Short Physical Performance Battery.	Follow-up at baseline, 5 days, 1, 4, and 12 months.	Geriatric group indicated better short physical performance battery (SPPB) score for primary outcome mobility than that in orthopaedic group (95%CI=0.18 to 1.30; p=0.01) in 4th month and in (95%CI=0.1 to 1.28, p=0.023) 12th month follow-up. Activities of daily living (ADL) score in geriatric group was significantly better than that in orthopaedic group (95%CI: 2.59 to 10.19; p=0.001).	"Immediate admission of patients aged 70 years or more with a hip fracture to comprehensive geriatric care in a dedicated ward improved mobility at 4 months, compared with the usual orthopaedic care. The results suggest that the treatment of older patients with hip fractures should be organised as orthogeriatric care."	Data suggest immediate comprehensive geriatric care group experienced improved mobility at 4 months.

			central Norway regional health authority, and foundation for scientific and industrial research at Norwegian institute of technology. The authors declared no COI.							
Vidán 2005 (Score= 5.0)	Geriatrics	RCT	Sponsored by the Fondo de investigaciones sanitarias in Spain. No mention of COI.	N=319 patients (≥65 years) with hip fracture.	Mean age: 81.9 years; 59 males, 260 females.	Intervention group: patients received multidisciplinary geriatric intervention includes psychosocial and medical problem and functional therapy per day (n=155) vs. Usual care group: patients received usual care in hip fracture acute phase with different specialists counseling during hospitalization (n=164).	Follow-up at baseline, 3, 6, and 12 months.	The intervention group indicated shorter hospital stay median length than that in usual care group (16 vs. 18; p=0.06). The intervention group showed less medical complications after surgery than that in usual care group (45.2% vs. 61.7%; p=0.003).	"Early multidisciplinary daily geriatric care reduces in-hospital mortality and medical complications in elderly patients with hip fracture, but there is not a significant effect on length of hospital stay or long-term functional recovery."	Data suggest early daily multidisciplinary geriatric care reduces in-hospital deaths and prevents complications.

Shyu 2012 (Score= 5.0)	Geriatrics / rehabilitation	RCT	Sponsored by National health research institute in Taiwan. No mention of COI.	N=299 patients received femoral neck fracture.	Mean age: 76.17 years; 108 males, 191 females.	Comprehensive group: patients received comprehensive care (n=99) vs. Interdisciplinary group: patients received interdisciplinary care with transitional and acute or subacute intervention (n=101) vs. Usual group: patients received usual care includes bed exercise and position transition training, and occasional internal medicine care (n=99).	Follow-up at baseline, 1, 3, 6, and 12 months.	The likelihood of complete independence recovery was significantly greater in comprehensive care group than that in usual care group (Odds ratio: 3.19; p<0.01). Emergency room (ER) visits was less likely in interdisciplinary care group than that in usual care group (Odds ratio: 0.4; p<0.05).	"In conclusion, researchers' comprehensive care program with nutrition consultation, depression management, and fall prevention along with interdisciplinary care components (geriatric hip-fracture assessment and rehabilitation and discharge support) appeared to be more beneficial than only interdisciplinary care for older persons with hip fracture in Taiwan."	Data suggest comprehensive care group better than other 2 groups.
Lamb 1998 (score= 5.0)	Rehab Programs for Geriatric Unit	RCT	No mention of COI or sponsors hip.	N = 24 Females over 75 years with hip fractures	Mean age: 83.5 years; 0 males, 24 females	Patterned neuromuscular stimulation (PNMS) of the quadriceps muscle vs. placebo stimulation	Follow-up at 7 and 13 weeks	Seventy-five percent compliance; PNMS participants recovered their pre-injury levels of mobility at 7 weeks ($p < 0.05$), but no differences in walking speed. Improvements for PNMS group in walking speed between 7 and 13 weeks after fixation, whereas control group did not ($p < 0.05$).	"Neuromuscular stimulation can improve recovery of mobility after surgical fixation for PFF, larger studies are needed to provide more precise estimates of the treatment effect."	Abstract
Watne 2014 (score= 4.5)	Rehab Programs for Geriatric Unit	RCT	No COI. Sponsored by the Research Council of	N = 332 with a femoral neck, trochanteri or sub-trochant	No mention of mean age – median age for acute geriatric	Acute geriatric ward – 20 bed ward, mainly admitting patients suffering from acute medical disorders with frailty, co-morbidities and polypharmacy, including a	Follow-up at 4 and 12 months	Cognitive function four months after surgery (Clinical Dementia Rating Scale (CDR)) Consortium to Establish a Register for Alzheimer's Disease battery (CERAD))	"Pre- and postoperative orthogeriatric care given in an acute geriatric ward was not effective in reducing delirium or long-term cognitive impairment in patients with hip fracture. The	The Oslo Orthogeriatric Trial. Data suggest lack of efficacy.

			Norway through the program 'Improving mental health of older people through multidisciplinary efforts', Oslo University Hospital, The Sophies Minde Foundation, The Norwegian Association for Public Health and Civitan's Research Foundation.	eric facture	ward: 84 years, median age for orthopedic ward: 85 years; 80 males, 252 females	Comprehensive Geriatric Assessment (all team members had daily meetings to coordinate treatments) (n=163) vs. Orthopedic ward – 52 bed ward, admitting elective and non-elective orthopedic patients, no multidisciplinary meetings or assessments (n=166)			intervention had, however, a positive effect on mobility in patients not admitted from nursing homes."	
Lahtinen 2015 (score= 4.5)	Rehab Programs for Geria	RCT	No COI. Sponsored by the Finnish Office	N = 538 non-pathological hip fracture patients	Mean age: 78.08 years; 105 males,	Geriatric rehabilitation – focused on physical training and associated geriatric problems, physiotherapist visits,	Follow-up at 4 and 12 months	No significant differences between groups in Health-Related Quality of Life categories, social status, psychological status, Mini-Mental State Examination,	"Physical rehabilitation reduced mortality. Physical and geriatric rehabilitation significantly improved the ability of	Usual care bias. Data suggest physical rehabilitation reduces mortality while improving mobility leading to

	tric Unit		for Health Technology Assessment (FinOHTA).	treated surgically	433 females	physiotherapy and group therapy, activities of daily living (ADL) and mobilization (n=171) vs. Physical rehabilitation – given assistance in ADLs, mobilization therapy, occupational therapy and rehabilitation physiotherapy including physical, balance and gym exercises (n=187) vs. Control group – routine basic level of rehabilitation, given assistance with ADL and mobilization (n=180)		Short Portable Mental Status Questionnaire, associated disease, or ADL (except for higher ADL toilet function in rehabilitation (p=0.011)). Physical rehabilitation produced more exercise events, ADL-exercises per day, and used more time in ADL-exercises than geriatric rehabilitation or control group (p<0.001). Mortality lower in physical rehabilitation group versus geriatric rehabilitation at 4 months (p=0.026) and versus control group (p=0.006).	independent living after 4 months especially among the femoral neck fracture patients but this effect could not be seen after 12 months."	independent living 4 months after hip fractures.
Galvard 1995 (score= 4.5)	Rehab Programs for Geriatric Unit	RCT	No mention of COI or sponsorship.	N = 371 Community dwelling hip fracture patients	Mean age: 79.26 years; 95 males, 276 females	Orthopedic (n=192) vs. geriatric rehabilitation (n=179) (scant descriptions of program components)	Follow-up at 1 year	Days in the hospital were orthopedic 28.0±24.2 vs. geriatric 53.3±47.7 days. Discharge to prior living were 72.0% vs. 72.4% (NS). Deaths were not different. Walking speeds not different. More orthopedic-related readmissions (27.9% vs. 11.9%) occurred in the orthopedic unit treated group. Total costs orthopedic group SKr84, 537 vs. SKr94, 026.	"[H]ip fracture patients may be rehabilitated under geriatric supervision and obtain results, that are fully comparable to orthopedic rehabilitation."	Baseline differences (younger age of males and fewer subtrochanteric fractures) favored orthopedic unit treatment. Results suggest rehabilitation in a geriatric unit possible. Geriatric unit had no prior prolonged experiences with rehabilitation of orthopedic patients.
Tinetti 1999 (score= 4.5)	Rehab Programs for Geria	RCT	No COI. Sponsored by the Claude D.	N = 304 27 home care agencies All had had	Mean age: 79.94 years; 55 males,	Home-based multicomponent rehabilitation program (n=148) vs. usual care (n=156); multi-component program	Follow-up at 6 and 12 months	Regaining prefracture level of self-care ADLs at 6 months: multicomponent rehabilitation 71% vs. usual care 75%, p = 0.40. Complete independence 67% vs. 71% (p	"The systematic multicomponent rehabilitation program was no more effective in promoting recovery than	Large size and multiple agencies may improve generalizability of results, however dropouts high.

	tric Unit		Pepper Older Americans Independence Center grant from the National Institute on Aging.	surgical repair of hip fracture	249 females	included identification of deficits and tailoring PT program plus functional therapy; usual care included home PT		= 0.49). Complete ADL independence at 6 months 9% vs. 16%, p = 0.07 and 12 months 19% vs. 25%, p = 0.23. No differences in mobility, balance of lower extremity strength. Gait performance at 6 months favored rehabilitation program (p = 0.08).	usual home-based rehabilitation."	Suggests multi-component rehabilitation program not superior to usual care.
Huang 2005 (score= 4.5)	Rehab Programs for Geriatric Unit	RCT	No mention of COI. Sponsored by the National Science Council, Taiwan and Chung Gung University.	N = 126 with hip fractures due to falling	Mean age: 77.0 years; 39 males, 87 females	Discharge planning intervention – gerontological nurse provided discharge service, visited patient at least every 48 hours during hospitalization, 3-7 days after patient discharge the nurse was available for patients to call but also initiated a weekly call up to three months, patients also provided with educational procures and individualized discharge plans (n=63) vs. Control group – received hospital routine discharge planning, given no educational materials (n=63)	Follow-up at 3 months	Discharge planning intervention lead to few hospitalized stays (8.17 days) versus the control intervention (10.06, p=0.002). The intervention also produced fewer readmissions (4 versus 13, p=0.02) and a higher number of survival in patients (100% versus 93.56%, p=0.04) when compared to the control. The intervention did not produce a statistically different number of repeat falls when compared to the control (5 versus 7, p=0.57)	"The discharge planning benefited older people with hip fractures. Relevance to clinical practice. A discharge planning intervention by a nurse can improve physical outcomes and quality of life in hip fracture patients."	Usual care bias. Data suggest the interventional group had decreased length of stay, rate of admissions and improved activities of daily living and increased survival.
Shyu 2010	Geriatrics /	RCT	Sponsored by national	N=162 patients with	Mean age: 78.2 years; 51	Intervention group: patients received 1) early postoperative	Follow-up at baseline, 1, 3, and	Ratio of hip flexion (RHF) and walling ability recovery were better in intervention group	"The interdisciplinary intervention for hip fracture benefited	Data suggest interdisciplinary group benefits included

(Score= 4.5)	reha bilita tion		health research institute in Taiwan. The authors declared no COI.	single side accident al hip fracture and underwe nt total hip replacem ent.	males, 111 females.	continuous rehab includes enhancing physical fitness intervention and hip fracture tailored intervention; 2)discharge planning service includes predischarge assessment and home environment assessment and modification; and 3) geriatric consultation with geriatric staff pre- and post-operatively (n=80) vs. Control group: patients received usual care includes orthopedists care and occasional internal medicine consultation pre- and post-operatively (n=82).	6 months, 1, 1.5, and 2 years.	than that in control group (p<0.001) Self-care ability was significantly improved in intervention group for activities of daily living than that in control group (p<0.001). Patients in intervention group also indicated significant better health related quality of life (HR QoL) physical score than that in control group (p<0.001).	elderly persons with hip fracture by improving clinical outcomes, self-care ability, and physical health–related outcomes and by decreasing depressive symptoms during the first 24 months after hospital discharge."	improved self-care and decreased depressive symptoms as well as improved walking ability and hip flexion.
Tseng 2016 (score= NA)	Reha b Progr ams for Geria tric Unit	Sec ond ary Ana lysis of Shy u 201 0	No COI. Sponsor ed by the National Health Research Institute, Taiwan.	N = 153 who had been hospitali zed for accident al single-side hip fracture, receiving hip arthropla sty or internal fixation,	Mean age: 78.01 years; 48 males, 105 females	Usual care – after surgery a nurse would teach the patient how to exercise in bed and change position and also provided education on health after hospital discharge, also included physical therapy (n=77) vs. Interdisciplinary program including geriatric consultation services, a continuous	Follow-up at 1, 3, 6, 12, 18 and 24 months	Those in the interdisciplinary group had lower risk for being persistently depressed (OR=0.23, p<0.05). Those in interdisciplinary group were not at lower risk for being marginally depressed (OR=0.34, p>0.05).	"Our interdisciplinary intervention reduced older persons' likelihood of having persistent depressive symptoms after hip fracture surgery."	Data suggest depressive symptoms decreased after interdisciplinary intervention.

				and have a diagnosis of depression		rehabilitation program, and discharge-planning services (n=76)				
Elinge 2003 (score=4.0)	Rehab Programs for Geriatric Unit	RCT	Sponsored by the Swedish National Board of Health and Welfare and the Geriatric Centre, Umeå University Hospital. No mention of COI.	N = 35 with a hip fracture who were part of a larger group learning program	Mean age: 73.38 years; 8 males, 27 females	Group learning program – educated about effects of osteoporosis, risk factors for osteoporosis, fall prevention, and how to perform activities of daily living (ADL), groups consisted of 5-8 participants, groups met for 2 hours weekly for 10 weeks (1 hour of education, 1 hour of physical training focused on muscle strength and balance) (n=21) vs. Control group – received no program except for scheduled assessments (n=14)	Follow-up at 12 months	Barthel ADL scores at pre-intervention (T1), post-intervention (T2), and 12 month follow-up (T3) for intervention group and control group, respectively: 20, 20, 20 (Within-group significance: p=0.58), 19, 19, 19 (p=0.46). Number of ALD items performed with difficulty: 3, 1, 4 (p=0.01), 2, 1.5, 1 (p=0.86). Perceived reduced ability to participate in activities with family and friends: 11, 4, 4, (p=0.01), 10, 8, 6 (0=0.14)	"When analysed between groups, however, the only significant difference was the ability to participate in social life after the intervention. Further research is needed to investigate whether an intensive or prolonged period of rehabilitation, at the hospital or in the patient's home, would increase the ability to resume meaningful participation in social life."	Small sample. Usual care bias. Data suggest lack of efficacy.
Swanson 1998 (score=4.0)	Rehab Programs for Geriatric Unit	RCT	No mention of COI or sponsorship.	N = 71 with non-pathological fracture, residing at home or in a hostel	Mean age: 78.17 years; 16 males, 55 females	Standard orthopedic management – daily visits with physiotherapist, social worker/occupational therapist, weekly discharge planning meetings, home visits as requested, referral to community services as needed (n=38) vs. Multidisciplinary team	Follow-up at 1 and 6 months	Multidisciplinary intervention produced a shorter length of stay compared to standard care (21 versus 32.5 days, p<0.01). Mean functional levels at discharge higher in intervention than standard care (92.8 versus 85.6, p=0.004).	"This early intervention program in an acute care setting results in significantly shorter length of hospital stay for elderly patients with femoral fractures."	Standard care bias. Data suggest early intervention program results in decreased length of stay.

						– early mobilization, daily assessment by occupational therapist and social worker, weekly case conference attended by all staff, postoperative care by orthopedic unit, home assessment visit before discharge (n=33)				
Cameron 1993 (score= 4.0)	Reha b Progr ams for Geria tric Unit	RCT	Support ed by Australia n Departm ent of Health, Housing and Commun ity Services. No mention of COI.	N = 252 All uncompli cated proximal femoral fractures with surgery within 7 days	Mean age: 83.9 years; 42 males, 210 females.	Accelerated rehabilitation (early mobilization after surgery, comprehensive rehabilitation program, liaison with a care-giver, early hospital discharge, community-based rehabilitation) (n=127) vs. conventional care (variously interdisciplinary program, discharge home, and transfer to nursing home) (n=125)	Follow up at 2 weeks and 1 and 4 months.	Length of hospital stay in limited disability group not in a nursing home before fracture was median 20 days for accelerated care vs. 32 days for conventional (p = 0.024). Those with moderate to severe pre-fracture disability not in a nursing home, hospitalization median 20 vs. 30.5 days (p = 0.324). Lengths of stays for accelerated care were under 1 month for 107 (84%) of accelerated care vs. 84 (67%) of conventional care.	"Accelerated rehabilitation led to a substantial reduction in length of hospital stay with a modest short-term improvement in level of physical independence and accommodation status after discharge."	Disparate care given in control group somewhat limits conclusions. Data suggest accelerated rehabilitation is superior.
Cameron 1994 (score= 4.0)	Reha b Progr ams for Geria tric Unit	RCT	Supporte d by Australia n Departm ent of Health, Housing and Commun ity	N = 252 All uncompli cated proximal femoral fractures with surgery within 7 days	Mean age: 84.0 years; 0 males, 252 females	Accelerated rehabilitation (early mobilization after surgery, comprehensive rehabilitation program, liaison with a care-giver, early hospital discharge, community-based rehabilitation) (n=127)	Follow-up at four months	Costs for treatment A $10,600 for accelerated rehabilitation vs. A $12,800 for conventional rehabilitation. There were no differences in recovered vs. worse vs. dead status.	"[A]ccelerated rehabilitation is cost-effective in treating (proximal femoral fracture) and appears superior to conventional orthogeriatric care."	Study based in Australia making generalizability and cost estimates difficult to compare.

			Services. No mention of COI.			vs. conventional care (variously interdisciplinary program, discharge home, and transfer to nursing home) (n=125)				
Quine 1994 (score= 4.0)	Rehab Programs for Geriatric Unit	RCT	Supported by Australian Department of Health, Housing and Community Services and the Department of Public Health, University of Sydney. No mention of COI.	N = 252 All uncomplicated proximal femoral fractures with surgery within 7 days	No mention of mean age; 31 males, 162 females.	Accelerated rehabilitation (early mobilization after surgery, comprehensive rehabilitation program, liaison with a care-giver, early hospital discharge, community-based rehabilitation) (n=127) vs. conventional care (variously interdisciplinary program, discharge home, and transfer to nursing home) (n=125)	Follow up immediately after discharge and at 1, 4, and 12 months.	Thirty-eight percent of carers assessed by social worker as having burden caring for fracture patient; 55% mild, 40% moderate, 5% severe. Initial assessment of burden highly correlated with initial disruption ($r = 0.9$, $p < 0.001$).	"Accelerated rehabilitation does not impact greatly on carer burden, but already severely burdened carers may benefit from additional counseling/information."	Suggests disruption results in care-giver burden.
Karumo 1977 (score= 4.0)	Rehab Programs for Geriatric Unit	RCT	No mention of sponsorship or COI.	N = 87 all femoral neck fractures. Thompson prostheses (n = 39) and 48 with	Mean age: 72.9 years; 22 males, 65 females.	Intensive physical therapy (usual plus 2nd PT a day) vs. usual therapy. Intensive PT included 30 minutes walking with crutches first post-operative day, early weight bearing mostly on 1st day, sitting in chair,	Follow up first day post-op and 2, 4, and 9 weeks post-op.	Total hospitalization days prosthesis group (intensive PT 31.8±19.6, routine PT 33.9±20.1) vs. internal fixation (intensive 32.5±23.6, routine 36.0±23.2). Intensive groups better able to move and sit up in bed on 1st post-operative day ($p < 0.001$).	"Postoperative mobilisation of elderly patients with femoral neck fractures causes a great deal of work to the nursing staff. Intensified physical therapy did not hasten the patients' recovery in this study."	Some method details sparse; 13 excluded due to inadequate follow-up, but apparently not part of study. Aspects of study dated, e.g., patients hospitalized average 6-7 days prior to operation; may have impacted results.

				internal fixation.		stair training on 2nd post-op day.				
Thingstad 2016 (score= 3.5)										Standard care bias. Data suggest comprehensive geriatric care improved gait up to 12 months post hip fracture.
Day 2001 (score= 3.5)										Some baseline differences of uncertain significance. Data suggest early rehabilitation program superior to standard care.
Galvard 1995 (score= 3.5)										Data suggest orthopedic hospital length of stay was less than geriatric rehabilitation length of stay but had more readmissions. There were no differences in walking ability.
Rubenstein 1984 (score= 3.0)										Data suggest control group had more hospital days, nursing home days, and readmissions.
Jette 1987 (score= 2.5)										Methods details sparse. Unclear if numbers of appointments differed in 2 programs. Programs appear to be exercise vs. exercise plus education.
Gilchrist 1988										Data suggest comparable results for

(score= 2.0)										length of stay and mortality.

Evidence for MR Arthrogram to diagnose femoroacetabular impingement

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Labral Tears, Femoroacetabular Impingement (FAI), treatment; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 102 articles in PubMed, 128 in Scopus, 154 in CINAHL, 2 in Cochrane Library, 4070 in Google Scholar, and 0 from other sources. We considered for inclusion 9 from PubMed, 4 from Scopus, 5 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 20 articles considered for inclusion, 10 diagnostic studies and 6 systematic studies met the inclusion criteria.

Evidence for the Use of Diagnostic Tests for Femoroacetabular Impingement (FAI)

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Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Magnetic Resonance Imaging (MRI)										
Magee 2015 (Score= 6.5)	Magnetic resonance imaging (MRI) / Magnetic resonance arthrography (MRA)	Diagnostic	No mention of sponsorship or COI.	N=43 patients experienced hip pain and underwent hip MR arthroplasty.	Mean age: 34 years; 28 males, 15 females.	Acetabular labral tears/ chondral defects	Conventional hip MR group: patients received 3 T Signa scanner which spins 550/10 ms at repetition time echo T1 weighted, and 4100/55 ms at repetition time echo T2 weighted (n=43) vs. MR arthrography group: patients received MR arthrography with 15 cc diluted Magnevist saline mixture (n=43).	To detect acetabular chondral defects, the conventional MR indicated 100% specificity and 65% sensitivity by reader 1, and same specificity and 59% sensitivity by reader 2. The MR arthrography indicated 91% specificity and 81% sensitivity by reader 1, and 82% specificity and 71% sensitivity by reader 2.	"In this series, 3.0-T MR demonstrated sensitivity for detection of acetabular labral tears that rivals the sensitivity of 3.0-T MR arthrography of the hip. In this series, 3.0-T MR arthrography was more sensitive than conventional 3.0-T MR for detection of acetabular chondral defects."	Data suggest MR with an arthrogram is more sensitive than conventional MR for acetabular chondral defect imaging.
Banks 2012 (Score= 6.5)	Magnetic resonance arthrography (MRA)	Diagnostic	The authors declared no sponsorship of COI.	N=66 patients underwent hip arthroscopy.	No mention of age or sex.	Labral tears/ chondral wear	Pre-operative MRA group: patients received magnetic resonance arthrography	To detect labral tears, MRA indicated 81% sensitivity, 51% specificity, and 58% accuracy. To	"In our institution, negative MRA would not prevent us from undertaking	Data suggest MRa for detecting labral tears and chondral wear in femoroacetab

							(MRA) with two 15 degree internal rotation planes on Siemens symphony 1.5 tesla machine with 14-20 cm view scans (n=66) vs. Intraoperative group: patients received arthroscopies with hip distracter and standardized 2 portal saline distension (n=66).	detect chondral damage, MRA indicated 17% specificity, 100% accuracy, and 100% specificity.	hip arthroscopy in patients with a clear clinical picture of impingement and radiological signs of FAI, with the caveat that it is not our intention to suggest the use of arthroscopy as a diagnostic tool."	ular impingement (FAI) was not as good as previous reports have suggested.
Sutter 2012 (Score= 6.5)	Magnetic resonance imaging (MRI) / Magnetic resonance arthrography (MRA)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=126 patients with FAI symptoms and volunteers without FAI symptoms.	Mean age: 34.9 years; 66 males, 60 females.	Femoral antetorsion	Volunteer group: volunteers with no symptoms of FAI underwent non- enhanced magnetic resonance (MR) imaging with a Siemens 1.5 T system and Syngo MR b17 software (n=63) vs. FAI group: patients with FAI symptoms underwent MR arthrography	MR imaging can assess femoral antetorsion with high agreement (Intraclass correlation coefficient=0.966). The two groups indicated similar antetorsion: reader 1: 12.7°± 10 vs. 12.6°±9.8; reader 2: 13.5°± 9.8vs.12.8°±10.	"Femoral antetorsion can be measured rapidly and with good reproducibility with MR imaging. Patients with pincer-type FAI had a significantly larger femoral antetorsion than patients with cam-type FAI."	Data suggest femoral ante torsion can be measured rapidly (approximately 80 seconds) and shows substantial reproducibility with MRI.

							with a Siemens 1.5 T system, Syngo MR b17 software, and T2 transverse weighted spin echo fast sequence (n=63).	1. Patients with FAI pincer type indicated higher femoral antetorsion than those with FAI cam type (P=0.02 by reader 1; p=0.04 by reader 2).		
Buck 2011 (Score= 6.5)	Ultrasound/Magnetic resonance arthrography (MRA)	Diagnostic	No mention of sponsorship or COI.	N=50 patients with suspected cam type FAI according to their clinical examination.	Mean age: 39.1 years; 26 males, 24 females.	Cam type femoroacetabular impingement (FAI)	Ultrasound group: patients received ultrasound scan by using a curved 2 to 5 MHz frequency array transducer in leg and hip joint (n=50) vs. Arthrography group: patients received a standard magnetic resonance (MR) arthrography with a 1.5 T Siemens system (n=50).	To detect anterosuperior cam deformity, Ultrasound (US) indicated 93% sensitivity and 36% specificity by reader 1, and 89% sensitivity and 14% specificity by reader 2. For bony protuberance anterosuperiorly, US indicated 71% sensitivity and 86% specificity by reader 1, and 32% sensitivity and 82% specificity by reader 2. For anterosuperior waist deficiency, US showed 25%	"A technique to evaluate cam type FAI using US is presented. The detection of an anterosuperior cam deformity is sensitive, and presence of an anterosuperior bony protuberance is specific for cam FAI."	Data suggest detection of an anterosuperior cam deformity can be detected using US but alpha angle measurements do not help make the diagnosis.

								sensitivity and 100% specificity by reader 1, and 54% sensitivity and 54% specificity.		
Sahin 2014 (Score= 6.0)	Magnetic resonance arthrography (MRA)/ Computed tomography arthrography (CTA)	Diagnostic	No mention of sponsorship or COI.	N=14 patients experienced hip FAI.	Mean age: 35 years; 3 males, 11 females.	Labral pathology/ hip articular cartilage disorder	MRa group: patients received magnetic resonance arthrography(MRa) by a 1.5 T Siemens scanner and a wraparound flexible surface oil (n=14) vs. CTa group: patients received multidetector computed tomography arthrography (CTa) by a 64 row scanner with 1.5 pitch, high resolution filter, 0.5 mm slice thickness, 512x512 matrix, and 15 cm view field (n=14).	To assess labral tearing, the MRa group indicated 100% sensitivity, 50% specificity, and 86% accuracy; and the CTa group showed 100% sensitivity, specificity, and accuracy; the differences between the groups were significant ($p<0.05$). For acetabular cartilage assessment, MRa indicated 89% sensitivity, 40% specificity, 71% accuracy; while CTa showed 56% sensitivity, 60% specificity, and 71% accuracy; but the differences were not	"Inter-observer reliability with CTa is excellent for labral tearing assessment. CTa seems to have an equal sensitivity and a higher specificity than MRa for the detection of labral pathology. MRa is better, but not statistically significantly, in demonstrating acetabular and femoral cartilage pathology."	Small sample. Data suggest CTa has equal sensitivity with better specificity for visualizing acetabular and femoral cartilage damage but this is not a statistically significant difference.

								significant (p>0.05)		
Aprato 2013 (Score= 6.0)	Magnetic resonance arthrography (MRA)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=41 patients with FAI clinical diagnosis	Mean age: 24 years; 24 males, 17 females.	Labral tears / os acetabuli / cam type FAI	Group A: patients underwent surgical dislocations had intraoperative magnetic resonance arthrography (MRA) with a 1.5 T scan equipment (n=21) vs. Group B: patients received hip arthroscopies took intraoperative MRA with a 1.5 T scan equipment (n=20).	To detect cam type FAI, MRA indicated 100% sensitivity, specificity, positive and negative predictive value (PPV/NPV). For femoral head cartilage lesions, MRA showed 46% sensitivity, 81% specificity, 55% PPV, and 73% NPV. To detect labral tears, MRA showed 91% sensitivity, 86% specificity, 97% PPV, and 67% NPV. For acetabular cartilage damage, MRA indicated 69% sensitivity, 88% specificity, 78% PPV, and 81% NPA.	"MRA appears to be an efficacious imaging modality in the evaluation of labral tears, cam-type impingement lesions and os acetabuli of the hip. MRA is less efficacious in the diagnosis of cartilage abnormalities in the hip, both femoral and acetabular."	Data suggest MRA is effective in imaging impingement lessons and os acetabuli of the hip both less effective in imaging femoral and acetabular cartilaginous abnormalities of the hip.
Domayer 2011 (Score= 5.5)	Radiograph/ Magnetic	Diagnostic	Sponsored by Siemens Healthca	N=60 patients with hip internal	Mean age: 28±10.2 years;	Cam deformity	Radiograph group: patients received 38 anteroposterio	Dunn view indicated 96.4% sensitivity to	"The 45◦ Dunn view can improve the first line of	Data suggest 45 degree Dunn view enhances first

	resonance imaging (MRI)		re. COI: One or more of the authors have received or will receive benefits for professional use.	rotation limitation and FAI clinical symptoms.	31 males, 29 females.		r and 45°Dunn views, 22 anteroposterior and lateral crossed table views (n=60) vs. Radial MRI: patients received magnetic resonance imaging (MRI) by a 1.5 T Siemens system and 8 channel flexile surface coil (n=60).	detect cam deformity, and 70.6% sensitivity by cross table lateral view. Radial MRI detected cam deformity in 75% cases. Dunn view showed higher accuracy to superior anterior aspect (Person correlation=0.772; p<0.05), while cross table review indicated best suitability to anterior superior aspect (Person correlation=0.511; p<0.05).	impingement diagnostics. Radial MRI however remains indispensable for pre-operative planning and the evaluation of symptomatic cases without obvious deformity."	line impingement diagnostics. However, in cases without clear deformity radial MRI is the imaging to use when planning femoral head-neck function osteoplasty.
Crespo-Rodríguez 2017 (Score= 5.0)	Magnetic resonance imaging (MRI) / Magnetic resonance arthrography (MRA)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=50 patients with radiological detection of FAI or clinical suspicion of it.	Mean age: 42.5 years; 30 males, 20 females.	Labrum and articular cartilage lesions	3T MRI group: patients received no contrast magnetic resonance imaging (MRI) with a 3-Telsa Achieva dual quasar magnet and 6 channel hoday phased array coil	3-T MRI indicated 97.7% sensitivity, 100% specificity, 98% accuracy, 100% positive predictive value (PPV) and negative predictive value (NPV) to	"Non-invasive assessment of the hip is possible with 3-T MR magnet. 3-T non-contrast MRI could replace MRA as the workhorse technique for assessing hip internal	Data suggest sequences of 3-T non-contrast MRI can help image and diagnose articular cartilage tears and are non-invasive compared with 1.5 T

							(n=50) vs. 1.5-Telsa MRA group: patients received direct magnetic resonance arthrography (MRA) with a tip Chiba echogenic needle intra-articular injection, a 1.5-Telsa Achieva nova magnet, and a 5 channel cardiac body coil (n=50).	detect labral chondral tears; while 1.5-T MRA showed 100% sensitivity, 85.7% specificity, 98% accuracy, 85.7% PPV, and 97.7% NPV.	damage. MRA would then be reserved for young adults with a strong clinical suspicion of FAI but normal findings on 3-T non-contrast MRI."	MRA. If, however, the 3-T non-contrast imaging is negative MRA should be considered.
Ratzlaff 2013 (Score= 4.5)	Hip internal rotation pain test/ Goniometer test/ Hip flex range of motion (ROM)/ Log roll test/ FARBER test/ Flexion 90° adduction internal rotation	Diagnostic	Sponsored by Canadian institutes of health research new emerging team grant. No mention of COI.	N=12 patients with symptomatic femoroacetabular impingement or with healthy hips.	Mean age: 36±8.2 years; 5 males, 7 females.	Femoroacetabular impingement (FAI)	All patients were included in 12 tests: Hip internal rotation pain test: patients were examined for ipsilateral side hip and hip and knee 90° passive flex (n=12) vs. Goniometer test: patients received hip internal rotation range of motion examination with hip and knee 90°	60% of the 12 hip tests indicated adequate reliability (overall raw agreement>0.75), 0.35-0.84 positive agreement, and 0.62-0.99 negative agreement. The average range of motion outcomes was 5° flexion and 7° internal rotation.	"The results provide evidence that the most common hip examination tests would likely be sufficiently reliable to allow agreement between examiners when discriminating between painful FAI and normal hips in a clinical setting."	Small sample (n=12). Data suggest clinicians of varying disciplines agree on diagnosis about 60% of the time.

	pain test/ Flexion 90° adduction internal rotation ROM test/ Flexion 120° adduction internal rotation pain test/ Flexion 120° adduction internal rotation ROM test/ Flexion 90° adduction compression pain test/ Flexion 120° adduction compression pain test/ Posterior						passive flex (n=12) vs. Hip flex range of motion (ROM) test: patients were examined by hip flex with neutral position opposite leg (n=12) vs. Log roll test: patients received passive leg rolls external rotation to internal, then to resistance point (n=12) vs. FARBER test: patients received flexion, abduction and external rotation (FARBER) examination with ipsilateral foot position (n=12) vs. Flexion 90° adduction internal rotation pain test: patients received hip and knee passive 90° flex and internal			

	impinge ment test						hip rotation (n=12) vs. Flexion 90° adduction internal rotation ROM test: patients received hip and knee passive 90° flex and endpoint hip adduction (n=12) vs. Flexion 120° adduction internal rotation pain test: patients received hip and knee passive 120° flex and internal hip rotation (n=12) vs. Flexion 120° adduction internal rotation ROM test: patients received hip and knee passive 120° flex and endpoint hip adduction (n=12) vs. Flexion 90° adduction compression pain test: patients			

							received hip and knee passive 90° flex and internal hip rotation, and femur long axis force compression (n=12) vs. Flexion 120° adduction compression pain test: patients received hip and knee passive 120° flex and internal hip rotation, and femur long axis force compression (n=12) vs. Posterior impingement test: patients received hip and knee active flex and ipsilateral hip passive external rotation (n=12).			
Cunningham 2017 (Score= 4.5)	Magnetic resonance imaging	Diagnostic	Sponsored by National center for	No mention of sample size of patients	No mention of age and sex.	Femoroacetabular impinge	MRI group: patients received MRI with intra-articular	The most cost-effective methods were H&P with/without	"H&P and radiographs with supplemental diagnostic	Data suggest in low prevalence diseases, providers

	(MRI) / Magnetic resonance arthrography (MRA)/ Injection		advancing translational sciences of the national institutes of health. One or more of the authors have received or will received benefits for personal or professional use.	with hip pain.		ment (FAI)	gadolinium contrast or no contrast vs. MRA group: patients received MRA as the golden standard to diagnose labral tears and FAI	injection among the 4 methods. Physical examination indicated 92% sensitivity, 33% specificity, 25% prevalence, and hip anesthetic injection indicated 85% sensitivity to detect FAI. Cost of History and physical examination (H&P) with supplemental diagnostic injection ($10,869) vs. Cost of H&P without supplemental diagnostic injection ($10.079) vs. Cost of H&P with magnetic resonance arthrography (MRA) ($12,225) vs. Cost of H&P with magnetic resonance imaging (MRI) ($11,198).	injection are preferred over advanced imaging, even with reasonable deviations from published values of disease prevalence, test sensitivity, and test specificity. Providers with low examination sensitivity in situations with low disease prevalence may benefit most from including injection in their diagnostic strategy.”	may benefits most from advanced imaging. Data suggests advanced imaging is not helpful in diagnosing most FAI.

Evidence for use of local glucocorticosteroid injections for hip impingement

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Labral Tears, Femoroacetabular Impingement (FAI), treatment; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 653 articles in PubMed, 694 in Scopus, 112 in CINAHL, 2 in Cochrane Library, 2590 in Google Scholar, and 0 from other sources. We considered for inclusion 9 from PubMed, 4 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 16 articles considered for inclusion, 8 randomized trials and 7 systematic studies met the inclusion criteria.

Evidence for Arthroscopy to diagnose and treatment patients with hip pain.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Labral Tears, Femoroacetabular Impingement (FAI), treatment; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 102 articles in PubMed, 128 in Scopus, 154 in CINAHL, 2 in Cochrane Library, 4070 in Google Scholar, and 0 from other sources. We considered for inclusion 9 from PubMed, 4 from Scopus, 5 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 0 from other sources. Of the 20 articles considered for inclusion, 10 diagnostic studies and 6 systematic studies met the inclusion criteria.

Evidence for Open surgical repair is recommended for "hip impingement" or labral tear cases

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Labral Tears, Femoroacetabular Impingement (FAI), treatment; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 653 articles in PubMed, 694 in Scopus, 112 in CINAHL, 2 in Cochrane Library, 2590 in Google Scholar, and 0 from other sources. We considered for inclusion 9 from PubMed, 4 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 16 articles considered for inclusion, 8 randomized trials and 7 systematic studies met the inclusion criteria.

Evidence for the Use of Treatments for Femoroacetabular Impingement (FAI)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Labral Tears, Femoroacetabular Impingement (FAI), treatment; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 653 articles in PubMed, 694 in Scopus, 112 in CINAHL, 2 in Cochrane Library, 2590 in Google Scholar, and

0 from other sources. We considered for inclusion 9 from PubMed, 4 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 16 articles considered for inclusion, 8 randomized trials and 7 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Surgery										
Strickland 2018 (score= 6.0)	Capsulotomy Repair	RCT	Sponsored by ArthroCare. One or more of the authors have received or will receive benefits for personal or professional use.	N = 15 patients (30 hips) who underwent simultaneous bilateral hip arthroscopy	Mean age: 29.2 years; 15 males, 10 females	Group 1: Allocated to capsulotomy repair (n=15 hips) vs Group 2: Allocated to capsulotomy non-repair (n=15 hips)	6, 24 weeks	A continuous hip capsule with no apparent defect was observed in 8 hips that had capsular repair and 3 that did not at 6 weeks post-op. The distance of separation across capsular fibers at the articular surface was greater than at the muscular surface in the hips with a capsulotomy defect at 6 weeks ($p=0.009$). In all hips, mean capsular thickness along capsulotomy defect was largest at the distal portion and smallest at the middle area of hip capsule ($p<0.001$). Mean hip capsular thickness decreased at 24 weeks post-op in comparison with 6 weeks post-op ($p<0.001$). Subchondral edema decreased from 6 to 24 weeks post-op across the entire	"Arthroscopic repair of a small interportal hip capsulotomy site yields an insignificant increase in the percentage of continuous hip capsules seen on MRI at 6 weeks postoperatively compared with no repair."	Small sample. Data suggest lack of efficacy of repaired vs unrepaired interportal Capsulotomies in simultaneous bilateral THA. Data suggest both groups progressed to healing at the 24 week follow up

								cohort (p=0.037).		
Krych 2013 (score= 5.5)	Labral Repair	RCT	No COI. No mention of sponsorship.	N = 36 female patients undergoing arthroscopic hip treatment for pincer of combined type femoracetabular impingement	Mean age: 38.5 years; 0 males, 36 females	Group 1: Underwent labral repair (n=18) vs Group 2: Selective labral debridement was performed with preservation of as much stable labrum as possible (n=18)	12-48 months	The mean ADL HOS improved from 68.2 preoperatively to 91.2 postoperatively in the repair group, (p<0.05). The mean ADL HOS improved from 60.8 preoperatively to 80.9 postoperatively in the debridement group, (p<0.05). The repair group had greater improvement in ADL HOS (p<0.05). The repair group (mean improvement from 47.5 to 88.7) showed greater improvement in sports HOS than the debridement group (mean improvement 40.6 to 76.3) (p<.05.05).	"Arthroscopic treatment of femoroacetabular impingement with labral repair in femail patients resulted in superior improvement in hip functional outcomes compared with labral debridement."	Data suggest arthroscopic labral repair of FAI in female patients led to significantly better hip function than selective labral debridement.
Mansell 2018 (score= 5.0)	Arthroscopic Hip Surgery vs. Physical Therapy	RCT	Sponsored by internal grant from the US Defense Health Agency. No COI.	N = 80 patients with femoroacetabular impingement syndrome	Mean age: 30 years; 47 males, 33 females	Group 1: Surgery group, underwent arthroscopic hip surgery (n=40) vs Group 2: Rehabilitation group, underwent 12-session physical	6 months, 1 year, 2 years	Mean HOS scores at 2 years were 45.8 among patients without surgery and 57.3 among patients with surgery. Mean iHOT-33 scores at 2 years were 42.0 among patients without surgery and 49.2	"There was no significant difference between the groups at 2 years. Most patients received little to no change in status at 2 years, and one-third of military patients were	Data suggest lack of statistically significant differences in groups at 2 years but both groups did show improvement

						therapy program (n=40)		among patients with surgery. (P values for this data not provided in article)	not medically fit for duty at 2 years."	
Injections										
Lee 2016 (score= 5.0)	Steroid vs. Hyaluronic Acid Injections	RCT	Sponsored by the SNUBH research fund. No COI.	N = 30 patients with femoroacetabular Impingement	Mean age: 37 years; 11 males, 19 females.	Group 1: Injected using steroid triamcinolone acetonide (TA) (n=16) Vs Group 2: Injected using hyaluronic acid (HA) (n=14)	12 weeks	At 4 weeks mean increase in HOOS was 10.2 in HA group and 5.3 in TA group (p=0.032). At 4 weeks after hip injections, mean decrease of pain was 0.9 in TA group and 2.7 in HA group (p=0.001). Instances of adverse events was 11 in TA group and 3 in HA group. Mean total pain intensity (NRS score) at 12 weeks was 2.0 in TA group and 2.4 in HA group.	"[I]ntra-articular hip injection with TA or HA may be effective as a conservative treatment in patients with FAI. TA can be use to obtain faster effect in pain relief, whereas HA can be used to obtain more delayed effect in functional improvement"	Data suggest HA and TA may be effective in FAI patient with TA being faster for pain relief and HA had a delayed effect on improving function. HA resulted in more adverse events.
Rafols 2015 (score= 4.5)	Platelet-Rich Plasma Injection	RCT	No mention of sponsorship. No COI.	N = 57 patients with hip impingement treated with arthroscopic hip surgery	Mean age: 35 years; 30 males, 27 females	Group 1: Received an intra-articular concentrated platelet-rich plasma (PRP) injection at the end of surgery (n=30) Vs Group 2: Did not receive PRP injection at the end of surgery (n=27)	3, 6, and 24 months	Mean HHS score at 3 months were 91.79 in PRP group and 90.97 in non-PRP group (p=0.65). Mean HHS score at 6 months were 94.8 in PRP group and 94 in non-PRP group (p=0.65). Mean HHS score at 24 months were 97.1 in PRP group and 94.76 in non-PRP group (p=0.54). Mean VAS scores 2 days post-op were 3.04 in PRP group and 5.2 in	"PRP resulted in lower postoperative pain scores at 48 hours and fewer joint effusions at 6 months. These findings suggest that PRP may have a benefit regarding postoperative inflammation; however, the long-term clinical benefit is unclear."	Data suggest PRP group had less pain 48 hours post-operatively, and fewer joint effusions at 6 months

								non-PRP group (p<0.05). 37% of patients in PRP group did not present with effusion compared with 21.1% in non-PRP group (p<0.05).		
Physical Therapy										
Aoyama 2017 (score= 4.5)	Muscle Training with Trunk Training	RCT	Sponsored by Smith & Nephew. No COI.	N = 20 patients with FAI	Mean age: 45.1 years; 0 males, 20 females	Group 1: Underwent pelvic floor muscle training with trunk training (n=10) Vs Group 2: Underwent pelvic floor muscle training only (control group) (n=10)	Mean follow-up period of 128.9 ± 82 days	There was an improvement in the range of motion of hip flexion at 4 weeks in the trunk training group compared with the control group (p<0.05). Hip abductor strength improved at 4 weeks in trunk training group compared with control group (p<0.05). Vail hip score increased at 8 weeks in trunk training group compared with the control group (p<0.05). iHOT12 score increased at 8 weeks in trunk training group compared with the control group (p<0.01).	"The addition of trunk stabilization exercise to a typical hip rehabilitation protocol improves short-term clinical outcomes and may augment nonoperative and postoperative rehabilitation."	Small sample. Data suggest adding trunk stabilization exercise to standard hip muscle exercises for FAI may improve ROM
Wright 2016 (score= 4.0)	Manual Therapy vs. Home Exercise	RCT	Sponsored by High Point University Research Advancement Explorer Grant. No mention of COI.	N = 15 patients with a FAI diagnosis	Mean age: 33.7 years; 4 males, 11 females	Group 1: 6 week manual therapy and exercise (MTEX) (n=7) vs Group 2: Advice and home exercise	7 weeks	Mean HOS ADL score at 7 weeks was 81.1% in MTEX group and 85.1% for Ad+HEP group. Mean HOS Sports score at 7 weeks was 70% in MTEX group and 72.4% for Ad+HEP group. "both of these	"[S]ymptomatic femoroacetabular impingement may be amenable to conservative treatment strategies however further full-scale	Pilot study. Small sample with 7 week follow-up. Data suggest PT administered over 6 weeks provided pain improvement in FAI patients

						(Ad+HEP) (n=8)		within group improvements met criteria for clinical significance" Mean change in pain score at 7 weeks was -17.6 in MTEX group and -18 in Ad+HEP group.	randomized controlled trials are required to demonstrate this."	

Evidence for use of MR to diagnose gluteus medius tendinosis or tears, and for greater trochanteric pain syndrome

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gluteus Medius Tendinopathy, Gluteus Medius Tears; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 55 articles in PubMed, 2 in Scopus, 3 in CINAHL, 1 in Cochrane Library, 6580 in Google Scholar, and 0 from other sources. We considered for inclusion 5 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 5 diagnostic studies and 2 systematic studies met the inclusion criteria.

Evidence for the Use of Diagnostic Tests for Gluteus Medius Tendinosis and Tears

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gluteus Medius Tendinopathy, Gluteus Medius Tears; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 55 articles in PubMed, 2 in Scopus, 3 in CINAHL, 1 in Cochrane Library, 6580 in Google Scholar, and 0 from other sources. We considered for inclusion 5 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 7 articles considered for inclusion, 5 diagnostic studies and 2 systematic studies met the inclusion criteria.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Trochanteric bursitis, greater trochanteric pain syndrome, GTPS**;** diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 63 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 852 articles (Went through first 100). We also found and reviewed 122 in Scopus, 88 in CINAHL, 56 in Cochrane Library, 17400 in Google Scholar (Went through first 100), and 16 from other sources. We considered for inclusion 7 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 13 articles considered for inclusion, 6 diagnostic studies and 5 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Steinert 2010 (Score =6.5)	Radiography/ Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=150 patients with hip pain.	Mean age: 58.7± 16.1 years; 57 males, 93 females.	Abductor tendon abnormalities	Radiographs group: patients received conventional radiographs with <3.2mm enthesophyte measurement in 20° rotated legs supine position (n=150) vs. MR group: patients received magnetic resonance (MR) imaging by a 1.5 Telsa Siemens system (n=150).	MR tendinopathy indicated 90% positive predictive value (PPS) for surface irregularities >2mm. The radiographs showed 40% sensitivity for changes, 94% specificity, 61% accuracy, 49% negative predictive value (NPV). The positive likelihood ratio of patients with trochanteric surface irregularities to have gluteus medius tendon abnormality (>2mm) was 5.8.	"Pronounced (>2 mm) surface irregularities of the greater trochanter on conventional radiographs were associated with abductor tendon MR abnormalities."	Data suggest significant surface irregularities (>2mm) of the greater trochanter imaged on plain radiographs are associated with abductor tendon abnormalities found on MRI.
Sutter 2013 (Score =5.5)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship or COI.	N=35 patients experienced total	Mean age: 64.6 years; 11 males,	Abductor tendon tears/ tensor fasciae latae	Tear group: patients with abductor tendon	46% patients indicated gluteus medius / minimus	"Patients with abductor tendon tears showed	Data suggest there is tensor fasciae latae

				hip arthroplasty or no experience.	24 females.	muscle hypertrophy	tear received magnetic resonance imaging (MRI) scanning with 1.5 Telsa Achieva MRI scanner and 16 channel Philips torso coil (n=16) vs. Non-tear group: patients without abductor tendon tear received magnetic resonance imaging (MRI) scanning with 1.5 Telsa Achieva MRI scanner and 16 channel Philips torso coil (n=19).	tendon tear. Abductor tendon tear group indicated higher tensor fasciae latae ratio (interquartile range IQR=1.97 to 3.21) than that in non-tears group (IQR=1.52 to 2.26) (p=0.028).	hypertrophy of the tensor fasciae latae muscle when compared to the contralateral healthy side and to patients without a tear."	muscle hypertrophy in patients with abductor tendon tears.
Chi 2015 (Score =5.0)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=185 patients with no or low-/high-grade gluteus medius partial or full tear.	Mean age: 65.7years; 102 males, 83 females.	Glutueus medius/ gluteus minimus	Radiologist 1 evaluation: patients received magnetic resonance imaging (MRI) in pelvis by using 1.5 Telsa scanner with body coil (n=185)	Tendon pathology insertion site and muscle atrophy location indicated statistically significant association with gluteus medius by Fisher's exact	"Gluteus medius and minimus tendon pathology and muscle atrophy increase with advancing age with progression of tendinosi	Data suggest that with increasing age there is more tendon pathology and muscle atrophy but no statistically significant association

							vs. radiologist 2 evaluation: patients received magnetic resonance imaging (MRI) in pelvis by using 1.5 Telsa scanner with body coil (n=185).	tests evaluation (p<0.0001). 79.5% patients showed no muscle atrophy if no insertion site emerged, 61.8% patients showed isolated superoposterior insertion involved, 68.4% patients showed isolated lateral insertion for gluteus medius.	s to low-grade tendon tears to high-grade tendon tears."	between age and both tendinopathy or atrophy of the iliopsoas.
Cvitanic 2004 (Score =5.0)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship or COI.	N=45 patients with tendon disruption signs (study group n=15 vs. control group n=30).	Mean age: 67 years; 2 males, 43 females.	Glutueus medius/ gluteus minimus tears	MRI evaluation: patients received magnetic resonance imaging (MRI) scanning for both hips by a 1.5 Telsa Signa General Electric MRI system (n=45) vs. Surgical evaluation: study group patients	To diagnose abductor tendon tears, MRI indicated 93% sensitivity, 91% accuracy, 79% positive predictive value (PPV), and 95% negative predictive value (NPV). Trochanteric bursitis was found to have	"MRI showed good accuracy for the diagnosis of tears of the gluteus medius and gluteus minimus tendons."	Data suggest MRI performed well for accurately identifying gluteus maximums and minimums tear with the highest sensitivity and specificity for identification of an area of T2 hypersensitivity

							received surgery to evaluate tendon injury by using binary end point (n=15).	strong association with abductor tendon tears (p<0.0001).		superior to the greater trochanter (73%, 99%).
Bird 2001 (Score =4.5)	Magnetic resonance imaging (MRI)/ Physical examination (PE)	Diagnostic	No mention of sponsorship or COI.	N=24 patients with greater trochanteric pain syndrome (GTPS).	Median age: 58 years; 0 male, 24 females.	Glutueus medius tears	Physical examination: patients received physical examination towards Trendelenburg's sign, pelvic tilt, and 45°resisted affected hip abduction (n=24) vs. MRI: patients received magnetic resonance imaging (MRI) to assess hip and pelvis by a 1.5 Telsa Signa General Electric MRI system (n=24).	For Trendelenburg's sign, magnetic resonance imaging (MRI) indicated 72.7% sensitivity and 76.9% specificity; for pain on resisted abduction, MRI showed 72.7% sensitivity and 46.2% specificity; for pain on resisted internal rotation in affected hip, MRI indicated 54.4% sensitivity and 69.2% specificity.	The results support the hypothesis that gluteus medius tendon pathology is important in defining GTPS. In this series, trochanteric bursal distension was uncommon and did not occur in the absence of gluteus medius pathology.	Data suggest the Trendelenburg sign in the most sensitivity and specific sign in the detection of gluteus medius tears.

Evidence for the Use of Diagnostic Tests for Trochanteric Bursitis or Greater Trochanteric Pain Syndrome

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Trochanteric bursitis, greater trochanteric pain syndrome, GTPS**;** diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 63 articles in PubMed using the most recent sorting function. We conducted a secondary review in PubMed using the best match sorting function and found and reviewed 852 articles (Went through first 100). We also found and reviewed 122 in Scopus, 88 in CINAHL, 56 in Cochrane Library, 17400 in Google Scholar (Went through first 100), and 16 from other sources. We considered for inclusion 7 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Of the 13 articles considered for inclusion, 6 diagnostic studies and 5 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Fearon 2010 (Score=6.0)	Ultrasound/ Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship or COI.	N=24 patients experienced combined bursectomy and gluteal tendon reconstruction.	Mean age: 56 years; 0 male, 24 females.	Greater trochanteric pain syndrome (GTPS)	Ultrasound group: patients received ultrasound with a 5000 Philips scanner and a 7 megahertz (MHz) probe (n=17) vs. MRI group: patients received MRI to confirm tendon tears (n=8).	To detect tendon tear, ultrasound indicated 79% sensitivity and 100% positivity predictive value (PPV). To detect bursa pathology, ultrasound showed 61% sensitivity, 100% specificity, 100% PPV, and 100% negative predictive value (NPV).	"Ultrasound appears to be clinically useful in greater trochanteric pain syndrome; reconstructive surgery seems to relieve pain and the histopathologic findings show tendinopathy and bursa pathology coexist in greater trochanteric pain syndrome."	Case series. Data suggest us showed a high PPV for gluteal tendon tear imaging prior to surgical repair.
Klontzas 2014 (Score=5.5)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=141 patients with peritrochanteric edema and bursitis.	Mean age: 53.99 years; 26 males, 66 females.	Greater trochanteric pain syndrome (GTPS)	Group A: patients received MRI by using 1.5 Telsa Siemens MRI system and showed peritrochanteric edema (n=91) vs. Group B: patients received MRI by using 1.5 Telsa Siemens	The association between bursitis and GTPS was statistically significant (p=0.0003), indicated 23.53% positive predicted value (PPV) (95%CI=10.75 % to 41.17%) and 97.14%	"Acetabular morphology is associated with GTPS and the absence of bursitis was proved to be clinically relevant. Peritrochanteric edema alone was not associated with local pain."	Data suggest there is a relationship between acetabular morphology and peritrochanteric bursitis.

							MRI system and showed bursitis with peritrochanteric edema (n=34).	negative predicted value (NPV) (95%CI=92.85 % to 99.22%). Symptomatic bursal maximum size and non-symptomatic size indicated no significant difference (p=0.2496).		
Ribeiro 2016 (Score=5.5)	Ultrasound/ X-ray/ Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=18 patients with hip tendinobursittis diagnosis.	Mean age: 49.8±14.6 years; 8 males, 10 females.	The trochanteric pain syndrome (TPS)	PRP group: patients received Platelet Rich Plasma (PRP) (n=9) vs. Control group: patients received 20 mg/ml Triancil hexacetonide triamcinolone infiltration (n=10).	Facial expressions pain scale (FEPS) in corticosteroid group changed from 1.9±0.568 to 4.8±1.549, while FEPS in PRP group changed from 3.6±1.17 to 4.8±1.22. The Harris hip score questionnaire (HHS) in corticosteroid group increased from 57.208±11.5 to 79.47±20.4, while HHS in PRP group changed from 65.229±12.2 to 70.645±14.0.	"There was no difference in pain and function between treatment of TPS with infiltration of PRP and corticosteroids. Only the control group had reduced pain and function according to HHS at 10, 30 and 60 days, as compared to pre intervention period."	Small sample single injection. Data suggest lack of efficacy of PRP on trochanteric pain syndrome when compared to corticosteroid.
Lequesne 2008 (Score=5.0)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship or COI.	N=17 patients with trochanteric tendinobursitis	Mean age: 68.1±10.8 years; 1 male, 16 females.	Greater trochanteric pain syndrome (GTPS)	MRI: patients received MRI scanning by using 1.5 Telsa system and surface coil (n=8) vs. Control: patients visited rheumatology department for greater trochanter (GT)	MRI indicated 100% sensitivity and 97.3% specificity to detect gluteus medius bursitis with tearing evidence. Single leg stance test showed 88% sensitivity and 97.3% specificity in	"The 30-second single-leg stance and resisted external derotation tests had very good sensitivity and specificity for the diagnosis of tendinous lesion and bursitis in patients with MRI-documented refractory GTPS."	Data suggest both tests showed good sensitivity and specificity for diagnosing gluteal tendinopathy in individuals with refractory GTPS.

							examination (n=9).	supine position.		
Blankenbaker 2008 (Score=4.0)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship or COI.	N=256 patients with trochanteric pain syndrome.	Mean age: 45 years; 99 males, 157 females.	Trochanteric pain syndrome (TPS)	MRI scanning: patients received MRI scanning for abductor tendon abnormality by using 0.7, 1.5 or 3 Telsa GE magnet medical system (n=125) vs. Clinical examination: patients received clinical examination to find hip and trochanteric pain symptoms (n=256).	91.4% patients with hip pain indicated abnormal change via MRI detection, and 88% patients with no hip pain showed abnormal change via MRI scanning, the difference indicated no significance (p=0.39)	"Thus, MR has a high sensitivity for trochanteric pain syndrome but the findings are not specific. As such, we have changed our reporting habits to point out that these findings can be seen in trochanteric pain syndrome but are often asymptomatic."	Data suggest MRI has high sensitivity for trochanteric pain syndrome with poor specificity.
Gandertion 2017 (Score=4.0)	Magnetic resonance imaging (MRI)	Diagnostic	No mention of sponsorship. The authors declared no COI.	N=46 patients with or without greater trochanteric pain syndrome.	Mean age: 50.7 years; o male, 46 females.	Greater trochanteric pain syndrome (GTPS)	GTPS group: patients with greater trochanteric pain syndrome received MRI scanning with 3 Telsa Siemens system and array surface coil (n=28) vs. Control group: patients with no symptoms of greater trochanteric pain received MRI scanning with 3 Telsa Siemens system and array surface coil (n=18).	The diagnostic tests indicated satisfied ≥83% specificity, high ≥75% positive predictive value (PPV). The greater trochanter palpation showed high 85.7% sensitivity and low 61.1% specificity.	"The study found the Patrick's or FABER test, palpation of the greater trochanter, resisted hip abduction, and the resisted external derotation test to have the highest diagnostic test accuracy for GTPS. Tendon pathology on MRI is seen in both symptomatic and asymptomatic women."	Small sample. Data suggest the FABER test, resisted hip abduction, resisted external derotation and greater trochanteric palpitation are most accurate for diagnosing GTPS.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gluteus Medius Tendinopathy, Gluteus Medius Tears, treatments, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 34 articles in PubMed, 118 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1280 in Google Scholar, and 2 from other sources. We considered for inclusion 3 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 11 articles considered for inclusion, 3 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence for Exercise for Trochanteric Bursitis:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gluteus Medius Tendinopathy, Gluteus Medius Tears, treatments, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 34 articles in PubMed, 118 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1280 in Google Scholar, and 2 from other sources. We considered for inclusion 3 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 11 articles considered for inclusion, 3 randomized trials and 8 systematic studies met the

Evidence Glucocorticosteroid Injections for Acute, Subacute, or Chronic Trochanteric Bursitis
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Trochanteric bursitis, greater trochanteric pain syndrome, GTPS; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 335 articles in PubMed (Went through first 100), 992 in Scopus (Went through first 100), 81 in CINAHL, 56 in Cochrane Library, 17400 in Google Scholar (Went through first 100), and 48 from other sources. We considered for inclusion 9 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 2 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for Surgical Repair of Gluteus Medius Tears
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Gluteus Medius Tendinopathy, Gluteus Medius Tears, treatments, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 34 articles in PubMed, 118 in Scopus, 4 in CINAHL, 0 in Cochrane Library, 1280 in Google Scholar, and 2 from other sources. We considered for inclusion 3 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 11 articles considered for inclusion, 3 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence for the Use of Treatments for Gluteus Medius Tendinosis and Tears

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Injections										
Cohen 2009 (score= 8.5)	Trochanteric Bursal Injections	RCT	Sponsored by grant from John P Murtha Neuroscience and Pain Institute, Johnstown, PA, the US Army, and the Army Regional Anesthesia and Pain Medicine Initiative Washington, DC. No COI.	N = 65 Greater trochanteric pain syndrome	Mean age: 55.2 years; 9 males, 56 females	Fluoroscopic vs. blind glucocorticoid injections with 60mg depomethylprednisolone plus 2.5mL 0.5% bupivacaine into most tender location	1, 3 months	Success rate at 1 month only in 7(22%) blind vs. 4 (13%) fluoro guided and 3 month success in 15(47%) blind vs. 13 (41%) fluoro guided, p = 0.38. Pain at rest at 3 months 2.6 vs. 1.9, p = 0.34; pain with activity 4.8 vs. 4.7, p = 0.90. Post-hoc analyses, no differences in successful injections by age, gender, BMI, opioid use.	"Although using fluoroscopic guidance dramatically increases treatment costs for greater trochanteric pain syndrome, it does not necessarily improve outcomes."	Data support blind injection, at least for the first injection. Data support efficacy even though only 37% of first attempts enter bursa. No placebo group.
Brinks 2011 (score= 5.0)	Steroid Injections	RCT	Sponsored by the funding program for common disorders in general practice by the Netherlands Organization for Health Research and Development (ZonMW). No COI.	N = 120 patients with greater trochanteric pain syndrome (GTPS)	Mean age: 56 years; 28 males, 92 females.	Local corticosteroid injections group: 40 mg of triamcinolone acetate combined with 1% or 2% lidocaine at most painful point of hip and 1mL of the substance at the maximal tenderness point. 2nd injection between 3 wks to 3 months. (n=60) vs Usual care group: Received analgesics as	Follow up at 6 weeks and at 3, 6, 9, and 12 months	At 3 months: 34% of patients in usual care had recovered vs 55% w/ injection group (adjusted OR = 2.38; 95% CI, 1.14-5.00.) Decreased pain severity (VAS scale: adjusted OR =1.18; 95% CI, 0.31-2.05) and on activity (adjusted OR =1.30; 95% CI, 0.32-2.29) in both groups, but greater in injection group. At 12 months: 60% of patients in usual care had recovered vs	"This study shows the additional value of injection therapy in primary care patients who have clinical signs of GTPS. The application of corticosteroid injections made no difference in the long-term resolution of pain, but the injection gave patients early relief. Although these effects have been assessed in only one trial, physicians now have a more evidence-based rationale for offering	Usual care bias. Data suggest at 3 months post injection, the treatment group reported improvement in pain but at 12 months there were no differences between groups.

						needed with usual care (n=60). Both groups were allowed to receive additional treatment from a physiotherapist		61% in injection group (VAS scale: OR = 1.05; 95% CI, 0.50-2.27). No significant differences between both groups.	corticosteroid injections to patients with symptoms of GTPS for the short-term relief of symptoms."	
Shbeeb 1996 (score= 4.0)	Trochanteric Bursal Injections	RCT	No mention of sponsorship or COI.	N = 83 Trochanteric bursitis	No mention of mean age or sex.	Betamethasone 6mg vs. 12mg vs. 24mg all mixed with 4mL 1% lidocaine. Fluoroscopy not used.	1, 6, 26 weeks	Percentages improving after injection: 1 week (77.1%), 6 weeks (68.8%), 6 months (61.3%). Those receiving 24mg more likely to have improvement ($p < 0.012$).	"Corticosteroid and lidocaine injection for trochanteric bursitis is an effective therapy with prolonged benefit."	No placebo control. Range of doses used corresponding to dose-response relationship suggests trochanteric bursal injections at least somewhat efficacious.
Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Rompe 2009 (Score= 4.5)	Home training/ corticosteroid injection/ shock wave therapy	RCT	No mention of sponsorship. The authors declared no COI.	N=229 patients with unilateral diagnosis of greater trochanter pain syndrome.	Mean age: 48 years; 67 males, 162 females.	Home training group: patients received training includes piriformis stretch, iliotibial band stretch standing, straight leg raise, wall squat with ball, and gluteal strengthening (n=76) vs. Injection group: patients received local corticosteroid injection with 5 ml 0.5% Mepivacain (n=75) vs.	Follow-up at baseline, 1, 4, and 15 months.	After 15 months of intervention, 74% radial shock wave therapy and 80% home training indicated more successful outcomes than that in 48% corticosteroid injection, and the difference was significant ($p<0.05$). Corticosteroid injection and home training's mean difference of change was -3.3 points ($p<0.001$), and corticosteroid injection and shock wave therapy's	"The role of corticosteroid injection for greater trochanter pain syndrome needs to be reconsidered. Subjects should be properly informed about the advantages and disadvantages of the treatment options, including the economic burden."	Data suggest administration of corticosteroid injection for GTP syndrome is better than home training or radial shock wave therapy but benefits start to decline after 1 month.

						Radial therapy group: patients received radial shockwave therapy by using 15 mm diameter metal applicator (n=78).		mean difference of change was -1.6 points (p<0.001).		
Brennan 2017 (Score= 4.0)	Dry needling (DN)/ cortisone injection	RCT	Sponsored by Baylor Scott & White Health. The authors declared no COI.	N=43 patients with iliac crest or mild iliotibial band lateral hip pain.	Mean age: 65.8 years; 6 males, 37 females.	DN group: patients received dry needling with needles of 0.3-0.5 mm diameter and 50-100 mm length (n=21) vs. Injection group: patients received cortisone injection with 2 ml of methylprednisolone acetate, 4 ml of 0.25% Marcaine, and 4 ml of 1% lidocaine (n=22).	Follow-up at baseline, 1, 3, and 6 weeks.	Patient specific functional scale (PSFS) scores between DN and injection groups by using time as mixed effects model indicated significance (p<0.01), but treatment indicated no significance (p=0.63).	"Cortisone injections for GTPS did not provide greater pain relief or reduction in functional limitations than DN. Our data suggest that DN is a noninferior treatment alternative to cortisone injections in this patient population. "	Short (6 weeks) follow-up. Data suggest comparable efficacy between groups for pain relief.

Evidence for X-Rays or MRI to Diagnosis Hamstring Strains and Tears

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hamstring muscles, hip flexor strains; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 171 articles in PubMed, 3 in Scopus, 2434 in CINAHL, 30 in Cochrane Library, 17400 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 4 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for Work Limitations for Treatment of Hamstring or Hip Flexor Strains

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hamstring muscles, hamstring injury, hip flexor strains; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and

prospective studies. We found and reviewed 107 articles in PubMed, 1179 in Scopus, 690 in CINAHL, 30 in Cochrane Library, 17900 in Google Scholar, and 4 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 9 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 14 articles considered for inclusion, 12 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for Bed Rest for Treatment of Hamstring or Hip Flexor Strains

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hamstring muscles, hamstring injury, hip flexor strains; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 107 articles in PubMed, 1179 in Scopus, 690 in CINAHL, 30 in Cochrane Library, 17900 in Google Scholar, and 4 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 9 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 14 articles considered for inclusion, 12 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence NSAIDS for Treatment of Hamstring or Hip Flexor Strains

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hamstring muscles, hamstring injury, hip flexor strains; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 107 articles in PubMed, 1179 in Scopus, 690 in CINAHL, 30 in Cochrane Library, 17900 in Google Scholar, and 4 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 9 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 14 articles considered for inclusion, 12 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for Ice or Heat or Wraps for Treatment of Hamstring or Hip Flexor Strains

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hamstring muscles, hamstring injury, hip flexor strains; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 107 articles in PubMed, 1179 in Scopus, 690 in CINAHL, 30 in Cochrane Library, 17900 in Google Scholar, and 4 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 9 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 14 articles considered for inclusion, 12 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for the Use of Treatments for Hamstring and Hip Flexor Strains

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Hamstring muscles, hamstring injury, hip flexor strains; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 107 articles in PubMed, 1179 in Scopus, 690 in CINAHL, 30 in Cochrane Library, 17900 in Google Scholar, and 4 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 9 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 14 articles considered for inclusion, 12 randomized trials and 2 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Sherry 2004 (score=5.0)	STST vs. PATS	RCT	Sponsored by grant from University of Wisconsin Sports Medicine Research Classic Fund. No mention of COI.	N = 24 Athletes with acute hamstring strains	Mean age: 23.7 years; 18 males, 6 females	STST (static stretching, isolated progressive hamstring resistance exercise, icing) vs. PATS (progressive agility, trunk stabilization and icing)	1 year	Time to return to sports was STST 37.4±27.6 days vs. PATS 22.2±8.3 days (p = 0.25). In first 2 weeks after return to sports, re-injury rate significantly greater (p = 0.0034) in STST group [6/11(54.5%) vs. 0/13 (0%)]. After 1 year of return to sports, re-injury rate also higher among completers in STST [7/10(70%)] vs. PATS [1/13(7.7%)], p = 0.0059.	"A rehabilitation program consisting of progressive agility and trunk stabilization exercises is more effective than a program emphasizing isolated hamstring stretching and strengthening in promoting return to sports and preventing injury recurrence in athletes suffering an acute hamstring strain."	Small sample size. Data suggest agility and trunk stabilization exercises superior. Reinjury rate also lower in that group both short and long term.
Petersen 2011 (score=5.0)	Eccentric Exercise	RCT	No mention of sponsorship. No COI.	N=942 male soccer players (professional and amateur)	Mean age: 23.3 years; 942 males, 0 females	Intervention Group: received 27 sessions of Nordic hamstring exercise (partner exercise-	10 weeks, 1 year	Control group showed a higher injury rate in preseason period ([RR] =1.76, 95% CI 0.54-5.67, p=0.35). No	"In male professional and amateur soccer players, additional eccentric hamstring exercise decreased the	Cluster randomized. Data suggest eccentric training decreased the number of new and recurrent hamstring

						kneeling, pressure, resistance, maximize eccentric phase) for 10 weeks (n=461) vs Control Group: received only usual training program (n=481)		injuries occurred during Nordic hamstring exercise. Overall injury rates were lower in the intervention group compared to controls ([RR] =0.293, 95% CI 0.150-0.572, p<.001), which was based on both lower injury rates for new injuries ([RR] =0.410, 95% CI 0.180-0.933, p=.034), and recurrent injuries ([RR] =0.137, 95% CI 0.037-0.509, p=.003).	rate of overall, new, and recurrent acute hamstring injuries."	injuries significantly.
Mendiguchia 2017 (score=4.5)	Rehabilitation	RCT	No sponsorship or COI.	N=48 male football players with suspected hamstring strain injury	Mean age: 23.5 years; 48 males, 0 females	RP Group: received exercise program emphasizing loading hamstrings during lengthening actions with general rehabilitation and	6 months	Re-injury occurrence within 6 months was 25% of RP group compared to 4% of RA group ([RR] =6, 90% CI 1-35). Return to sport was quicker in RP group	"Although return to sport was slower, male football players who underwent an individualized, multifactorial, criteria-based algorithm with a performance- and primary	Data suggest a multifactorial algorithm did not shorten return to sport, the re-injury rate was decreased.

						progressive running program (n=24) vs RA Group: received a modified version on hamstring injury rehabilitation that removes acute phase (5 days postinjury) with a regeneration phase directed at correcting different risk factors and mechanisms related to hamstring injury (functional phased-3 day block training and basic aerobic conditioning) (n=24)		(23.2±11.7 days) compared to RA group (25.5±7.8 days).	risk factor-oriented training program from the early stages of the process markedly decreased the risk of reinjury compared with a general protocol where long-length strength training exercises were prioritized.”	
Seymore 2017 (score=4.0)	Nordic exercise	RCT	No mention of sponsorship or COI.	N=20 healthy participants	Mean age: 19.1 years; 6 males, 14 females	NH Group: received injury-prevention protocol with a progressive eccentric	4, 6, 8 weeks	No group main effect, condition main effect, or fascicle length showed significance	“The NH intervention was an effective training method for muscle	Data suggest lack of efficacy. Data suggest NH intervention did not increase fascicle length, improve

						overload over the course of 6 weeks (pressure, resistance, contraction of hamstring muscles) (n=10) vs Control Group: received group sessions with a warm-up on a cycle ergometer, then 3 sets of static hamstring stretches, then same schedule of sessions as the training group (n=10)		(p=0.093, p=0.842, p=0.377, respectively). NH group showed increased volume by 10% compared to control group (d_{rmg}=0.47). Stiffness in NH group was lower than control group (16.2 kPa, 95% CI 14.59-17-76, 17.76, p=0.006).	hypertrophy, but, contrary to common literature findings for other modes of eccentric training, did not increase fascicle length. The data suggest that the mechanism behind NH eccentric strength training mitigating hamstring injury risk could be increasing volume rather than increasing muscle length. Future research is, therefore, warranted to determine if muscle hypertrophy induced by NH training lowers future hamstring strain injury risk."	stiffness or eccentric hamstring strength.

Akazawa 2016 (score=4.0)	Massage	RCT	No sponsorship or COI.	N=37 healthy males	Mean age: 27.1 ± 6.8 years; 37 males, 0 females	Massage group: received education of self-massage at the musculotendinosis junction using fingertips in sitting position (1-handed petrissage (n=37) (21 right legs, 16 left legs) vs Control Group: received no massage. (n=37) All participants received control and massage (randomized either leg).	12 weeks	Max HFA and max passive pressure showed interaction of p<0.001. At 6 and 12 weeks, the same interaction was higher in the after intervention (p<0.001, 95% CI 1.8-6.0; p<.001, 95% CI 4.3-8.6, respectively). VAS scale at maximum hip flexion angle (HFA), stiffness of hamstring, and structural indices were not different between groups at 12 weeks.	"The results of this study suggest that long-term self-massage at The musculotendinous junction increases hamstring extensibility by improving stretch tolerance. Then, this effect was greater after 12 weeks of massage than after 6 weeks. However, this intervention does not change hamstring stiffness and muscle structure."	Data suggest long-term self-massage improves stretch tolerance but does not change muscle stiffness.

Evidence X-rays or MRI to Diagnose Groin Strains or Adductor-related Groin Pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: groin strain, groin pain, adductor related groin pain; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 395 articles in PubMed, 73 in Scopus, 70 in CINAHL, 6 in Cochrane Library, 41000 in Google Scholar, and 2 from other sources. We considered for inclusion 12 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 17 articles considered for inclusion, 7 diagnostic studies and10 systematic studies met the inclusion criteria.

Evidence for the Use of Diagnostic Tests for Groin Strains or Adductor-related Groin Pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: groin strain, groin pain, adductor related groin pain; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 395 articles in PubMed, 73 in Scopus, 70 in CINAHL, 6 in Cochrane Library, 41000 in Google Scholar, and 2 from other sources. We considered for inclusion 12 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 2 from other sources. Of the 17 articles considered for inclusion, 7 diagnostic studies and10 systematic studies met the inclusion criteria.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Miller 2014 (score= 6.5)	Ultrasonography vs Magnetic Resonance Imaging (MRI)	Diagnostic	No mention of sponsorship. No COI.	N = 76 patients with clinical suggestion of inguinal hernia	Mean age: 53.1 years; 22 males, 54 females	Inguinal Hernia	Diagnostic examination: Hernia repair or Ultrasonography then hernia repair vs Nondiagnostic examination: Ultrasound (if +, then hernia repair; if -, then MRI and then repair if +) or MRI (if + then hernia repair)	Sensitivity for US was 0.33, CT was 0.54, MRI was 0.91. Specificity for US was 0, CT was 0.25, and MRI was 0.92. PPV for US was 1.00, CT was 0.86, and MRI was 0.95. NPV for US was 0, CT was 0.06, and MRI was 0.85. MRI accurately detected 91% of an occult hernia (10 out of 11 subjects)	"Ultrasonography and CT cannot reliably exclude occult groin abnormalities. Patients with clinical suspicion of inguinal hernia should undergo MRI as the definitive radiologic examination."	Data suggest MRI should be utilized as the definitive imaging test for inguinal hernia as US and CT cannot reliably determine occult groin abnormalities
Serner 2016 (score= 5.5)	Magnetic Resonance Imaging (MRI)	Diagnostic	The study was sponsored by Aspetar Orthopaedic and Sports Medicine Hospital. Outside this work, AG has received consultan	N = 81 athletes with acute groin injuries.	Mean age: 25.8 years; 81 males, 0 females.	Acute groin injuries	Clinical examination: palpation, muscle resistance and stretch tests vs Magnetic Resonance Imaging assessment: performed on a 1.5 T system. Protocol	MRI detected 85 acute injuries. Squeeze test with hip neutral and long lever, resisted outer range adduction and passive adductor stretch tests showed 80–81% (95% CI 63% to 91%) probability of an MRI+ lesion with high accuracy of a correct location (PPV 93–97% (95%	"Specific adductor examination tests (resisted outer range adduction, adductor stretch and the squeeze test in hip neutral position) individually provided ~80% probability of predicting a positive MRI in the adductors. These adductor examination tests also provided very high probability of predicting an accurate	Data suggest a good clinical exam can accurately diagnose acute adductor injuries but MRI can locate acute hip flexor injuries

			cies, speaking fees and/or honoraria from Sanofi-Aventis, Merck Serono and TissuGene, and is President and shareholder of Boston Imaging Core Lab (BICL), LLC, a company providing image assessment services. FR is Chief Medical Officer and shareholder of BICL, LLC.				included two coronal T1-weighted and short T1 inversion recovery (STIR), one sagittal fat-suppressed proton density-weighted, three axial T1-, fat-suppressed proton density-, and fat-suppressed T2-weighted, and two axial oblique fat-suppressed proton density- and T2-weighted sequences.	CI 76% to 100%)). Hip flexor tests was rated poorly for predicting MRI+ lesions (PPV 34–63% (95% CI 20% to 84%)) and had a low accuracy (PPV 17–71% (95% CI 7% to 85%)).	injury location. In contrast, individual hip flexor pain provocation tests had poor ability to predict a positive MRI, and poor accuracy. The absence of palpation pain was the best test result to predict a negative MRI in athletes with acute groin injuries."	
Verrall 2005 (score= 5.0)	Single Adductor (SA) test, Squeez	Diagnostic	No mention of sponsorship or COI.	N = 89 Australian Rules football players w/	No mention of age; 81	Sports-related chronic groin pain	All subjects went through an initial comprehensi	The sensitivity for the SA test ranged from 30-32%, SQ ranged from 40-49%, and BA ranged from 54-65%.	"If positive all three pain provocation tests, but in particular the BA test, demonstrate a high likelihood for the athlete	Data suggest high specificity in the 3 pain provocation tests with the BA test

	e (SQ) test and the Bilateral Adductor (BA) test			and w/o groin symptoms; 47 had chronic groin pain, 46 had bone marrow oedema, and 37 had both	males, 0 females.		ve musculoskeletal examination of the groin region, hip, and back. Three pain provocation tests (Single Adductor (SA) test, Squeeze (SQ) test and the Bilateral Adductor (BA) test) were then conducted in the order they were named with the athlete supine. Tests were performed statically and the contraction lasted less than 2s. 25 athletes were re-examined within one week of the initial examination to assess examiner reliability.	The specificity for the SA and SQ test ranged from 88-91%, and the BA test ranged from 92-95%. The Bilateral Adductor (BA) test was the most sensitive test, showed highest positive predictive values (86-93%), and had the highest specificity.	having MR detected parasymphyseal pubic bone marrow oedema. However, further research is needed to assess accurately the clinical value, in particular the specificity, of these pain provocation tests in the assessment of sports-related chronic groin pain diagnosed as pubic bone stress injury."	having highest sensitivity and PPV

Martin 2008 (score= 4.5)	Clinical Examination	Diagnostic	No mention of sponsorship. No COI.	N = 105 subjects with hip pain	Mean age: 49 years; 25 males, 24 females.	Intra-articular Hip Pain	Intra-articular injection group: A diagnostic/therapeutic anesthetic-steroid injection was performed under sterile conditions by use of fluoroscopic guidance with 6 mL of 1% lidocaine, 6 mL of 0.25% bupivacaine, and 80 mg of triamcinolone (n=49) Vs non-injection group: received everything but the injection (n=47). All patients completed an intake	Sensitivities (95% CI) for groin pain is 0.59 (0.41-0.75), catching 0.63 (0.44-0.78), pinching pain sitting is 0.48 (0.31-0.66), lateral thigh pain is 0.78 (0.59-0.89), FABER test is 0.6 (0.41-0.77), Impingement test is 0.78 (0.59-0.89), Trochanteric tenderness is 0.57 (0.39-0.74). Specificities (95% CI) for groin pain is 0.14 (0.05-0.33), catching 0.54 (0.35-0.73), pinching pain sitting is 0.54 (0.35-0.73), lateral thigh pain is 0.36 (0.2-0.57), FABER test is 0.18 (0.07-0.39), Impingement test is 0.10 (0.03-0.29), Trochanteric tenderness is 0.45 (0.27-0.65).	"The symptoms and signs investigated in this study did not accurately or consistently identify subjects with primary intra-articular pain sources. Furthermore, candidates for hip arthroscopy with a labral tear identified on MRI arthrogram had varied responses to anesthetic intra-articular injection. Therefore, all labral tears identified on MRI arthrogram may not be major contributors to patients' pain complaints, and medical personnel should look for other causes of pain."	Data suggest labral tears identified on MRI may or may not be the source of pain

							form that questioned the nature and location of their symptoms. A routine clinical examination (flexion abduction external Rotation and flexion– internal rotation– adduction impingement tests & palpation to determine trochanteric tenderness) was then performed. Series of standard plain radiographs were performed. Conventional unilateral direct MRI arthrogram by use of gadolinium contrast was used to describe the			

							condition of the labrum.			
Garvey 2012 (score= 4.5)	Computed tomography scan	Diagnostic	No mention of sponsorship. No COI.	N = 158 consecutive patients presenting over a period of 5 years with undiagnosed groin pain or lower abdominal pain	Mean age: 43 years; 121 males, 37 females.	Occult Groin Hernia	All patients received two separate series of contiguous 3-mm-thick axial images using a GE Sytec Spiral CT scanner obtained through the inguinal and lower abdominal regions with the patient in the supine position. Each series was obtained as a continuous helical acquisition using a slice thickness of 3–5 mm and a slice pitch of 1.0 during a single breath-hold of 10–25 s. The Wrst image series was	Positive predictive value (PPV) of pre-operative CT was 92% and a negative predictive value (NPV) of 96%, with an overall accuracy of 94%. There were a total of 45 true-positive cases, 4 false-positive cases (92% PPV), 111 true-negative cases and 5 false-negative cases (96% PPV). The overall accuracy for CT scan was 94%.	"This prospective non-contrast CT study of patients with undiagnosed chronic groin pain detected the majority of occult hernias requiring surgical intervention. These results suggest that CT can be a useful adjunct to the evaluation of patients presenting with chronic undiagnosed groin pain, but that experienced clinical judgment remains a critical element in the diagnostic pathway."	Data suggest non-contrast CT detected most occult hernias in those with undiagnosed chronic groin pain

							acquired with the patient at rest. The second image series was acquired while the patient was actively straining. The exposure factors of 120–140 kV and 160–380 mAs varied by patient size.			
Grant 2010 (score= 4.5)	Sonography	Diagnostic	No mention of sponsorship or COI.	N = 87 patients with groin pain	No mention of mean age; Median age: 44.6 years; 0 males, 87 females.	Groin Hernias	All patients had a standardized sonographic examination (HDI 5000 SonoCT or an iU22 ultrasound machine equipped with a 12–5-MHz multifrequency transducer) of the groin. All examinations were	Sonography correctly depicted and classified groin hernias in 18 of the 21 groins that had surgical confirmation. Six women without groin hernias also had surgical exploration of the affected side. The sensitivity, specificity, positive predictive value, and negative predictive value for the patients with surgical confirmation were 95%, 75%, 95%, and 75%, respectively.	"Groin hernias in women can be occult and confound the clinical diagnosis. In a woman with groin pain and normal or indeterminate physical examination findings, we have found that sonography can accurately depict and classify groin hernias and other pathologic processes."	Data suggest US may identify occult hernias in women

							performed in the supine position during quiet breathing and with the Valsalva maneuver.			
Alabraba 2014 (score= 4.0)	Ultrasound	Diagnostic	No sponsorship or COI.	N = 375 symptomatic adult patients	Mean age:	Groin Hernias	All patients had an Ultrasound scanned with a linear array probe 8e15MHz on a superficial musculoskeletal setting, supine or erect, using Valsalva manoeuvres to identify groin hernias by direct of a sac or a positive cough impulse.	The PPV of USS for groin hernia diagnosis was 0.70 (95% CI 0.62-0.78) while the accuracy of USS at distinguishing inguinal from femoral hernias was 0.95 (95% CI 0.89-0.99). The odds of a hernia being present during surgery were increased by indication with pain (OR = 2.08 vs. no pain; 95% CI 0.72 to 5.98; p = 0.175) and age _65 years (OR = 1.9 vs. age <65 years; 95% CI 0.76 to 4.79; p= 0.171).	"Ultrasound is poor in diagnosing occult groin hernias with a PPV of 70% suggesting a 30% chance of negative groin exploration. The equivocal ultrasound group requires careful follow-up as a considerable number were later diagnosed with hernia. The absence of subsequent hernia diagnosis in the negative ultrasound group suggests it may be a useful rule-out test to exclude occult groin hernias in symptomatic patients."	Data suggest US has a modest PPV (70%) for diagnosing occult groin hernias

Evidence Work Limitations for Treatment of Groin Strains or Adductor-related Groin Pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: groin strain, groin pain, adductor related groin pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 847 articles in PubMed, 2524 in Scopus, 74 in CINAHL, 6 in Cochrane Library, 27000 in Google Scholar, and 6 from other sources. We considered for

inclusion 16 from PubMed, 4 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 27 articles considered for inclusion, 19 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence Bed Rest for Treatment of Groin Strains or Adductor-related Groin Pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: groin strain, groin pain, adductor related groin pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 847 articles in PubMed, 2524 in Scopus, 74 in CINAHL, 6 in Cochrane Library, 27000 in Google Scholar, and 6 from other sources. We considered for inclusion 16 from PubMed, 4 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 27 articles considered for inclusion, 19 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence for use of NSAIDS for Treatment of Groin Strains or Adductor-related Groin Pain

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: groin strain, groin pain, adductor related groin pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 847 articles in PubMed, 2524 in Scopus, 74 in CINAHL, 6 in Cochrane Library, 27000 in Google Scholar, and 6 from other sources. We considered for inclusion 16 from PubMed, 4 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 27 articles considered for inclusion, 19 randomized trials and 8 systematic studies met the inclusion criteria.

*Evidence for use of Ice or Heat or Wraps for Treatment of Groin Strains or Adductor-related Groin Pain*A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: groin strain, groin pain, adductor related groin pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 847 articles in PubMed, 2524 in Scopus, 74 in CINAHL, 6 in Cochrane Library, 27000 in Google Scholar, and 6 from other sources. We considered for inclusion 16 from PubMed, 4 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 27 articles considered for inclusion, 19 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence for the Use of Treatments for Groin Strains or Adductor-related Groin Pain A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date *limits using the following terms: groin strain, groin pain, adductor* related groin pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly;

systematic, systematic review, retrospective, and prospective studies. We found and reviewed 847 articles in PubMed, 2524 in Scopus, 74 in CINAHL, 6 in Cochrane Library, 27000 in Google Scholar, and 6 from other sources. We considered for inclusion 16 from PubMed, 4 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 6 from other sources. Of the 27 articles considered for inclusion, 19 randomized trials and 8 systematic studies met the inclusion criteria.

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Physical Therapy or Occupational Therapy										
Holmich 1999 (score=7.0)	Physical Therapy	RCT	Sponsored by grants from the Danish Research Council of Sport, the Danish Sports Federation, and the Scientific Commission of TEAM Denmark. No mention of COI.	N = 68 Male athletes with long-standing groin pain (median 40 weeks)	Mean age: 30 years; 68 males, 0 females	Active training program (12 exercises) with physical therapy (laser, friction massage, stretching TENS) vs. no active training for 8 to 12 weeks	4 months	23 AT patients vs. 4 in PT returned to sports without groin pain [OR = 12.7 (95% CI 3.4-47.2)]. Subjective global assessments of effect of treatments favored active training (p = 0.006). Treatment outcomes (excellent plus good): AT 25/34 (73.5%) vs. 10/34 (29.4%), p = 0.001. Per-protocol analysis not appreciably different.	"AT with a programme aimed at improving strength and coordination of the muscles acting on the pelvis, in particular the adductor muscles, is very effective in the treatment of athletes with long-standing adductor-related groin pain. The potential preventive value of a short programme based upon the principles of AT should be assessed in	Variable length of treatment course (8-12 weeks); numbers of treatments reduces ability to conclude efficacy of any one treatment intervention. Data suggest the active training plus physical therapy program superior to physical therapy alone.

									future, randomised, clinical trials."	
Exercise Therapy										
Weir 2011 (score=4.0)	Manual /Exercise Therapy	RCT	No mention of sponsorship or COI.	N=54 patients with pain at proximal insertion of the adductor muscles on palpation and resisted adduction for at least 2 months	Mean age: 28.1 years; 53 males, 1 female	Exercise Therapy: received exercise therapy (static adduction, abdominal sit ups, balance training) 3 times per week at home for 8 weeks vs Multi-modal treatment: received heat followed by manual therapy (paraffin pack for 10 min, then flexion, external rotation and abduction, warm bath) for 14 days	6, 16, 24 weeks	Fifty-five percent of exercise therapy group returned to full sports in 17.3 weeks compared to 50% in the manual therapy group (p=0.043). Mean VAS score improved in manual group from 58.9±21.3 to 36.1±30.1 (p=0.01). Mean VAS score for exercise therapy group improved from 58.5±26.2 to 21.0±27.0 (p=0.000). Range of motion of hip joint did not alter after treatment or	"The multi-modal program resulted in a significantly quicker return to sports than ET plus return to running but neither treatment was very effective."	Data suggest MMT group resulted in faster return to athletic activity but both groups were modestly effective as only 50-55% of participants in both groups made a complete return to sports.

								between groups (p=0.45, p=0.65).		
Fibrin Glue										

Tolver 2013 (score=9.0)	Fibrin Glue/Tacked Fixation	RCT	Sponsored by Region Zealand's Health Research Fund (RESUS). COI: One or more of the authors have received or will receive benefits for personal or professional use.	N=112 men with unilateral inguinal hernia	Mean age: 49.5 years; 112 males, 0 females	Fibrin Glue: received fibrin glue for fixation (n=56) vs Tacks: received 4-6 tacks in the mesh for fixation (n=56). All patients underwent elective transabdominal preperitoneal groin hernia repair (TAPP)	1,3 days, 1 month	Fibrin group showed lower VAS pain scores during coughing compared to tacks group (p=.02) and during rest (p=.001). VRS pain score was lower in fibrin group compared to tacks group (p<.001). Discomfort and fatigue were lower in fibrin group compared to tacks group (p=.002; p=.02, respectively).	"In this double-blinded, randomized, controlled trial, fibrin glue compared with tacks fixation significantly reduced postoperative pain, discomfort, fatigue and foreign-body sensation without higher risk of recurrence."	Data suggest fibrin glue group reduced early post-operative pain but the results at 6 months are comparable.
Testini 2010 (score=6.0)	Fibrin Glue/Sutures/N-butyl-2cyanoacrylate	RCT	No mention of sponsorship. No COI.	N=156 patients with inguinal hernia	Mean age: 58 years; 144 males, 12 females	Human Fibrin Glue: (n=52) vs Sutures: (n=59) vs N-butyl-2-cyanoacrylate: (n=56)	3, 7, 15 days, 1, 3, 6, 12 months	Incidence of postoperative pain, local numbness and hematoma were higher in the suture group than in glue groups. Mean time to return to work was 20.4±3.38 days for	"The use of human fibrin glue or *N*-butyl-2-cyanoacrylate is better tolerated than sutures in tension-free inguinal open repair using the plug and	Data suggest use of fibrin glue is better tolerated than sutures in short term follow-up with a trend towards superiority long term.

								suture group compared to 20.3±3.94 days in the fibrin group and 19.8±3.63 days in the N-butyl group (p=0.60). Morbidity rate was 38.98% for suture group, 9.62% in the fibrin glue group, and 10.71% in the N-butyl group (suture vs fibrin p<0.001; suture vs n-butyl p<.001, fibrin vs n-butyl p=0.85).	mesh technique in terms of overall immediate results, and there is a better trend in the long-term data."	
Polypropylene Mesh Vs Other										

Koch 2008 (score=7.0)	Titanium Mesh/Polypropylene Mesh	RCT	No mention of sponsorship or COI.	N=317 male patients undergoing an elective repair of a unilateral primary inguinal hernia	Mean age: 56 years; 317 males, 0 females	Standard Mesh: received a 10 x 15-cm standard polypropylene mesh weighing more than 80 g/m^2 (n=161) vs Lightweight Mesh: received a 10 x 15-cm titanium-coated polypropylene lightweight mesh of 35 g/m^2 (n=156)	1 year	No differences were observed between groups for mean VAS scores. Lightweight mesh group patients returned to work after 4 days compared to 6.5 days in standard mesh group (p=.04). Lightweight mesh patients that performed light physical work returned to work the 1 day post-operation compared to standard mesh at 4 days (p=.004). Similar observations	"Patients with the lightweight mesh had a shorter convalescence than those with the standard heavyweight mesh."	Data suggest short term benefit with the use of light weight mesh compared to standard mesh in terms of return to work and normal activities but at one year post surgery, there were no differences for pain or hernia recurrence.

								were shown for return to normal activity for 7 days in lightweight mesh group compared to 10 days in standard mesh group (p=.005)		
Sadowski 2011 (score=6.5)	Polypropylene Mesh/Polyester Mesh	RCT	No mention of sponsorship or COI.	N=78 patients undergoing standard anterior Lichtenstein hernia repair	Mean age: 55 years; 76 males, 2 females	Polyester Mesh: (n=39) vs Polypropylene Mesh: received heavy-weighted mesh (n=39)	2 weeks, 3, 12, 24, 48 months	Mean VAS score at 2 weeks in polyester group was 1.18±1.42 compared to the polypropylene group with 1.39±1.36 (p=0.4989). Mean VAS score at 3 months in polyester group was 0.46±1.22	"Compared to standard polypropylene mesh, polyester mesh placed in open inguinal hernia repair does not reduce postoperative pain or discomfort significantly, nor does it improve quality of life as	Data suggest comparable efficacy at 3 months.

								compared to polypropylene group with 0.56±1.13 (p=0.7213).	measured by a standardized questionnaire."	
Paajanen 2011 (score=6.0)	Laparoscopic Surgery /Nonoperative	RCT	No mention of sponsorship or COI.	N=60 patients with a diagnosis of chronic groin pain and suspected sportsman's hernia	Mean age: 31 years; 52 males, 8 females	Operative: received total extraperitoneal (TEP) mesh placement (n=30) vs Nonoperative: received active training program (improving coordination and strength of msucles, static adduction exercises, sit ups, hip flexion, balance	1, 3, 6, 12 months	Mean pain scores during exercise decreased more in the operative group compared to the nonoperative group (p<.0001). Complete return to sports activity was achieved for 90% of operative	"This randomized controlled study indicated that the endoscopic placement of retropubic mesh was more efficient than conservative therapy for the treatment of sportsman's hernia (athletic	Data suggest laparoscopic repair of sports hernias is more effective than active PT as 90% vs 23% of individuals in surgical group returned to sports activities.

						training) for 8 weeks (n=30)		group compared to 27% of nonoperative group at 3 months (p<.0001).	pubalgia)."	
Chui 2010 (score=5.0)	Lightweight Mesh/Heavyweight Mesh	RCT	No mention of sponsorship. No COI.	N=50 patients with bilateral inguinal hernias	Mean age: 61.6±11.7 years; 49 males, 1 female	Heavyweight mesh vs Lightweight mesh. All patients received both types of mesh, but randomized to one side of the body.	1, 3, 6, 12 months	A higher VAS pain score was observed for the side of hernia repaired by heavyweight mesh compared to lightweight mesh. At 3 months, 8% of patients reported being able to feel a foreign body in the lightweight	"Lightweight polypropylene mesh may be preferable to heavyweight mesh for TEP inguinal hernia repair because it provides less postoperative foreign body sensation; however, there was no significant difference in	No difference between groups. Data suggest comparable efficacy for chronic pain between both groups.

								mesh compared to 24% feeling a foreign body with the heavyweight mesh (p=0.05). Similarly, at 6 months 6% felt foreign body in lightweight mesh compared to 18% for the heavyweight mesh (p=0.04). At 12 months, 2% of patients felt foreign body in lightweight mesh compared to 12% felt foreign body in heavyweight mesh (p=0.033).	the incidence of chronic pain."	

Chowbey 2010 (score=4.0)	Lightweight Mesh/Heavyweight Mesh	RCT	No mention of sponsorship. No COI.	N=402 patients with bilateral groin hernias	Mean age: 53.1 years; 368 males, 34 females	Prolene: received polypropylene mesh (n=211) vs Ultrapro: received lightweight composite mesh (n=191) All patients received endoscopic totally extraperitoneal (TEP) groin hernia repair	3 months, 1 year	Ultrapro group had a recurrence of 5 hernias compared to 1 in prolene group (p=0.078). Chronic pain at 3 months was observed in 15 patients in the prolene group compared to 7 patients in the ultrapro group (p=0.164). At 1 year, 10 patients in prolene group had chronic pain compared to 3 patients in the ultrapro group (p=0.178).	"Lightweight meshes appear to have advantages in terms of lesser pain and early return to normal activity. However, more patients had hernia recurrence with lightweight meshes, especially for larger hernias. We surmise that the lightweight meshes have greater tendency to get displaced from their intended position during desufflation at the conclusion of endoscopic TEP repair."	Data suggest lightweight mesh may have less pain and earlier return to routine activities but was associated with hernia recurrence.

Surgical Procedure										
Lam 2015 (score=7.0)	Ultrasound and Electrical Stimulator-Guided Obturator Nerve Block	RCT	No mention of sponsorship. No COI.	N=26 patients with bilateral severe chronic hip adductor spasticity	Mean age: 77±14 years; 7 males, 19 females	Treatment Group: received 1 dose of 5 mg diazepam orally 30-60 min before procedure, then an ultrasound was used to identify an anterior branch of the obturator nerve, then injected 1-2% lidocaine. A 1mA nerve stimulation was applied and given 5% Phenol in aqueous solution (total 10 mL solution) (n=16) vs Placebo Group: (n=10)	6, 24, 36 weeks	Treatment group showed 12/16 patients with at least 1-point reduction in MAS on both hip adductors compared to 1/10 patients in the placebo group (p=.001). GAS scores showed better improvement in the treatment group compared to the control group (p<.001).	"Obturator neurolysis with 5% aqueous phenol as guided by both ultrasound and electrical stimulation can safely and effectively reduce hip adductor spasticity, thus, improving hygiene scores and patient-centered outcomes measured by the GAS in affected long-term care residents."	Small sample, short flu time. Data suggest at 6 weeks, treatment group reported at least a one point reduction of modified Ashworth Scale on both hip adductors as well as improvement in GAS.

Bansal 2013 (score=4.0)	TEP/TAPP	RCT	No mention of sponsorship. No COI.	N=314 patients with uncomplicated groin hernia	Mean age: 47.1 ± 17 years; no mention of sex.	TAPP Group: received technique of transabdominal preperitoneal procedure (n=154) vs TEP Group: received technique of totally extraperitoneal procedure (n=160)	24 hrs, 1, 6 weeks, 3, 6, 12 months; and yearly thereafter	Only 1 hernia recurrence was observed in the TAPP group compared to the TEP group. TAPP group showed higher pain scores at 6 hours (p=0.006) and 24 hours (p=0.001). Pain score was higher in TAPP group compared with TEP group at 1 week (p=0.002) and 6 weeks (p=0.002).	"In summary, the TEP and TAPP techniques of laparoscopic repair of inguinal hernia have comparable long-term outcomes in terms of incidence of chronic groin pain, quality of life, and resumption of normal activities."	Data suggest comparable long term outcomes but the TAP procedure was associated with a higher incidence of seromas.

Evidence for use of Magnetic Resonance Neurography for the Diagnosis of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency, systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 12 in Scopus, 14 in CINAHL, 15 in Cochrane Library, 2080 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 3 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 6 diagnostic studies and 5 systematic studies met the inclusion criteria.

Evidence for use of Nerve Conduction Study to Confirm Diagnosis of Meralgia Paresthetica and Localize Entrapment

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency, systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 12 in Scopus, 14 in CINAHL, 15 in Cochrane Library, 2080 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 3 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 5 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 6 diagnostic studies and 5 systematic studies met the inclusion criteria.

Evidence for the Use of Diagnostic Tests for Meralgia Paresthetica

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Diagnoses:	Comparison:	Results:	Conclusion:	Comments:
Chhabra 2012 (score=6.5)	Magnetic Resonance Neurography (MRN)	Diagnostic	No mention of sponsorship or COI.	N = 11 patients with Meralgia Paresthetica	Mean age: 46 years; 4 males, 7 females	Meralgia Paresthetica (MP)	All patients - Magnetic Resonance Neurography (MRN) vs Lateral Femoral Cutaneous Nerve (LFCN): Axial T1-weighted and T2 spectral adiabatic inversion recovery. Two blinded reading sessions performed in a 4 wk interval. All examinations performed on 3-T scanners using a body matrix and spine array coil.	For both readers: sensitivity, specificity, positive predictive value, and negative predictive value of LFCN neuropathy diagnosis were ≥71 % and ≥94 % & the diagnostic test accuracy was ≥90 %.	"Three-Tesla MRN neurography provides reliable and accurate diagnostic evaluation of MP."	Data suggest 3-Tesla magnetic resonance neurography is beneficial for accurately diagnosing MP.
Suh 2013 (score=5.0)	Sonographic vs Electrophysiologic	Diagnostic	Sponsored by a Korea University Grant. No	N = 35 participants, 23 with unilateral Meralgia	Mean age: 49.3 years; 11	Meralgia Paresthetica (MP)	All patients - Nerve conduction study: Lateral Femoral Cutaneous Nerve	Sensitivity of 95.7% (95% confidence interval, 78.1–99.9%),	"Ultrasonography is useful in the diagnosis of MP as a supplemental diagnostic tool,	Data suggest US may be useful as an additional

			mention of COI.	Paresthetica and 12 healthy controls	males, 12 females.		were performed using a Nicolet Viking IV Electrodiagnostic System (sensitivity, 5 lV/division; sweep speed, 1 ms/division; and bandwidth, 20–3000 Hz. Electrical stimuli of duration 0.1-ms and frequency 1-Hz) Electrodes with 9 mm diameters and 30 mm spacing positioned on lateral thigh vs Sonographic examination: performed immediately after nerve conduction study. The Lateral Femoral Cutaneous Nerve of both thighs were identified around the ASIS using a 5–12 MHz linear transducer	specificity of 95.5% (95% confidence interval, 77.2–99.9%), positive predictive value of 95.7%, and a negative predictive value of 95.5% for the accuracy of diagnosing MP using sonography.	which gives important information about the morphologic changes that occur in the LFCN and its course."	diagnostic test for MP.
Nouraei 2006 (score= 4.0)	Pelvic Compression Test vs Surgical Technique	Diagnostic / retrospective review	No mention of sponsorship or COI.	N = 45 patients with Meralgia Paresthetica	Mean age: 47 years; 27 males,	Meralgia Paresthetica (MP)	Pelvic compression test: ipsilateral hand on the symptomatic area and applying a lateral	Sensitivity of 95% and a specificity of 93.3% for the pelvic	"The pelvic compression test is a sensitive and specific test for MP, helping to distinguish it from	Data suggest pelvic compression is best for distinguishing MP from

					18 females.		compressive force on the pelvis for 45 seconds (n=25) vs Surgical technique: A 2- to 3-cm incision is placed inferomedial to the anterior superior iliac spine inferior and along the line of the inguinal ligament. Using an artery clip, the inferior leaf of the inguinal ligament is lifted and, with the nerve protected with a dissector, divided and splayed. (n=20)	compression test	lumbosacral radicular pain. Most patients with this condition can be managed successfully with conservative measures, and those requiring surgery can be treated effectively with nerve decompression."	lumbosacral radicular pain.
El-tantawi 2009 (score=3.5)										Data suggest dermatomal SEP may help identify those individuals with MP.
Lagueny 1991 (score= 3.5)										Data suggest while SNAP amplitudes have the most diagnostic value, they are not solely predictive of meralgia paresthetica.

Po 1009 (score=3.0)										Data suggest somatosensory evolved potentials may be of diagnostic value for identification of MP.

Evidence for Weight Loss/Avoidance of Aggravating Exposures/Loose Clothing for Treatment of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 214 in Scopus, 10 in CINAHL, 15 in Cochrane Library, 1520 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for use of NSAIDS for Treatment of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 214 in Scopus, 10 in CINAHL, 15 in Cochrane Library, 1520 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for use of Topical Lidocaine Patches for Treatment of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar wthout date limits using the following terms: Meralgia Paresthetica; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 214 in Scopus, 10 in CINAHL, 15 in Cochrane Library, 1520 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for use of Glucocorticosteroid Injections for Treatment of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 214 in Scopus, 10 in CINAHL, 15 in Cochrane Library, 1520 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for Surgical Release for Treatment of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 214 in Scopus, 10 in CINAHL, 15 in Cochrane Library, 1520 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for use of Spinal Cord Stimulator for Treatment of Meralgia Paresthetica

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Meralgia Paresthetica; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 214 in Scopus, 10 in CINAHL, 15 in Cochrane Library, 1520 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.

Evidence for Culturing Urine to Diagnose Epididymitis or Epididymito-orchitis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epididymitis, Epididymo-orchitis; diagnostic, diagnosis, sensitivity, specificity, positive predictive value, negative predictive value, and predictive value of tests, efficacy, and efficiency. We found and reviewed 85 articles in PubMed, 78 in Scopus, 27 in CINAHL, 40 in Cochrane Library, 7,550 in Google Scholar, and 0 from other sources. We considered for inclusion 0 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero of the articles considered for inclusion met the inclusion criteria.

Evidence for Work Limitations for Treatment of Epididymitis or Epididymo-orchitis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epididymitis, Epididymo-orchitis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 94 articles in PubMed, 1,002 in Scopus, 26 in CINAHL, 40 in Cochrane Library, 3,050 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria

Evidence for use of Bed Rest for Treatment of Epididymitis or Epididymo-orchitis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epididymitis, Epididymo-orchitis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 94 articles in PubMed, 1,002 in Scopus, 26 in CINAHL, 40 in Cochrane Library, 3,050 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources.Zero articles met the inclusion criteria

Evidence for use of NSAIDS or Age-appropriate Antibiotics for Treatment of Epididymitis or Epididymo-orchitis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epididymitis, Epididymo-orchitis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 94 articles in PubMed, 1,002 in Scopus, 26 in CINAHL, 40 in Cochrane Library, 3,050 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria

Evidence for the use of Ice or Intermittent Elevation for Treatment of Epididymitis or Epididymo-orchitis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epididymitis, Epididymo-orchitis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 94 articles in PubMed, 1,002 in Scopus, 26 in CINAHL, 40 in Cochrane Library, 3,050 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria

Evidence for the use of Therapy for Treatment of Epididymitis or Epididymo-orchitis

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epididymitis, Epididymo-orchitis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 94 articles in PubMed, 1,002 in Scopus, 26 in CINAHL, 40 in Cochrane Library, 3,050 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria

Evidence for use of Surgical Wound Infiltration with Local Anesthetic

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Caudal Blocks with Buprenorphine, Posterior Lumbar Plexus Block, Psoas Compartment Block (PCB) with or without IV Clonidine, Surgical Wound Infiltration with Local Anesthetic, Femoral Nerve Block; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 103 articles in PubMed, 2132 in Scopus (Went through the first 150), 42 in CINAHL, 7 in Cochrane Library, 160 in Google Scholar, and 149 from other sources. We considered for inclusion 18 from PubMed, 14 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 20 from other sources. Of the 51 articles considered for inclusion, 38 randomized trials and 13 systematic studies met the inclusion criteria.

Evidence for use of Posterior Lumbar Plexus Block

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Caudal Blocks with Buprenorphine, Posterior Lumbar Plexus Block, Psoas Compartment Block (PCB) with or without IV Clonidine, Surgical Wound Infiltration with Local Anesthetic, Femoral Nerve Block; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled

trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 103 articles in PubMed, 2132 in Scopus (Went through the first 150), 42 in CINAHL, 7 in Cochrane Library, 160 in Google Scholar, and 149 from other sources. We considered for inclusion 18 from PubMed, 14 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 20 from other sources. Of the 51 articles considered for inclusion, 38 randomized trials and 13 systematic studies met the inclusion criteria.

Evidence for use of Psoas Compartment Block (PCB) with or without IV Clonidine

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Caudal Blocks with Buprenorphine, Posterior Lumbar Plexus Block, Psoas Compartment Block (PCB) with or without IV Clonidine, Surgical Wound Infiltration with Local Anesthetic, Femoral Nerve Block; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 103 articles in PubMed, 2132 in Scopus (Went through the first 150), 42 in CINAHL, 7 in Cochrane Library, 160 in Google Scholar, and 149 from other sources. We considered for inclusion 18 from PubMed, 14 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 20 from other sources. Of the 51 articles considered for inclusion, 38 randomized trials and 13 systematic studies met the inclusion criteria.

Evidence for use of Regional Blocks – Caudal Block with Buprenorphine

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Caudal Blocks with Buprenorphine, Posterior Lumbar Plexus Block, Psoas Compartment Block (PCB) with or without IV Clonidine, Surgical Wound Infiltration with Local Anesthetic, Femoral Nerve Block; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 103 articles in PubMed, 2132 in Scopus (Went through the first 150), 42 in CINAHL, 7 in Cochrane Library, 160 in Google Scholar, and 149 from other sources. We considered for inclusion 18 from PubMed, 14 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 20 from other sources. Of the 51 articles considered for inclusion, 38 randomized trials and 13 systematic studies met the inclusion criteria.

Evidence for use of Femoral Nerve Block

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Caudal Blocks with Buprenorphine, Posterior Lumbar Plexus Block, Psoas Compartment Block (PCB) with or without IV Clonidine, Surgical Wound Infiltration with Local Anesthetic, Femoral Nerve Block; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 103 articles in PubMed, 2132 in Scopus (Went through the first 150), 42 in CINAHL, 7 in Cochrane Library, 160 in Google Scholar, and 149 from other sources. We considered for inclusion 18 from PubMed, 14 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 2 from Google Scholar, and 20 from other sources. Of the 51 articles considered for inclusion, 38 randomized trials and 13 systematic studies met the inclusion criteria.

Evidence for the Use of Regional Blocks

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Bogoch 2002 (score= 9.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No sponsorship or COI.	N=115 undergoing primary total hip arthroplasty or total knee arthroplasty	Mean age: 64.5 years; 43 males, 72 females	Lumbar paravertebral nerve block compared with sham procedure	4, 8, 24 hours	Morphine use lower in immediate postoperative period of 0-4 hours (11.6±9.7 versus 21.5±10.7mg, p = 0.001). Morphine use trended towards less use over 24 hours, but was not significant. Pain ratings trended towards favoring the blocks. Length of hospital stay trended in favor of the blocks (7.0±2.9 vs. 8.0±3.3 days, p = 0.09).	Block group required approximately 10mg less morphine for pain control than controls first 4 hours post-op (p < 0.001). No significant differences in morphine use between groups 4 to 24 hours post-op. "Visual analog scale pain score measurements at 4, 8, and 24 hours did not differ significantly between groups. Paravertebral nerve block of lumbar plexus is an invasive procedure with some risk. Considering the added risk and minimal benefits, routine use of this procedure is not supported."	Results suggest lack of power for statistical significance for a shorter hospital stay. Data suggest less immediate post-op opioid usage.
Gao 1995 (score= 8.5)	Regional Block Anesthesia and	RCT	No mention of sponsorship or COI.	N=30 patients requiring hip or knee	Mean age: 69.6 years; 11 males,	Bupivacaine vs. bupivacaine with buprenorphin	24 hours	The duration of analgesia was much longer (mean 606 minutes vs. 126 minutes p <0.001) in those receiving added	No significant differences in incidence of complications although group which had added buprenorphine had a lower incidence of vomiting.	Relatively low cost to add buprenorphine to caudal black increasing analgesic time on average 8 hours.

	Analgesia for Hip/Knee Arthroplasty			replacement surgery	19 females	e in caudal block for post-operative pain relief in hip and knee arthroplasty		buprenorphine; mean morphine consumption in the first 24 hours was halved (14mg vs. 28mg) and patient satisfaction greatly increased.		
Xing, 2015 (Score = 8.5)	Femoral Nerve Block	RCT	No mention of sponsorship or COI	N=50 patients undergoing hip arthroscopy	Mean Age: 31.54 ± 9.62 yrs. 35 males and 15 females	FNB group: Received preoperative ultrasound-guided with 20 mL of 0.5% bupivacaine (n=27) vs Control group: Receive saline (n=23)	0.5hr, 1hr, 1.5hr, 2hr, 4hr, 6hr, 1-day,2-day, 7-day	Postoperative pain scores were lower in FNB compared to control group at 0.5, 1, 2, 4, and 6 hrs. (p = 0.009, 0.004, 0.003, 0.006, 0.0002 respectively)	"In this study, we aimed to confirm previous findings that preoperative FNB leads to better pain control and less opioid consumption after hip arthroscopy."	Data suggest FNB may decrease early pain after hip arthroplasty was associated with a high number of patients falls
Chaudet, 2016 (Score = 8.5)	Femoral Nerve Block	RCT	Sponsored by the Angers University Hospital. No COI	N = 55 Clinical suspicion of hip fracture	Mean Age: 82.42 ± 11.19, 9 male and 46 females	Ropivacaine Group: 2 mg/mL at a rate of 8 mL/h using an elastomeric pump of 400mL (n=26) vs Placebo Group: received saline solution (n=29)	No Mention of follow Up	Significant decrease in pain scores after catheter Insertion in each group (VAS 50[30-80] versus 23 [0-40] for group R, p = 0.003 and 50 [30-60] versus 20 [5-45] for group p, p <0.001)	"In conclusion, this study demonstrated that continuous femoral blockades using ropivacaine performed at ED admission reduce morphine side effects (mainly nausea), but not morphine consumption or pain intensity, during the perioperative period for hip-fracture patients."	Data suggest continuous femoral blockades with ropivacaine preoperative decreases nausea but morphine consumption was comparable in both groups as was pain.
Foss 2007 (score= 8.0)	Fascia Iliaca Compartment	RCT	So mention of sponsorship or COI	N = 48 suspected hip fracture.	Mean Age: 80 ± n/a. 13 males,	FICB Group: received FICB with 1.0% mepivacaine and a placebo	60 min	Pain relief was superior in the FICB group both at rest (p < 0.01) and movement (p = 0.02)	"Pain relief was superior at all times and at all measurements in the FICB group. The study supports the use of FICB in acute management of hip	Short follow up. Same sample size. Data suggest FIC provided superior pain relief for the management of acute

	Block (FICB)				35 females	intramuscular injection of isotonic saline (n=24) vs Morphine Group: received a placebo FICB with 0.9% saline and an intramuscular injection 0.1 mg /kg morphine (n=24)			fracture pain because it is an effective, easily learned procedure that also may reduce opioid side effects in this fragile, elderly group of patients."	hip fracture and morphine consumption was decreased.
Solovyova 2013 (score= 7.5)	Regional Block/Local Continuous Anesthesia	RCT	No sponsorship or COI.	N=105 surgical patients	No mention of mean age; range: 18-80 years; no mention of sex.	Group 1: received an infiltration with an admixture of 0.2% ropivacaine (50 mL), ketorolac (15mg), and adrenaline (0.5mg) followed by a continuous infusion of 0.2% ropivacaine at 5 mL/hr for 48 hours (n=35) vs Group 2: received an infiltration with 0.2% ropivacaine	4-48 hours	Differences between groups in intraoperative hydromorphone administered was not significant (p=0.36) and the same was observed for fentanyl intraoperative administered (p=0.99).	"Local infiltration analgesia alone or followed by continuous infusion of ropivacaine as part of multimodal analgesia provides no additional analgesic benefit or reduction in opioid consumption compared with placebo following total hip arthroplasty."	Baseline characteristics missing from article. Data suggest lack of efficacy compared to placebo for decreasing the amount of post-operative opioid consumption.

						(50mL), ketorolac (15mg), and adrenaline (0.5mg) followed by a continuous infusion of normal saline solution 5mL/hour (n=35) vs Group 3: received infiltration with normal saline solution of 50 mL followed by infusion of normal saline solution at 5mL/hour (n=35)				
Shariat, 2013 (Score = 7.5	Fascia Iliaca Compartment Block (FICB)	RCT	No mention of sponsorship or COI	N = 32 patients scheduled for total hip analgesic	Mean Age: 59 ± 14.06, 15 male and 17 females.	FIB group: received ultrasound-guided injections of 30 mL 0.5% ropivacine (n=16) vs SB Group 30 mL 0.9% NaCl (n=16).	No Mention of follow Up	FIB group reported more pain compared to SB group at 24 hr. (5 ± 2 vs 2 ± 2, respectively, p < 0.01); opioid consumption did not differ between groups at 24 hr. (49 ± 30 vs 50 ± 34 mg, respectively)	"In summary, under the conditions of our study, the data suggest that the difference in average pain intensity after FIB versus SB was not significant (95% confidence interval, j2.2Y1.4 NRS units)."	Data suggest lack of efficacy for FIB compared to sham including opioid consumption.
Foss, 2005 (Score= 7.0)	Surgical Wound infiltration with local	RCT	No mention of sponsorship or COI	N = 60 patients	Mean Age: 82.47 ± 11.09, 10 males,	Group A: Received postoperative epidural infusion with	No mentions of	Significantly larger portion of group B were restricted by pain in all functions on the first and second postoperative	"In conclusion, the current study showed that postoperative epidural analgesia with local anesthetic and low dose	Data suggest post-operative epidural analgesia post hip fracture surgery better analgesia than placebo but

	anesthetic				and 45 females	a local anesthetic and low-opioid (n=30) vs. Group B: saline infusion (n=30)	follow up	days (P < 0.01, for all functions but hop flexion p <0.05).	morphine provided superior pain control during dynamic exercise in patients who underwent surgery for hip fracture and that patients were significantly less restricted by pain in their ability to perform basic functions without motor blockade."	without subsequent better rehabilitation.
Mannion 2005 (score= 7.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=36 patients scheduled to undergo surgical repair for traumatic hip fractures	Mean age: 79.7 years; 11 males, 25 females	Psoas Compartment Block (PCB) with 0.4 ml/kg of 0.5% levobupivacaine in combination with intravenous saline vs. intravenous clonidine (1µg/kg) vs. clonidine (1µg/kg) in PCB	24 hours	"The interval from time of completion of block injection to first supplementary analgesic administration was longer in IV clonidine group compared with placebo (mean ±sd.13.4 ±6.1 versus 7.3 ±3.6h; P=0.03). There was no difference between IV and PCB clonidine. Pain scores at rest or on movement were similar among groups except at rest on 24 h when IV clonidine group had a lower pain score than placebo, P= 0.02. There were no significant differences among groups regarding postoperative adverse events."	"IV, but not perineural, administration of clonidine (1 µg/kg) prolonged the duration of analgesia of PCB with 0.5% levobupivacaine in patients undergoing hip fracture surgery."	Small numbers in groups (n=12). Short follow-up time frame. Data suggest 4 clonidine prolonged analgesic effects with low numbers of adverse events. Despite increasing duration of post-op analgesia, there were no differences in analgesic requirements or pain scores, leading this result to be of uncertain clinical significance.

Biboulet 2004 (score= 6.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=45 patients undergoing elective total hip arthroplasty	Mean age: 55.9 years; 25 males, 20 females	PCA morphine: (n=14) vs. femoral nerve block: (n=16) versus psoas compartment block: (n=15)	4, 8, 12, 24, 48 hours	VAS pain scores lower in both block groups. Cumulative morphine consumption over 48 hours were median 17 vs. 21 vs. 8mg, however the results were not significant other than in the initial assessments.	"PCA morphine associated with proparacetamol and indomethacin, was a safe and effective analgesic technique, after (4th post-operative hour). Systematic administration of morphine at the end of the intervention has been proposed to improve immediate postoperative analgesia. The addition of a FNB provided no analgesic advantage, except just after the extubation. The PCB was an effective analgesic technique but only during the 4 postoperative hours, and this benefit could be offset by a high rate of potentially dangerous epidural diffusion. According to these results, FNB and PCB should not used routinely after THA."	The results suggest a lack of power to detect a beneficial effect of psoas compartment blocks on total post-operative opioid consumption.
Bianconi 2003 (score= 6.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by AstraZeneca, Basiglio, Milano, Italy. No mention of COI.	N = 37 patients undergoing elective hip and knee arthroplasties	Mean age: 65.0 years; 7 males, 30 females	Patients undergoing hip replacement with bupivacaine/ fentanyl spinal block and receiving either morphine (0.5mg/hour) plus ketorolac (3.6mg/hour) i.v. infusion with saline wound	4, 8, 12, 24, 48 and 72 h after surgery	Ropivacaine wound instillation group showed a significant reduction in post-operative pain at rest and on mobilization ($p < 0.05$); rescue medication requirements greater in morphine group. Ropivacaine group had significant reduction in length of hospital stay compared with morphine group (6.34 (0.67) and 8.79 (1.39) days respectively; $p < 0.05$). Total ropivacaine	"Infiltration and wound instillation with ropivacaine 0.2% is more effective in controlling postoperative pain than systemic analgesia after major joint replacement surgery."	Positive association between pain control and better clinical outcome (shortened hospital stay).

						infusion vs. saline i.v. infusion with ropivacaine irrigation and wound instillation (0.2% at 5ml/hour)		plasma concentration remained below toxic concentrations and no adverse effects occurred.		
Fournier 1998 (score= 6.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=40 patients scheduled for total hip replacement	Mean age: 69.4 years; 13 males, 27 females	General anesthesia (GA) with sham block vs. general anesthesia with a "3-in-1" femoral nerve block (FNB)	24, 48 hours	"There was no difference in anesthetic requirements during surgery. The time from extubation to 1st analgesic intervention (min): 61±44 vs. 298±39 P<0.05. Pain scores and the analgesic requirements in the postoperative periods (24 and 48 hr) were similar."	"There is a short-term benefit during the first few postoperative hours in using a single shot "3-in-1" femoral nerve block to complement general anesthesia for elective hip surgery."	Technique appears inadequate for long term pain relief for hip replacement surgery.
Morrison, 2016 (Score= 6.5)	Regional Blocks	RCT	So mention of sponsorship or COI	N = 161hip fractures patients > 60 yr.	No mention of age or sex.	Intervention group: Received a bolus of 15 mL of 0.2% ropivacaine was injected followed by a continuous infusion of 0.2% ropivacaine at 5 mL/h (n=79) vs Control group: recieded oral and intravenous	6 wks,	Pain scores 2 hours following emergency department presentation favored the intervention group compared to controls (3.5 versus 5.3 respectively, P=.002).	"Femoral nerve blocks performed by emergency physicians followed by continuous fascia iliaca blocks placed by anesthesiologists are feasible and result in superior outcomes."	Data suggest at 2 hours post nerve block, pain scores were improved over controls, and at 6 weeks walking and stair climbing better than in control group.

						analgesic therapy at the discretion of the physician (n=82)				
Unneby, 2017 (Score= 6.5)	Femoral Nerve Block	RCT	Sponsored by grants from Dementia foundation. No COI	N = 266 patients ≥ 70 with a hip fracture	Mean Age: 84.1 ± 6.9 yr.	Intervention Group: Femoral nerve block (n= 129) vs Control Group: conventional pain treatment using opioids if required (n=137)	No mention of follow up	Self-rated pain scores decreased significantly from in intervention group's baseline to 12h compared to control(p <0.001 and p = 0.003 respectively)	"In this study, patients with hip fracture, including those with dementia, who received FNB had lower pain scores and required less opioids before surgery."	Data suggest femoral nerve block subjects reported lower pain scores and required less opioids pre-surgery
Fletcher, 2003 (Score = 6.5)	Femoral Nerve Block	RCT	No mention of Sponsorship or COI	N = 50 patients that sustained fractured neck of femur	Mean Age: 78.08 ± 10.92. 15 males and 35 females	Study Patients 3-in-1 femoral nerve block with 20 mL of 0.5% bupivacaine(n =26) vs Control Group: receive 4 morphine (n=24)	6 months	Patients receiving 3 in 1 nerve blocks recorded a faster time to reach the lower pain score, and nerve block recipients required significantly less morphine per hour than control patients. (mean difference [95% CI]:-0.68 mg/h [-1.23 to -0.12 mg/h])	"Three-in-one femoral nerve block is an effective method of providing analgesia to patients with fractured neck of femur in the ED."	Pain follow- up at 24 hours and complications followed at 6 months. Data suggest patients reported quickness pain relief (2.88 hours versus 5.81 hours for controls) and required much less morphine in the 3 in 1 femoral nerve block group
Wardhan 2014 (score= 6.0)	Regional Block/Lumbar Plexus Block	RCT	No mention of sponsorship. No COI.	N=60 patients undergoing minimally invasive total hip arthroplasty	Mean age: 60.5 years; 28 males, 25 females	L2 PVB Group: received a L2 level bilateral paravertebral block of 18 gauge 9cm Tuohy needle 5 mL 0.5%	24 hours	L2 PVB group showed more consumption of morphine with 32±15 mg (95% CI 26-38 mg) compared to LPB group with 24±15 mg (95% CI 18-30 mg) (p=0.05).	"Our study demonstrates that use of a LPB results in slightly less morphine consumption but comparable pain scores when compared with continuous L2 PVB."	Short follow-up of 24 hours. Data suggest no difference between L2 paravertebral block versus lumbar plexus block (comparable efficacy).

						ropivacaine and 10 mL 0.5% ropivacaine injected in 5mL increments throught the catheter for total of 15 mL (n=27) vs LPB Group: received lumbar plexus block of 18 guage 10 cm Tuohy needle 5 mL 0.5% ropivacaine and an additional 10ML 0.5% ropivacaine in 5 mL increments for total of 15 mL(n=26)				
Parras, 2016 (Score= 6.0)	Femoral nerve block	RCT	No Mention of Sponsorship, NO COI	N=104 with the neck of the femur fracture undergoing hemiarthraplasty	Mean Age: 76.165 ± 9.730 yr. No mention of sex	Femoral group: 10 ml of 0.25% levobupivacaine injected lateral to the femoral artery and below the fascia lata and iliaca (n = 49) vs Quadratus	No mention of follow up	Opioid consumption in the PACU and the 24h was lower in the QLB group (3.6 mg vs 7.2, p < 0.01)	” This study shows that ultrasound-guided QLB provides superior analgesia to ultrasound-guided femoral block in patients undergoing surgery for femoral neck fracture.”	Short follow up time. Data suggest QLB was better than femoral block for improving pain, decreasing morphine consumption and resulted in shorter PACU stays during the first 24 hours

						lumborum block (QLB): 30 ml of 0.125% levobupivacacaine administered in anterolateral aspect of the quadratus lumborum muscle (n = 48)				
Siddiqui 2007 (score= 6.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by the Department of Anesthesia of Tufts-New England Medical Center. No mention of COI.	N=32 patients undergoing elective hip arthroplasty	Mean age: 55.5 years; 16 males, 18 females	Continuous lumbar plexus block combined with PCA (n=17) vs. PCA only (n=17)	36 hours	Intra-operative fentanyl use trended to favoring lumbar plexus block (423±180 vs. 315 ±159µg, p = 0.07). Estimated blood loss trended similarly (707±360 vs. 1,031±569, p = 0.07). Morphine requirements: 62±34 vs. 37±27mg, p = 0.02. Pain lower 36 hours follow-up in umbar plexus block (approximately VAS 5 vs. 3 at 20 hours, graphic representation). Patient satisfaction also favored blocks (p = 0.02).	Continuous perioperative lumbar plexus block provides superior analgesia, and reduces opioid requirements and opioid-related adverse effects compared with systemic opioids after hip arthroplasty.	Data suggest continuous lumbar plexus block in combination with PCA is better than PCA alone and is associated with less opioid requirements and the adverse events of opioids.
Stevens 2000 (score= 6.0)	Regional Block Anesthesia and Analgesia for Hip/Kn	RCT	Sponsored by Department of Anesthesia, Pharmacologyand	N = 60 patients undergoing total hip arthroplasty	Mean age: 60 years; 30 males, 30 females	General anesthesia vs. general anesthesia with posterior lumbar plexus block (bupivacaine)	48 hours	Plexus vs. control: supplemental fentanyl (no. of patients requiring): 6 vs. 20 p = 0.001; blood loss (ml) intraoperative: 420±187 vs. 538±254 p = 0.04; blood loss (ml) post-	"Posterior lumbar plexus block provides effective analgesia for total hip arthroplasty, reducing intra- and postoperative opioid requirements. Moreover, blood loss during and after the procedure is diminished. Epidural anesthetic distribution	Suggestive of attractive option for postoperative pain management.

	ee Arthroplasty		Surgical Intensive Care. No mention of COI.					operative (48 hour): 170±125 vs. 310±204 p = 0.003.	should be anticipated in a minority of cases."	
Tûrker, 2003 (Score= 5.5)	Psoas compartment block (PCB)	RCT	No mention of sponsorship, or COI	N = 30 who under when partial hip replacement	Mean age: 62.25 ± 6.9 yr. 17 males and 13 females	Group E: 18-G Tuohy with a 20-G catheter inserted through the L3-4, epidural was located using loss-of-resistance method. 3-ml test dose of solution (2% lidocaine and 1:2000,000 epinephrine injected catheter, then 15ml of 0.5% bupivacaine (n= 15) vs Group P: spinous process of L4 was used to find the puncture cite. 20ml of contrast solution (omnipaque) (n=15)	No mention of follow up	The number of attempts required to perform the block significantly higher in Group E than P (P<0.01).	" The continuous psoas compartment block provides excellent intraoperative and postoperative analgesia with a low incidence of complications for partial hip replacement surgery".	Short follow-up time. Small group size (15 each) Data suggest advantages of psoas block include fewer adverse events, Less epinephrine supplementation and longer ambulation time.
Monzon, 2010 (score= 5.5)	Regional Block Anesthesia	RCT	No mention of sponsorsh	N= 154 patients who had a previously	Mean age: 75.9 years; 58 males,	Group A (n=62) had 0.9 ml/kg normal saline	15 min, 2 hrs, and 8 hrs.	Parenteral block was deemed more effective at 15 min (p=0.001) while both treatments	"This study demonstrates that: (1) parenteral NSAIDs are very effective as analgesics after hip fractures	Short follow-up of 8 hrs. Dissimilar numbers in groups. Data suggests comparable efficiency at 2 hours but the

	and Analgesia for Hip/Knee Arthroplasty		ip. No COI.	untreated or undiagnosed hip fracture.	96 females	with IV NSAID analegics vs group B (n=92) had 0.3 ml/kg 0.25% bupivacaine with 3-5ml of 5% dextrose via IV.		had similar analgesic effects at 2 hrs (p=0.764). At 8 hrs there was no statistical difference between the two groups (p=0.083).	in elderly patients, (2) fascia-iliaca regional blocks are nearly as effective for up to about 8 h after administration and (3) regional fascia-iliaca blocks effectively control post-hip fracture pain. (4) Fascia iliaca regional block has a rapid onset."	regional block was more effective at 15 minutes.
Souron, 2003 (score= 5.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N= 53 ASA physical status I–II patients with advanced osteoarthritis of the hip scheduled for primary unilateral hip arthroplasty	Mean age: 67.2 years; 21 males, 32 females.	Group 1 (n=27) was given local anesthesia and then had a spinal needle enter the L4-L5 space and had 0.1 mg of morphine administered with 1 mL saline over 15 sec vs group 2 (n=26) was given local anesthesia and then a psoas block was done to give 1.5 mA, 2Hz, and 0.1 msec perpendicularly. 25 mL ropivacaine was given when there was negative	Every 30 min for 2 hrs, then every 6 hours until 48 hrs.	Group 1 used less morphine in PACU 1.07 vs 4.38mg, during first 24 hr 0.56 vs 9.42mg, and during first 48 hr 1.67 vs 12.5md ($p<0.05$). More patients received morphine during first 24 hr in group 2 ($p<0.05$).	"0.1 mg intrathecal morphine administration provides better postoperative analgesia than single-shot psoas compartment block after primary hip arthroplasty."	Data suggests 0.1 mg intrathecal morphine better than psoas compartment block after primary hip arthroplasty for analgesia.

						blood aspiration.				
Haddad, 1995 (score= 5.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No sponsorship or COI.	N=50 patients with extracapsular fractures of the femoral neck.	Mean age: 77 years; 15 males, 35 females.	Group 1 was given a femoral nerve block with 0.3 ml/kg of 25% bupivacaine (n=25) vs Group 2 given systemic analgesia alone (n=25).	15 min, 2 hrs, and 8 hrs.	Post-op respiratory complication decreased ($p<0.05$). At 15 min group 1 had a pain score of 4.8 vs group 2 pain score 6.4 ($p<0.05$). At 2 hrs group 1 had a pain score of 3.7 vs group 2 pain score 5.9 ($p<0.01$).	"Femoral nerve block seems to be a useful adjunct in the management of fractures of the femoral neck. It requires minimal instruction, can be performed by junior staff, and is rapidly effective. It has few side-effects and allows pain relief in patients who are unable to receive systemic analgesia."	Short follow-up time of 8 hours, sparse methods. Data suggest femoral nerve block significantly reduced perioperative analgesia and resulted in few adverse events.
Scucs, 2012 (score= 5.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N= 24 patients with fractured neck of femur.	Mean age: 78.1 years; 8 males, 16 females.	Group 1 was given 1 g paracetamol orally 6 hourly with parenteral morphine capped at 0.1 mg/kg intramuscularly 4 hourly (n=12) vs group 2 was given 10 ml of 2% lidocaine, 10 ml of 0.5% bupivacaine, 0.25% bupivacaine at a rate of 4ml/hr for 72 hrs, and 1 g paracetamol orally 6 hourly (n=12).	Every 6 hrs for 72 hrs.	At 6 hrs group 1 had larger pain scores 67.0 vs 30.7 ($p=0.004$). Group 1 had a lower heart rate at 66 and 72 hrs 74.09 vs 81.7 ($p=0.03$) and 73.27 vs 84.88 ($p=0.02$). At 12 hrs group 2 had a higher respiratory rate 17.81 vs 16.16 ($p=0.04$). Patients were more satisfied in group 2 concerning analgesia ($p=0.014$).	"CFNB provides more effective perioperative analgesia than a standard opiate-based regimen for patients undergoing fixation of FNF. It is associated with lesser opiate use and greater patient satisfaction."	Data suggest CFN13 was best for perioperative analgesia compared to routine opioid based analgesia for fixation of femoral neck fractures.

Badiola, 2018 (score= 5.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No sponsorship. No mention of COI.	N=48 ASA physical status 1-III and English speaking patients undergoing a primary hip arthroscopy.	Mean age: 39.3 years; 16 males, 32 females.	Group 1 was given a lumbar plexus block with 30 ml of 0.25% bupivacaine with 1:200,000 epinephrine (n=23) vs group 2 was given a fascia iliaca block with 30 ml of 0.25% bupivacaine with 1:200,000 epinephrine (n=25).	Every 15 min for 2 hrs and 24 hrs.	The pain before the block was similar in both groups (p=0.689). At 15 min there was no statistical difference in pain between groups (p=0.054). Group 1 used less opioids (p=0.02).	"A fascia iliaca block is not inferior to a lumbar plexus block in reducing PACU pain scores in patients with moderate to severe pain following hip arthroscopic surgery and is a viable option to help manage postoperative pain following hip arthroscopic surgery"	Short follow-up (24 hr). Data suggest comparable efficiency.
Coad, 1991 (score= 4.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N= 50 patients undergoing either compression-screw or pin and plate fixation of femoral neck.	Mean age: 77.32 years; 8 males, 42 females.	Group 1 had no nerve block (n=16) vs group 2 had lateral cutaneous nerve block with 1:200,000 ratio of 15 ml of 0.5% bupivacaine with adrenaline (n=17) vs group 3 had a 3 in 1 femoral nerve block with 1:200,000	24 hrs.	It took longer for groups 2 and 3 to need pethidine ($p<0.01$). At 12 hrs, group 3 used less pethidine than both groups 1 and 2 ($p<0.05$).	"3 in 1 femoral nerve block is simple to perform) safe and provides excellent post-operative analgesia following surgery for fractures of the femoral neck and the need for post-operative opioid administration is reduced."	Follow-up of 24 hr. Relatively small sample and group sizes. Data suggest 3 in 1 femoral nerve block provided best analgesia.

						ratio of 15 ml of 0.5% bupivacaine with adrenaline (n=17).				
Kratz, 2015 (score= 4.5)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No sponsorship or COI.	N=52 patients undergoing elective hip surgery.	Mean age: 66.35 years; 24 males, 28 females.	Group 1 received general anesthesia and a single shot of femoral nerve block with 0.4 mA, 5 mg bupivacaine, 20 µg clonidine (n=26) vs group 2 received only general anesthesia (n=26).	30 min, 2 hrs, 6 hrs, and 24 hrs.	Group 1 had less doses of ibuprofen in the first 24 hrs ($p<0.05$). In the PACU, group 1 required less piritramide ($p=0.0011$).	"Femoral nerve block improved perioperative hemodynamic stability mostly likely attributable to an overall reduced sympathico adrenergic tone."	Data suggest femoral nerve block group required less post-operative opioids as well as NSAIDS and had significantly lower blood pressures pre and post-surgery with reduced diastolic blood pressures post-operatively.
Hood, 1991 (score= 4.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N= 50 patients with intertrochanteric fractures	Mean age: 81 years; 6 males, 44 females.	Group 1 was given 0.2 mg/kg etomidate and 0.25mg doses of alfentanil (n=25) vs group 2 (n=25) was given a subcostal nerve block and a triple nerve block in addition to	24 hrs.	Group 2 had shorter recovery times ($p<0.05$). Group 2 had more patients that did not need analgesia ($p<0.01$) and had fewer injections ($p<0.05$).	"[…] the described technique is a safe and convenient method of reducing the peroperative anaesthetic requirements and alleviating the need for opioid analgesics in a significant number of patients during the first 24 hours after surgical correction of fractured neck of femur"	Data suggest nerve block group required much less opioid post-surgery up to 24 hr.

						the anesthesia given in group 1.				
Deniz, 2014 (score= 4.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship. No COI.	N= 60 patients undergoing hip prosthesis surgery	Mean age: 63.3 years' 27 males, 33 females.	Group 1 was given fascia iliaca compartment block with 2% prilocaine and 30 mL of 0.25% bupivacaine (n=20) vs group 2 was given 2% prilocaine and 30 ml of 0.25% bupivacaine lateral of femoral artery (n=20) vs group 3 was given general anesthesia (n=20).	0, 2, 4, 6, and 24 hrs.	At 0 and 2 hrs groups 1 and 2 had a difference in VAS scores compared to group 3 ($p<0.05$). No difference between groups 1 and 2 ($p>0.05$). VAS scores were not different between any groups at 4, 6, and 24 hrs ($p>0.05$). At 2, 4, 6, and 24 hrs groups 1 and 2 had a difference in tramadol consumption compared to group 3 ($p<0.05$).	"We believe that the safe and efficient application of the ultrasound-guided 3 in 1 block and the FICB is necessary in multimodal analgesic treatment in order to enable postoperative analgesia in hip prosthesis surgery"	Sparce methods. Data suggest 3 in 1 block group had decreased opioid use as well as pain scores.
Dickman, 2016 (score= 4.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by National Institute on Aging. No mention of COI.	N= 68 patients with a hip fracture	Mean age: 82.6 years; 18 males, 50 females.	Group 1 had intracapsular hip fractures (n=31) vs group 2 had extracapsular fractures (n=37).	2 and 3 hrs.	At 2 and 3 hrs pain scores were similar between both groups (p=0.39, p=0.38).	"USFNB is equally effective in reducing pain from hip fracture in both IC and EC subtypes. Health care providers offering emergency care to elderly patients who have sustained an IC or EC hip fracture should strongly consider using USFNB to treat pain"	Very short follow-up of 3 hrs. Data suggest comparable efficiency of US guided nerve blocks for both intracapsular and extracapsular hip fractures.

White, 1980 (score= 4.0)	Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=56 patients undergoing surgery for fractured neck of femur	Mean age: 78.7 years; 8 males, 48 females.	Group 1 was given 50 mcg with 1-1.5 ml althesin. They had a lumbar puncture and were given 0.6-0.8 hyperbaric cinchocaine (n=20) vs group 2 was given thiopentone and suxamethonium to induce sleep and was maintained using nitrous oxide in oxygen, halothane, and 50-100 mcg fentanyl via IV (n=20) vs group 3 was given general anaesthesia and a psoas compartment block was performed with 30 ml mepivacaine and 8.5 mL althesin.	4 weeks.	No fatalities during data collection period. Group 1 and 2 each had a patient experience nausea and vomiting. There was no significant difference in pneumonia prevalence between groups.	"This study has shown no difference in postoperative morbidity or mortality between the different anaesthetic groups. Close co-operation with the surgeons, adequate patient resuscitation and a carefully administered anaesthetic, regardless of technique, is the key to obtaining a lower mortality rate."	4 week follow up period to monitor adverse events. Data suggest comparable efficiency (both pre-op intra-op and post-op) in all 3 groups.
De Visme,	Regional Block	RCT	Sponsored by Brest	N= 29 patients	Mean age: 84.7	Group 1 was given a	5 days.	Surgery for group 1 was longer (p=0.13). The VAS	"[…] plain bupivacaine SA and block produce satisfactory	Small sample and group sizes. Data suggest comparable

2000 (score= 4.0)	Anesthesia and Analgesia for Hip/Knee Arthroplasty		University of Medicine. No mention of COI.	with proximal femoral fracture	years; 5 males, 24 females.	combined peripheral nerve block using 5 mL/kg Hartman solution pre-op and during first 15 min post-op and then 5 mL/kg/hr until transferred Vs group 2 was given an injection of 3 mL 0.5% plain bupivacaine at L3-L4 (n=14).		scores were not different between groups. Group 2 required more ephedrine to remain stable. There was a correlation between initial blood pressure decrease and age over 85 ($p<0.01$).	quality of anesthesia. It must be emphasized that both spinal and peripheral nerve block anesthesia occasionally resulted in marked hypotension in patients over 85 years of age."	efficiency with prolonger hypotension resulting from spinal anesthesia.
Luger 2013 (score= 4.0)	Regional Blocks	RCT	No mention of sponsorship. No COI.	N=34 patients scheduled for acute hip fracture surgery	Mean age: 87.3 years; no mention of sex.	Group A: received continuous 3-in-1 block of initial bolus of 0.25% bupivacaine, then 0.125% bupivacaine 6 mL/hour for a total of 2.5-4 mL(n=10) vs Group B: (n=10) vs Group C: received an initial dose of 0.05 mg/kg piritramide iv and	12, 24 hours	VAS and verbal pain scale (VPS) were similar for all groups. Analgesia response in group A for motion was 86.7% and rest was 86.7%, 100% for both in group B respectively (Group A vs Group B, p=0.001), and 70% for motion and 46.7% in rest for group C, respectively. Control group showed elevated consumption of additional analgesics compared to treatment groups. Increased need for paracetamol was seen in treatment groups (p=0.02).	"In the specific situation of acute hospital admission, the ultrasound-guided continuous 3-in-1 block appears to be indicated as a stress-free means of providing adequate preoperative pain relief in very elderly patients with hip fracture."	Pilot study. Data suggest ultrasound guided 3-1 block provided adequate analgesia for preoperative pain.

						additionally systemic analgesics, either piritramide 3 mg sc as a bolus, or paracetamol (Perfalgan, Bristol-Myers Squibb, Vienna, Austria) 1 g as a short infusion with a maximal daily dose of 3 g (n=14)				
Aksoy 2014 (score= 4.0)	Regional Block	RCT	No mention of sponsorship. No COI.	N=70 patients undergoing elective hip replacement surgery	Mean age: 73.1 years; 39 males, 31 females	CSA Group: received 2.5 mg of isobaric bupivacaine 0.5% continuous spinal anaesthesia (n=35) vs PCSNB Group: received psoas compartment -sciatic nerve block 30 mL of 0.25% bupivacaine with 1:200.000 epinephrine (5 µgr/mL) (n=35)	5^{th}, 10, 20^{th} minutes of surgery	More patients in the PCSNB group required rescue analgesic compared to CSA group (p=0.0001). MMSE post-operative scores were similar for both groups (18.37±4.37 CSA vs 18.57±4.08 PCSNB). PCSNB group showed higher MABP values at beginning, and 5^{th}, 10^{th}, and 20^{th} minutes of surgery compared to CSA group (p=0.038, p=0.029, p=0.012, p=0.009).	"CSA and PCSNB produce satisfactory quality of anaesthesia in elderly high-risk patients with fewer hemodynamic changes in PCSNB cases compared with CSA cases."	Data suggest both CSA and PCSNB have comparable anesthetic effects but PCSNB demonstrated fewer hemodynamic changes.

Spansberg 1996 (score= 4.0)	Regional Block	RCT	No mention of sponsorship or COI.	N=20 patients with femoral neck fractures	Mean age: 80.4 years; 5 males, 18 females	Bupivacaine: received bolus of 0.4 mL kg^{-1} bupivacaine 0.5%, continuous infusion: 0.14 mL $kg^{-1}h^{-1}$ bupivacaine 0.25% (n=10) vs Saline: received identical volumes of saline via the lumbar plexus catheter (n=13)	16 hours	Median use of morphine in saline group was 12.5 mg (p=0.24). No significant differences in VAS pain scale were observed between groups.	"In conclusion, the addition of continuous blockade of the lumbar plexus to post-operative rectal acetylsalicylic acid provides no important additional pain relief after surgical correction of a fractured neck of femur under spinal anaesthesia."	Very small sample (n=20) with sparse demographic data. Data suggest lack of efficacy as no significant differences in morphine consumption or pain were detected.
Jones 1985 (score= 4.0)	Regional Block	RCT	No mention of sponsorship or COI.	N=19 patients undergoing internal fixation of intertrochanteric fractures of the femoral neck	Mean age: 82 years; 1 male, 18 females	Group 1: did not receive a nerve block (n=9) vs Group 2: received lateral cutaneous nerve block using 15 mL 0.5% bupivacaine with adrenaline (n=9)	24 hours	Four patients in group 1 required analgesia compared to 1 patient in group 2, and only 44% of group 2 required no analgesia. Fewer patients required pethidine in first 12 hours in group 2 compared to group 1 and received it later as well ($p<0.05$, $p<0.01$; respectively).	"It is concluded that the technique of lateral cutaneous nerve block is simple, safe and rapidly performed and can contribute considerably to postoperative analgesia and greatly reduce or obviate the need for opioid analgesia following femoral neck surgery."	Small sample, sparse methods. Data suggest lateral cutaneous nerve block may decrease narcotic consumption to having femoral neck surgery significantly.

Evidence for use of Epidural – Single Injection-Extended Release Epidural Morphine

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epidural Anesthesia-Analgesia; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 299 articles in PubMed, 264 in Scopus, 17 in CINAHL, 5 in Cochrane Library, 14300 in Google Scholar, and 13 from other sources. We considered for inclusion 7 from PubMed, 0 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 13 from other sources. Of the 24 articles considered for inclusion, 16 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence for use of Continuous Epidural Local Anesthetics Only

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Epidural Anesthesia-Analgesia; Acetabular Fracture, Femur Fracture, Hip-Pelvic fracture, latrogenic femoral fracture, occult hip fracture, hip fractures, trochanteric fractures, intertrochanteric fractures, sub trochanteric fractures, femoral neck fracture, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 299 articles in PubMed, 264 in Scopus, 17 in CINAHL, 5 in Cochrane Library, 14300 in Google Scholar, and 13 from other sources. We considered for inclusion 7 from PubMed, 0 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 13 from other sources. Of the 24 articles considered for inclusion, 16 randomized trials and 8 systematic studies met the inclusion criteria.

Evidence for the Use of Epidural Anesthesia/Analgesia

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Viscusi 2005 (score= 9.5)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship. COI: One or more of the authors have received or will receive benefits for personal or professional use.	N=200 patients scheduled to undergo total hip arthroplasty	Mean age: 60.6±12.5 years; 102 males, 98 females	Extended release epidural morphine (EREM) 15mg (N=51) vs EREM 20mg (N=50) vs EREM 25mg (N=49) vs. epidural saline placebo (n=50)	Follow up at 24, 48 hours post operation.	Total Fentanyl use over 48 hours post dose was lower in all three EREM groups vs placebo (Exact values not given; p<0.0001 for all three). Median time to first dose of fentanyl was 21.3 min for the pooled EREM groups vs 3.6 hours for the placebo (p<0.0001) Area under the curve of pain control at rest through the first 24 hours was 1.4 in the placebo group vs 0.8 for the 15 mg (p<0.0004), 0.6 for the 20	"EREM provided significant postoperative pain relief over a 48-h period after hip surgery, without the need for indwelling epidural catheters."	All active groups used less opioid. May be particularly beneficial in post-op rehabilitation as no indwelling epidural catheter is required in this often anti-coagulated cohort.

								mg group (p<0.0001) and 0.6 in the 25mg group (p<0.0001)		
Murdoch 2002 (score= 9.5)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by a research grant from Chiroscience Ltd. No mention of COI.	N=105 patients undergoing elective hip or knee joint replacement	Mean age: 63.7 years; 49 males, 42 females	Continuous epidural infusion of levobupivacaine at three different concentrations 0.0625% (n=32) vs 0.125% (n=27) vs 0.25% (n=32) for post-op pain relief in patients undergoing knee or hip arthroplasty.	Follow up at baseline, 1, 2, 3, 4, 6, 8, 10, 12, 18, and 24 hours.	Mean time to first request for rescue analgesia was 16.7 minutes in the 0.25% group vs 8.1 in the 0.0625% group (p<0.001) and 9.5 in the 0.125% group (p<0.001). Hazard ratios using cox proportional hazard models for requesting morphine vs the 0.25% group were 1.791 for the 0.125% group and 4.181 for the 0.0625% group.	"Levobupivacaine as a continuous epidural infusion provided adequate postoperative analgesia. The 0.25% concentration provided significantly longer analgesia than 0.125% or 0.0625% levobupivacaine without any significant increase in detectable motor blockade relative to the 0.125% group."	Alternative to opioid pain control. Side effect profile high for hypotension (60%).
Berti 1998 (score= 7.5)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=30 ASA physical status 1-2 patients undergoing total hip replacement	Mean age: 63.4 years; 15 males, 15 females	Post-operative anesthesia by continuous epidural infusion of bupivacaine 0.125% at 4ml/hour in combination with fentanyl 0.005mg/ml (N=15) vs. in combination with morphine 0.05mg/ml (N=15)	Follow up at 1, 3, 6, 9, 12, 24 hours	Mean pain scores on the 100 mm visual analogue scale ranged from 15 mm and 53 mm in the morphine group vs 11 mm and 58 mm in the fentanyl group (No P value provided). At 3, 6, 9, 12, and 24 hours SpO_2 was lower in the morphine group than in the fentanyl group (No values provided; p<0.05)	"Continuous epidural infusion of bupivacaine-morphine or bupivacaine-fentanyl mixtures provided similar pain relief. Patients receiving morphine showed a more marked decrease in SpO2 than those receiving fentanyl. However, the average SpO2 remained > 90% in both groups."	Equivocal results in pain management. Questionable clinical significance of oxygen saturation difference.

Smet 2008 (score= 7.5)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N = 78 patients undergoing total hip or knee replacement	Mean age: 63.5 years; 39 males, 39 females	Patients who received an epidural mixture of ropivacaine 0.165% with sufentanil 1 µg ml^{-1} post operatively (N=38) vs patients who received an epidural mixture of levobupivacaine 0.125% with sufentanil 1 µg ml^{-1} post operatively (N=40)	Follow up at baseline, 12, 24, 36, and 48 hours postoperation.	After 48 hours total colume of local anaesthetic and sufentanil solution consumed was 221 ml in the Ropivacaine group vs 178 ml in the Levobupivacaine group (p=0.02). There were 38.5 PCEA device demands for the ropivacaine group after 48 hours vs 28 in the levobupivicaine group (p=0.04)	"In conclusion, the present study found that both local anaesthetics provide satisfactory analgesia in the concentrations used. Despite a 25% higher ropivacaine concentration, the volume consumed was higher during a 48 h period when compared with levobupivacaine. This suggests either a potency difference between both local anaesthetics of more than 25% or a different duration of action. Regardless of the exact explanation, using lower concentrations of ropivacaine may be unwise as it could mean that more PCEA demands are made which may increase the total opiate dose if its concentration is not changed to allow for this."	Data suggest comparable analgesic effects but during the first 48 hours post-surgery the ropivacaine group consumed 25% more local anesthesia.
Gedney 1998 (score= 7.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=160 patients undergoing hip replacement surgery	Mean age: 71.3 years; 80 males, 80 females	Study groups received epidural infusions of bupivacaine (6-8ml an hour) in combination with	Follow up at 6, 12, 18, 24, 36 hours	No significant difference in pain scores between the groups. Severe nausea with vomiting was seen in 47% of the morphine group vs 12.5% in the fentanyl group (p=0.0069) Pruritis occurred in 44% of morphine and diamorphine groups vs 12.5% in the	"Fentanyl had the lowest incidence of severe nausea and vomiting. Methadone the lowest incidence of pruritus, methadone and pethidine the lowest overall incidence of urinary catheterization and	Pethidine is also known as meperidine (Demerol). There is no clear conclusion by these authors as to which opioid is superior.

						morphine 0.05 mg/ml (N=32) vs. fentanyl 2.0 µg/ml (N=32) vs. methadone 0.1 mg/ml (N=32) vs. diamorphine 0.05 mg/ml (N=32) vs. pethidine 1.0 mg/ml (N=32).		methadone group (p=0.012) and 15.6% in the pethidine group (p=0.027).	pethidine the lowest overall incidence of side effects. Pethidine is known to have local anesthetic properties which may reduce the total dose required and contribute to the low incidence of side-effects observed."	
White 1992 (score= 7.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=66 patients that underwent elective total replacement of the knee or hip joint	Mean age: 57.5 years; no mention of sex	Bolus followed by continuous epidural infusion of morphine (N=34) vs. fentanyl (N=32). (dosages were variable)	Follow up at 3, 6, 12, 24, 36, and 48 hours	Pain relief similar in both groups. In morphine group, $PaCO_2$ elevation and nausea occurred over 12 hours ($p < 0.05$). In fentanyl group, there was no $PaCO_2$ elevation. Nausea more severe ($p < 0.01$) at 6 hours and more frequent (24 hour cumulative incidence, 53 vs. 28%, $p < 0.05$) in morphine group. There was a quadratic increase in pruritus over time ($p < 0.001$), and it was more severe in the morphine group ($p < 0.001$).	"Side effects of both groups were less on the second day of infusion with the notable exception of pruritus. Side effects were generally less in the fentanyl group. The continuous epidural infusion of opioids, after the initial bolus-related side effects, appears to be a safe technique to provide prolonged and steady pain relief with minimal side effects."	Methodology issues related to treatment (variable bolus and infusion dosages without explanation) make comparison to other studies challenging.
Carabine 1992 (score= 6.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by grant from Department of Health and Social Services for N. Ireland. No	N=100 patients undergoing total hip replacement	Mean age: 63.8 years; 26 males, 54 females	Extradural clonidine 25µg/ mL/hour (N=25) vs. extradural clonidine 50µg/ mL/hour (N=25) vs.	Follow up at baseline, 10, 20, 30, 40, 50, and 60 minutes, 2, 3, 4, 5, 6,	Mean arterial blood pressures were lower in clonidine groups. Patients more likely to be awake in clonidine 25µg and combination groups at 30 minutes compared with morphine group ($p<0.05$). PCA morphine doses were 14.5/10.5/15.9/9.3mg respectively. Times to first PCA	The requirements for systemic analgesia were least in the combination and larger dose clonidine group.	Data suggest the addition of clonidine to morphine resulted in the best analgesic outcomes while not increasing respiratory depression. In addition, emetic events did not differ between the groups, but arterial pressure did decrease with clonidine, but with few cases of clinical hypotension.

			mention of COI.			extradural morphine 0.1mg/ mL/hour (N=25) vs. clonidine plus morphine 50µg/ mL/hour and 0.1mg/mL/hr (N=25).	7, 8, 9, 10, 11, 12, 18 and 24 hours.	use: 144/286/109/283 minutes respectively.		
Foss 2005 (score= 6.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Apotekerfonden af 1991, Copenhagen, Denmark, IMK-fonden, Copenhagen, Denmark, and The Danish Research Council, Copenhagen, Denmark. No mention of COI.	N = 55 elderly patients with primary hip fracture	Mean age: 82.5 years; 10 males, 45 females	Post-operative pain relief by continuous epidural 4 ml/hour infusion of bupivacaine 0.125% and morphine (50µg) (N=28) vs. saline placebo (N=27)	Follow up at 1, 2, 3, 4 days	The number of patients that reported pain on hip flexion after 1 day in the treatment group was 2 vs 10 in the placebo group (p=0.02). The number of patients that reported pain on walking after 1 day in the treatment group was 2 vs 17 in the placebo group (p<0.001). The treatment group spent 85 mins in the PACU vs 120 min for the placebo group (p = 0.007). No other statistically significant differences were seen in postoperative complications.	"In conclusion, the current study showed that postoperative epidural analgesia with local anesthetic and low dose morphine provided superior pain control during dynamic exercise in patients who underwent surgery for hip fracture and that patients were significantly less restricted by pain in their ability to perform basic functions without motor blockade. However, overall ability to perform basic mobility functions independently was not significantly improved, potentially because of other confounding limiting factors, such as nausea and exhaustion, that impeded physical function despite the absence of pain."	4 day follow-up Data suggest postop epidural anesthesia post hip fracture surgery provides excellent analgesia but this did not result in enhanced rehabilitation.
Gustafson	Epidural Anesthes	RCT	Sponsored by grants	N=21 patient	Mean age: 65.7	1 mg/kg of pethidine IM	Follow up at	Area under the curve of the pain score was not significantly	"The present study shows that extradural pethidine	Blinding unclear, small sample size.

1986 (score= 5.5)	ia and Analgesia for Hip/Knee Arthroplasty		from Swedish Medical Research Council and the Swedish Cancer Society. No mention of COI.	s that underwent total hip replacement	years; no mention of sex	(N=7) vs.20mg of pethidine IM (N=7) vs. 60mg of extradural pethidine (N=7)	baseline, 15, 30, 60, 90, 120, 150 minutes and 3, 4, 5, 6, 8, 10 and 18 hours post drug administration	different between groups after 18 hours.	produces short-lived analgesia, in contrast to the long-lasting effect of morphine found in other studies."	
Reiz 1981 (score= 5.5)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=33 patients undergoing hip surgery	Mean age: 65 years; 17 males, 16 females	Single epidural morphine (2mg) injection (N=15) vs. morphine (10mg) IM injection (N=18) after hip replacement surgery using epidural anesthesia	Follow up at baseline, 15, 30, 45, and 60 minutes and continuous until discharge (mean 15 hours, range between 14-17 hours)	Epidural pain score dropped from 5.3±1.6 to 0.7±0.2 ($p < 0.001$) vs. IM morphine 5.2±1.2 to 2.7±1.0 ($p < 0.01$). After the first dose of ED morphine, 5 of the 15 patients were totally pain-free vs 1 of the 18 patients in the IM group.	"The quality of pain relief was substantially higher and the duration of action markedly longer after epidural morphine."	Lack of clear statistical analysis weakens inferences.
Sun 2017 (score= 5.5)	Epidural Anesthesia and Analgesia for	RCT	No mention of sponsorship. No COI.	N = 300 ASA class 2-3 patient	Mean age: 82.9 years; 141 males,	Patients received intravenous infusions during	Follow up at baseline, 10, 30, and	Incidence of POCD was 18.7% for M3 vs 5.3% in the control group ($p<0.05$), 6.7% in M1 ($p<0.05$), and 6.7% in M2 ($p<0.05$). At the end of the	"In conclusion, intravenous infusion of methoxamine at 2–3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ was demonstrated effective in	Data suggest IV methoxamine infusion (2-3 µg/kg/min) can maintain stable hemodynamics without increasing POCD.

	Hip/Knee Arthroplasty			s undergoing unilateral hip-joint replacement surgery under epidural anesthesia	159 females	surgery of 2 μg·kg^{-1}·min^{-1} methoxamine (M1; N=75) vs 3 μg·kg^{-1}·min^{-1} methoxamine (M2; N=75) vs 4 μg·kg^{-1}·min^{-1} methoxamine (M3; N=75) vs the same volume of saline at the same rate (C; N=75)	60 minutes and at the end of operation as well as 1, 6, 12, 18, 24, 36, and 48 hours post operation.	operation Mean arterial pressure in mmHg was 115.7 in M3 vs 75.9 in the control ($p<0.05$), 93.3 in M1 ($p<0.05$), and 98.3 in M2 ($p<0.05$) Similar differences were seen in Rate pressure product, central venous pressure, cardiac output and systolic volume.	maintaining stable hemodynamics in elderly patients during epidural anesthesia for hip joint replacement surgery, without increasing the incidence of POCD."	
Koch 2008 (score= 5.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Abbott GmBH & Co. KG, Max Planck-Ring 2. No mention of COI.	N = 71 ASA classes 1-3 patients from German academic hospitals under-going hip surgery.	Mean age: 61.8 years; No mention of gender.	Patients who received a perioperative epidural with 10-18 ml Bupivacaine (N=22) vs 10-18 ml Levobupivacaine (N=24) vs 10-18 ml Ropivacaine (N=25).	Follow up at baseline, 3, 6, 9, 12, and 15 minutes post drug administration follow by every 5 mins until sensory block level T10 followed by every	No statistically significant differences observed in epidural volumes, sensory and motor block development and regression. No statistically significant differences observed in pain course.	"The results of this prospective, randomized single blind study were able to demonstrate in most parameters equal epidural anesthesia and postoperative analgesia with 0.5%/0.125% levobupivacaine and 0.5%/0.125% bupivacaine or 0.75%/0.2% ropivacaine for major orthopedic and traumatologic hip surgery."	Data suggest comparable efficacy.

							10 minutes intraoperatively, then every 15 minutes post operatively until sensory block regression to T12.			
Turner 1996 (score= 5.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Astra Pharmaceuticals. No mention of COI.	N=151 patients undergoing total hip or knee arthroplasty or cruciate ligament reconstruction	Mean age: 60.1 years; 64 males, 71 females	Patients received an extradural infusion of 0.2% Ropivacaine at a rate of 6 ml h^{-1} (N=22) vs 8 ml h^{-1} (N=23) vs 10 ml h^{-1} (N=23) vs 12 ml h^{-1} (N=24) vs 14 ml h^{-1} (N=23) vs control group which did not receive any postoperative extradural infusion.	Follow up at 0-4, 4-8, and 8-21 hours	Median VAS scores after 10 hours were between 18-30 in the control group vs all below 8 for the ropivacaine groups during the same period (Exact values were not provided). Percent of patients that rated the quality of treatment as excellent was 80% in the 6 ml group vs 75% in the 10 ml group vs 68% in the 12 ml group vs 65% in the 8 ml group vs 61 in the 14 ml group vs 59% in the control group.	"The overall incidence of side effects was similar, with the exception of a higher incidence of urinary retention and hypotension in the groups receiving the higher rates of ropivacaine. The quality of treatment scores were similar for all treatment groups."	Study suggests 10ml/hr group as best dose for analgesia and limited side effects. The results are weakened by lack of blinding and presence of co-interventions.

Modig 1981 (score= 5.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=32 patients subjected to total hip replacement	Mean age: 65.2 years; 18 males, 14 females	Epidural morphine (n=15) vs. 0.5% bupivacaine with epinephrine (n=17)	Continuous follow up over 32 hours	Mean duration of analgesia was 28 hours in morphine group vs. 4.3 hours for bupivacaine (p <0.001). Epidural morphine group tended to have lower frequency of reduced blood pressures.	"Epidural morphine certainly has a role in the management of postoperative pain. Administration both by the lumbar and by the thoracic route resulted in satisfactory pain relief in all patients, without sympathetic block. The time of onset of analgesia was somewhat slower with morphine than with bupivacaine, but its duration was much longer. The quality of postoperative analgesia obtained by epidural morphine was less profound than that following bupivacaine and was not accompanied by sensory, proprioceptive or motor loss, as in the latter case."	Data suggest significantly longer pain relief occurred in the epidural morphine group (28 hours vs 4.3 hours). However, due to the potential for delayed adverse events such as respiratory depression, epidural morphine needs careful monitoring after administration.
Wulf 1999 (score= 5.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Astra Pain Control. No mention of COI.	N = 90 ASA classes 1-3 patients scheduled for unilateral total hip replacement.	Ages >18; 44 males, 46 females	EDA group received an epidural of 12-15 ml main dose of ropivacaine 10mg/ml (N=44) vs GA/PCA group received general anesthesia with thiopental or	Follow up before surgery, during surgery, end of surgery, 0-24 and 24-48 hours after surgery as well	Area under the curve (AUC) based on the visual analog scale pain score at 24 hours was 14 mm in the EDA group vs 24 mm in the GA/PCA group (p=0.007). Time until deemed ready for discharge from PACU was 5.6 min in the EDA group vs 39.7 in the GA/PCA group (No P-value provided)	"Our results indicate that patients in the EDA group are in a stable and comfortable condition much sooner after operation than patients in the GA/PCA group. Nevertheless, improvement of pain management does not automatically result in improvement in other outcome	Small follow-up period of 24 hours. Data suggest ropivacaine administered epidurally was superior for pain relief during the first 24 hours post surgery and was associated with faster PACU discharge compared to general anesthesia and post-op patient-controlled analgesia.

						etomidate, fentanyl, and nondepolarizing muscle relaxant (N=46).	as total after surgery.		variables. This is mainly because hospital routines do not take advantage of the improved pain management. Early mobilization, early enteral feeding, etc. have been proposed as additional components of a multimodal approach to control postoperative pathophysiology and to enhance rehabilitation."	
Kilickan 2000 (score= 4.0)	Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N = 60 ASA type 1 or 2 patients undergoing total hip or knee replacement	Mean age: 51.4 years; no mention of sex.	Pre-dermal incision intravenous morphine 0.15mg/kg (Pre-iv group; N=20) vs. pre-emptive epidural 75 µg/kg morphine (Pre-epi group; N=20) vs. IV saline in hip and knee arthroplasty (N=20)	Follow up at 3, 4, 6, 8, 12, 16, 20, 24, and 48 hours	Pre-iv group had a mean morphine dose of 52.35 vs 69.05 for the control group ($p<0.0009$) and 65.55 for the pre-epi group ($p<0.0003$). VAS pain score at 3, 6, 12, 24 and 48 hours were lower in the pre-epi group than in the pre-iv and placebo groups ($p<0.001$; Exact values not provided)	"Although pre-emptive epidural morphine has failed to decrease postoperative analgesic consumption, it has been able to suppress the surgical stress more significantly than intravenous morphine and a saline control."	Lack of blinding, concealment of treatment allocation.

Evidence for the use of Spinal/Local Anesthetic Only

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Intrathecal Anesthesia or Analgesia, Local Anesthetic, Continuous Anesthetic, Clonidine with Anesthetics, Ziconotide, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic

review, retrospective, and prospective studies. We found and reviewed 360 articles in PubMed, 386 in Scopus, 2540 in CINAHL, 220 in Cochrane Library, 6620 in Google Scholar, and 18 from other sources. We considered for inclusion 4 from PubMed, 6 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 18 from other sources. Of the 32 articles considered for inclusion, 28 randomized trials and 4 systematic studies met the inclusion criteria.

Evidence for the use of Spinal Continuous/Local Anesthetic

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Intrathecal Anesthesia or Analgesia, Local Anesthetic, Continuous Anesthetic, Clonidine with Anesthetics, Ziconotide, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 360 articles in PubMed, 386 in Scopus, 2540 in CINAHL, 220 in Cochrane Library, 6620 in Google Scholar, and 18 from other sources. We considered for inclusion 4 from PubMed, 6 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 18 from other sources. Of the 32 articles considered for inclusion, 28 randomized trials and 4 systematic studies met the inclusion criteria

Evidence for the use of Clonidine in Combination with Local Anesthetics

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Intrathecal Anesthesia or Analgesia, Local Anesthetic, Continuous Anesthetic, Clonidine with Anesthetics, Ziconotide, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 360 articles in PubMed, 386 in Scopus, 2540 in CINAHL, 220 in Cochrane Library, 6620 in Google Scholar, and 18 from other sources. We considered for inclusion 4 from PubMed, 6 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 18 from other sources. Of the 32 articles considered for inclusion, 28 randomized trials and 4 systematic studies met the inclusion criteria

Evidence for the use of Spinal Infusion – Ziconotide

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Intrathecal Anesthesia or Analgesia, Local Anesthetic, Continuous Anesthetic, Clonidine with Anesthetics, Ziconotide, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 360 articles in PubMed, 386 in Scopus, 2540 in CINAHL, 220 in Cochrane Library, 6620 in Google Scholar, and 18 from other sources. We considered for inclusion 4 from PubMed, 6 from Scopus, 0 from CINAHL, 1 from Cochrane Library, 3 from Google Scholar, and 18 from other sources. Of the 32 articles considered for inclusion, 28 randomized trials and 4 systematic studies met the inclusion criteria

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Atanassoff 2000 (score= 8.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by grant from Elan Pharmaceuticals, South San Francisco, California. No mention of COI.	N=30 patients undergoing hysterectomy, radical retropubic prostatectomy, and total hip replacement	Mean age: 62.8 years; no mention of sex.	Continuous intrathecal infusion post-operatively of placebo (n=12) vs. Ziconotide (an N-type calcium channel blocker) high dose 7µg/hour (n=6) vs. Ziconotide (an N-type calcium channel blocker) low dose 0.7µg/hour (n=12)	8, 16, 24, 32, 40, 48 hours	Use of morphine equivalents for pain relief from all sources of administration (PCA, injection, Ketorolac) compared. High-dose of ziconotide group (7µg/hour) used 6.6±7.7mg of morphine equivalent compared with 26.2±20.3mg for placebo group (pairwise comparison p = 0.01), while low-dose ziconotide group (0.7µg/h) used 20.7±17.7mg of morphine equivalent (pairwise comparison vs. placebo p =. 487; vs. high-dose p = 0.081). No statistical significances in adverse events, although 4 of 6 patients in high dose group developed dizziness, blurred vision, nystagmus, and sedation, which contributed to study drug being discontinued after 24 hours. Symptoms resolved after discontinuation of ziconotide infusion.	"The high dose group required significantly less narcotic and non-steroidal medication than placebo as shown by decreased PCA morphine equivalent consumption and lower VASPI scores. The low dose group required less morphine, but was not statistically significant. Because of a favorable trend of decreased morphine consumption with an acceptable side-effect profile in the low-dose ziconotide group, 0.7 µg/h may be closer to the ideal dose than 7µg/h."	This was a phase II trial with discontinuation of the higher dose infusion, and no difference in placebo vs. low dose therapy group.
Grace 1995 (score= 8.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by a grant from the Department of Health and Social Services for	N=90 patients undergoing total hip replacement	Mean age: 67 years; 42 males, 48 females	Intrathecal co-administration of clonidine hydrochloride (75µg) and morphine sulfate (0.5mg) vs. intrathecal	2, 4, 6, 24 hours	Patient-controlled analgesia (PCA) morphine requirements significantly reduced (p <0001) post-operation by both comparison groups vs. placebo. No significant additional reduction shown in clonidine-morphine group compared to morphine-alone group. Mean arterial blood pressure	"Co-administration of clonidine 75 µg and morphine 0.5 mg provided profound analgesia after total hip replacement under IT anesthesia, but this combination conferred no additional analgesic benefit over IT morphine	No added benefit of IT clonidine.

			Northern Ireland. No mention of COI.			morphine (0.5mg) vs. saline placebo in spinal anesthesia for hip replacement surgery		significantly lower in clonidine/morphine group than others. Incidence of emesis similar to morphine-alone group, and significantly higher than control group.	0.5 mg alone, and, furthermore, it was associated with marked reductions in mean arterial pressures between 2-5 hours after IT administration."	
Fournier 2005 (score= 8.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=40 patients scheduled for total hip arthroplasty	Mean age: 80 years; 15 males, 25 females	Intrathecal (7.5 µg) vs. intravenous sufentanil (1.25 mg) for postoperative pain relief after total-hip replacement where total spinal anesthesia was used.	24 hours	"Post-operatively, patients administered one of the treatment protocols upon reaching VAS pain scale of 3. Intrathecal sufentanil treated patients had significantly faster relief of pain than intravenous group. More patients needed rescue bupivacaine in intravenous group (7 of 20 vs. 0 of 20, p <0.008), significantly more in intrathecal group reached a pain score of 0 (20 of 20 vs. 9 of 20, p <0.001). Time to first analgesic intervention for pain score greater than 3 significantly longer in intrathecal group (224 +/- 100 vs. 98 +/- 60 minutes, p <0.001). Pruritus observed in 5 patients of intrathecal group (p <.047), whereas peripheral oxygen saturation under 95% observed only in 6 patients in intravenous group (p <.045)."	"After total-hip replacement, intrathecal route of sufentanil administration rapidly offers excellent analgesia of better quality and longer duration when compared with the intravenous route."	Effective pain management strategy in patients undergoing continuous intrathecal anesthesia. In this study, all patients were age 75 or older.
Grace 1996 (score= 8.5)	Intrathecal Anesthesia and Analgesia for Hip/Kne	RCT	Sponsored by a grant from the Department of Health	N=75 patients undergoing total hip replacement	Mean age: 65 years; 31 males, 44 females	Intrathecal morphine-6-glucuronide (M6G) at 100µg and 125µg vs. intrathecal	1, 2, 4, 6, 8, 10, 12, 24 hours	Analgesia excellent and similar to that obtained after intrathecal administration of morphine. VAS pain scores recorded post-op low (median = 0) and similar in all groups. Compared to control morphine	Intrathecal M6G provides excellent postoperative analgesia. More subjects in the intrathecal M6G groups were pain free at 4, 10, and 24 hours than the morphine sulfate	Pain relief as measured by subjective pain scale was improved in treatment group, but no clinical difference was observed by objective measures of

	e Arthroplasty		and Social Services for Northern Ireland. No mention of COI.			morphine sulfate (500µg) for post-operative hip replacement pain control		group, significantly more patients in M6G125 group reported pain as 0 at 6 and 10 hours, while significantly more in M6G 100 group reported 0 pain at 24 hours. No significant difference in consumption of post-operative analgesia (PCA) or onset of time to first PCA demand. Incidences of nausea and vomiting high in all groups with no significant differences.	group. Side effects were high in all groups but not significantly different.	patient-controlled analgesia (PCA).
Lydon 1999 (score= 8.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N = 24 patients undergoing hip arthroplasty	Mean age: 69.4 years; 14 males, 10 males	Intrathecal bupivacaine (17.5mg) vs. combination of intrathecal morphine (0.6mg) and bupivacaine (17.5mg) in spinal anesthesia for hip arthroplasty	No mention of follow-up.	Gastric emptying rates, as quantified by acetaminophen administration and blood concentration studies were reduced in both groups pre- and postoperatively, respectively; the magnitude of the reduction was greater in the group given morphine.	"The combination of intrathecal morphine (0.6 mg) and intrathecal bupivacaine (17.5 mg) delays gastric emptying postoperatively."	Study may allow inferences in the association of morphine and common side effects of nausea and vomiting, but does not address implications related to effectiveness of opioid treatment.
Fournier 2000 (score= 7.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=40 scheduled for elective total hip replacement	Mean age: 79.5 years; 7 males, 17 females	Morphine 160µg vs. nalbuphine 400µg	24, 48 hours	VAS pain scores decreased more rapidly in nalbuphine group with time to pain score<3 of 8±6 vs. 31±32 minutes, p <0.001 and similar results for time to lowest pain score (18±11 vs. 66±75 minutes, p <0.001).	After total hip replacement, administration of intrathecal nalbuphine resulted in a significantly faster onset of pain relief and shorter duration of analgesia than intrathecal morphine.	Study prematurely terminated due to slow onset of action in morphine group. Dosage of morphine is significantly lower than other studies, making comparison difficult.
Fogarty 1993 (score= 7.5)	Intrathecal Anesthesia and Analgesi	RCT	No mention of sponsorship. COI:	N=90 patients undergoing elective	Mean age: 65 years; 55 males, 35 females	Intrathecal clonidine 75µg (100µg if over 76kg)	2, 4, 6, 8, 10, 12 hours	Post-operative morphine consumption much lower in intrathecal morphine group and diverged within 4 hours (graphic representation). Time	"Both intrathecal clonidine and intrathecal morphine prolonged the time to first analgesia compared with saline	This demonstrated a weak effect of intrathecal clonidine and a strong effect of morphine.

	a for Hip/Knee Arthroplasty		Fogarty and Milligan were in receipt of DHSS research grants.	total hip replacement		vs. morphine 1mg vs. saline		to first post-operative analgesia 278 vs. 497 vs. 153 minutes (p <0.05 for morphine). Total morphine used 27.9 vs. 5.5 vs. 31mg (p <0.05 for morphine).	(mean 278 (SD 93.2) min, 498 (282.4) min and 54 (61.9 (min., respectively) (P< 0.001). Total morphine consumption on the first night after operation was significantly less in the intrathecal morphine group. There were no differences between the clonidine and the control group. Intrathecal clonidine prolonged the duration of spinal analgesia, but was markedly inferior to the intrathecal morphine in providing subsequent post-operative analgesia."	
Pitkanen 1993 (score= 7.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=54 patients undergoing hip or knee surgery	Mean age: 68.1 years; 15 males, 39 females	Tropisetron 5mg (5-HT3-receptor antagonist) vs. saline placebo in patients undergoing intrathecal bupivacaine (0.5%)/ morphine (0.3mg) block for lower extremity surgery	24 hours	No significant differences found between number of patients experiencing nausea/ vomiting for tropisetron (17/11) vs. saline (20/13). No significant differences in pain relief or consumption of analgesic medications between the two groups.	"Tropisetron has no effect on postoperative nausea, emesis, or pain control in patients who underwent spinal anesthesia with bupivacaine and morphine."	Negative study.
Fournier 2000 (score= 7.0)	Intrathecal Anesthesia and	RCT	No mention of	N=42 patients scheduled for	Mean age: 79.5 years; 17	Intrathecal sufentanil (7.5µg) vs. fentanyl	24 hours	There were no significant differences between the groups in pain scores, rescue analgesia, adverse effects,	"After total hip replacement, both lipid soluble opioids produce excellent analgesia with	No recommendation of one over the other from this study. Both effective

	Analgesia for Hip/Knee Arthroplasty		sponsorship or COI.	elective total hip replacement	males, 25 females	(40µg) in bupivacaine spinal anesthesia		elapsed time for pain relief, time to lowest pain score and duration of pain relief.	comparable onset, duration of action, and low incidence of minor adverse effects."	in post-operative pain management.
Niemi 1993 (score= 7.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by a grant from Sigrid Jesulius Foundation, Finland. No mention of COI.	N=60 patients undergoing hip arthroplasty	Mean age: 69 years; 16 males, 44 females	Post-op intrathecal fentanyl infusion (120µg/24 hour) vs. intrathecal morphine infusion (200µg/24 hour) vs. intrathecal morphine bolus (200µg)	24 hours	"The number of patients given IM administered opioid was larger in fentanyl infusion (18 patients) than in morphine infusion (8 patients) ($p < 0.01$). The IM opioid was requested sooner in fentanyl group (18 patients, mean 480 min) after the intrathecal injection than in morphine bolus group (13 patients, mean 786 min) ($P < 0.01$). Patients in morphine bolus had significantly higher incidence of urinary bladder catheterization than the other two groups. Nausea and pruritus occurred equally often in all three groups."	"Intrathecal infusion of fentanyl at 5 pg/h, instituted together with bupivacaine spinal block, was inadequate for postoperative analgesia after hip surgery in elderly patients. Intrathecal morphine (200 µg) as a single dose or as a continuous infusion provided better analgesia, and the quality of analgesia after the two modes of administration was similar for the first 18 h."	Fentanyl infusion (without bolus) is less effective in this population than morphine infusion.
Grace 1994 (score= 7.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by a grant from the Department of Health and Social Services for Northern Ireland. No mention of COI.	N=90 patients undergoing hip replacement	Mean age: 66.3 years; 42 males, 48 females	IT bupivacaine vs. IT bupivacaine with morphine sulfate (0.5mg) vs. IT pethidine (0.75mg/kg) and clonidine (75µg)	4, 6, 10 hours	Pethidine-clonidine (PC) anesthesia comparable in quality with that obtained with conventional isobaric bupivacaine. PC was associated with greater hypotension. PC inferior to bupivacaine with morphine. Incidence of side effects did not differ between groups.	"The combination did not offer any major advantage over conventional agents. The greater incidence or hypotension and the lack of additional analgesia suggest the technique is not indicated for routine use."	May be useful in rare occasions when a patient is allergic to bupivacaine.

Harsten 2014 (score= 7.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by institutional grants from Hasslehom Hospital and Lund University. No COI.	N=118 patients with osteoarthritis scheduled for total hip arthroplasty.	Mean age: 72.5 years; 59 males, 59 females	Group 1: Received general anaesthesia (GA) with target-controlled infustion of remifentanil and propofol (n=60) vs Group 2: Received intrathecal bupivacaines pinspinal anaesthesia (SA)	6, 10, 24, and 48 hours post-op, 6 month follow-up after procedure	Average length in hospital stay was 26h in GA group in comparison with 30h in SA group(p=0.004). Patients in the GA group had lower dizziness scores than the SA group (p<0.001). 26 subjects in SA group were able to walk 5m at 6h post-op in comparison with 56 in GA group (p=0.008).	"general anaesthesia resulted in a more favourable recovery profile compared with spinal anaesthesia"	Data suggest general anesthesia was better than spinal anesthesia for a slightly shorter LOS, less nausea and dizziness & better orthostatic function
Dobryd njov 2005 (score= 6.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Orebo County Council. No mention of COI.	N=60 patients undergoing hip arthroplasty	Mean age: 65 years; 41 males, 19 females.	Group B-R: Received bupivacaine and ropivacaine 1mg/ml, plus 1ml sterile saline (n=20) vs Group B-RC: Received bupivacaine and ropivacaine 1mg/ml, plus 1ml sterile saline, plus 10µg/ml clonidine (n=20) vs	24 hours post-procedure	Duration of anesthesia, analgesia and motor block were longer in Group BC-RC compared to Groups B-R and B-RC (P<0.02). Postoperatively, both VAS score on movement and PCA-morphine consumption were higher in Group B-R than in Groups B-RC and BC-RC (P<0.01). The arterial pressure and heart rate in Groups B-RC and BC-RC were significantly lower than in Group B-R at 10—24 and 15—24 h, respectively, after spinal injection.	"Low-dose intrathecal clonidine provided a better quality of anesthesia and longer lasting analgesia. Epidural clonidine-ropivacaine infusion resulted in imporovedpost-operative analgesia but was associated with a moderate decrease in blood pressure."	Short term intervention. Data suggest low dose intrathecal clonidine resulted in better anesthetic quality as well as longer lasting anesthesia. Epidural clonidine with ropivacaine provided good post-operative analgesia but mildly depressed blood pressure.

						Group BC-RC: bupivacaine and ropivacaine 1mg/ml, plus 15µg/ml clonidine (n=20) *all patients received spinal anesthesia with 3.5ml of plain bupivacaine				
D'Ambrosio 2015 (score= 6.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by the University of Foggia, Italy. No COI.	N=32 patients scheduled for major orthopedic surgery	Mean age: 75.4 years; 15 males, 17 females	Group A: received sufentanil 1mcg/h plus levobupivacaine 0.125%-1 ml/h (n=16) vs Group B: received sufentanil 1mcg/h plus 0.0625%-2 ml/h (n=16)	48h post-op	Median VAS score in Group A was lower than in Group B at 1hr post-op (8 vs 16; p<0.05). Median VAS score in Group A was lower than in Group B at 4hrs post-op (11 vs 18; p<0.05). There were no significant differences between groups for postoperative joints mobility post-op	"Levobupivacaine at a dose of 1.25mg/h administered by CSA provides good quality analgesia independent of concentration and solution volume in patients undergoing total knee hip replacement."	Short follow up (96 hours.) Data suggest levobupicaine (1.25 mg/hr) via CSA is an appropriate dose for good analagesia in total joint arthroplasties.
McNamee 2002 (score= 6.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee	RCT	Sponsored by AstraZeneca Pharmaceuticals Ltd. No	N=66 patients scheduled for total hip arthroplasty	Mean age: 66.5 years; 43 males, 23 females	Group R: Received spinal anesthesia with 3.5ml of plain ropivacaine 5mg/ml	24h, once at 14-21 days post-surgery	Median duration of sensory block at the T10 dermatome was longer in the bupivacaine group: 3.5h compared with 3.0h in the ropivacaine group (p<0.0001). Median time of onset of sensory block at T10 dermatome was 2 min in both	"Intrathecal administration of either 17.5mg plain ropivacaine or 17.5mg plain bupivacaine was well tolerated and an adequate block for total hip arthroplasty was	Ultra short trial with no long term follow-up. Data suggest ropivacaine led to a more rapid sensory and motor function recovery otherwise comparable efficacy.

	Arthroplasty		mention of COI.			(n=32) vs. Group B: Received spinal anesthesia with 3.5ml of plain bupivacaine 5mg/ml (n=34)		groups (p-value not given, results not statistically significant).	achieved in all patients. A more rapid postoperative recovery of sensory and motor function was seen in Group R compared with Group B."	
Gentili 1996 (score= 6.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=40 patients undergoing hip surgery	Mean age: 63 years; 29 males, 11 females	Intrathecal morphine (0.2mg) vs. clonidine (75µg) in combination with bupivacaine spinal anesthesia (15mg) for hip surgery	12, 24 hours	All in morphine group, and 5 in clonidine group had bladder distension at 12 hours. At 24 hours, present in 7 and 1 patient in morphine and clonidine groups, respectively ($p < 0.001$). Naloxone given in 16 of morphine and 1 clonidine group. Catheter placed in 1 and 6 in morphine and clonidine groups respectively ($p < 0.001$).	"We conclude that spinal clonidine impaired bladder function to a lesser extent than morphine."	No description provided on methodology of measuring bladder distension. Study did not include any measures for symptomatic distension.
Fournier 2002 (score= 6.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=45 patients for elective total hip arthroplasty using continuous spinal anaesthesia.	Mean age: 77.67 years; 24 males, 21 females	Group 1: Received 7.5 µg sufentanil alone. (n=15) vs Group 2: Received 7.5 µg sufentanil and 200 µg epinephrine (n=15) vs Group 3: Received 7.5 µg sufentanil	24 hours	Time to a pain score of <3 was 6 min in Group 1, vs 6 min in Group 2, and 5 min in Group 3. Time to the lowest pain score was 7 min in Group 1, vs 8 min in Group 2, and 8 min in Group 3. Adverse effects and analgesic requirements during the first 24h were similar. No P-Values were given for the results.	"After total hip replacement, all three analgesic regimens gave good analgesia with comparable onset and duration of action, and minor adverse effects."	Short follow-up of 24 hours. Data suggest comparable efficacy between all 3 groups with a trend towards a slightly shorter onset and longer duration in the sufentanil-clonidine group.

						and 30 µg clonidine in 2ml normal saline (n=15)				
Fogarty 1995 (score= 6.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship. COI: Fogarty and Milligan both received DHSS research grants.	N=60 patients undergoing elective total hip replacement	Mean age: 65.5 years; 37 males, 23 females	Intrathecal diamorphine 0.75mg vs. intrathecal morphine 1.0mg	2, 4, 6, 8, 10 ,12, 24 hours	The cumulative post-operative morphine consumption diverged within 4 hours post-operatively with higher consumption in diamorphine group and remained throughout 24-hour observation period (graphic representation). Cumulative morphine consumption was 13.0±14.25 vs. 5.8±7.56mg. Adverse effects not demonstrated.	"This study demonstrated that in the doses used intrathecal morphine provided superior postoperative analgesia to that after intrathecal diamorphine with no increase in side effects."	Data suggest similar efficacy for post-operative pain scores between both groups, but significantly less additional IV morphine requirements occurred in the IT morphine group ($p<0.05$).
Hooda 2006 (score= 6.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of COI or sponsorship.	N=90 patients over the age of 60 years scheduled to undergo open surgical repair of hip fractures under spinal anaesthesia.	Mean age: 70 years; 55 males, 35 females	Group 1: Received 4mg of 0.5% hyperbaric bupivacaine and 20µg fentanyl (n=30) vs Group 2: Received 5mg of 0.5% hyperbaric bupivacaine and 20µg fentanyl (n=30) vs Group 3: Received 6mg of 0.5% hyperbaric	Every 10 minutes until two-segment regression, and then every 20 minutes until recover to S2 dermatome	Mean time to achieve max sensory blockade was similar in all groups ($p>0.05$). Significantly intense motor blockade was achieved in 3 patients from Group 1, 13 patients from Group 2, and 22 patients from Group 3 ($p<0.05$). Mean duration of motor block was 64min in Group 1, 67min in Group 2, and 70min in Group 3 ($p>0.05$). Hypotension was observed in 0 patients from Group 1, 4 patients from Group 2, and 10 patients from Group 3 ($p<0.05$).	"5 mg intrathecal bupivacaine with 20mg fentanyl provides reliable and satisfactory sensory and motor blockade for hip surgery in elderly patients. The 6 mg dose of bupivacaine is associated with significant hypotension."	Data suggest the 5 mg of intrathecal bupivacaine plus 20 mg fentanyl provides good motor and sensory blockade for hip surgery but 6 mg of bupivacaine is associated with increased hypotension.

						bupivacaine and 20µg fentanyl (n=30)				
Maurer 2003 (score= 6.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=68 patients undergoing total hip replacement surgery	Mean age: 72.1 years; 30 males, 35 females	Continuous spinal anesthesia and post-operative analgesia vs. single-shot spinal anesthesia	24 hours	"From 3 hours postoperation, VAS score were significantly lower in the continuous spinal anesthesia group than in the single-shot spinal anesthesia group (P<0.05). Mean arterial pressure dropped less in the continuous vs. single shot group during induction (P<0.05). Postoperative nausea and vomiting was lower in continuous group (P<0.05)."	"Continuous spinal anesthesia/analgesia is a very practicable method providing better postoperative analgesia and better hemodynamic stability during anesthesia induction than SPA followed by morphine PCA analgesia after total hip replacement surgery."	Results suggest continuous spinal anesthesia provides advantages over single shot anesthesia with PCA analgesia.
Strebel 2004 (score= 6.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=75 patient scheduled for elective hip or knee arthroplasties	Mean age: 62 years; 36 males, 39 females	Group 1: Received 0.5% bupivacaine, 18mg, plus saline (n=20) vs Group 2: Received 0.5% bupivacaine, 18mg, plus clonidine 37.5µg (n=17) vs Group 3: Received 0.5% bupivacaine, 18mg, plus	15 min intervals for the first hour post-op. 1 hr intervals for the first 8 hrs post-op. 4 hr intervals from 8h to 24h	Duration of the sensory block was increased in patients receiving intrathecal clonidine: 288min in Group 1, 311min in Group 2, 325min in Group 3, and 337min in Group 4 (estimated parameter for dose 0.23[95%C.I.-0.05–0.50], no p-value). Time until the first request for rescue analgesia for pain was: 295min in Group 1, 343min in Group 2, 381min in Group 3, and 445min in Group 4 (estimated parameter for dose 1.02 [95% confidence interval 0.59–1.45] no p-value).	"[S]mall doses of intrathecal clonidine (≤ 150µg) significantly prolong the anesthetic and analgesic effects of bupivacaine in a dose-dependent manner and that 150µg of clonidine seems to be the preferred dose, in terms of effect versus unwarranted side effects, when prolongation of spinal anesthesia is desired."	Short intervention. Data suggest the addition of small doses of intrathecal clonidine (≤ 150µg) to isobaric bupivacaine prolongs spinal anesthesia in a dose-dependent manner.

						clonidine 75µg (n=18) vs Group 4: Received 0.5% bupivacaine, 18mg, plus clonidine 150µg (n=20)	post-op.			
Souron, 2003 (score= 5.5)	Intrathecal Anesthesia	RCT	No mention of sponsorship or COI.	N= 53 ASA physical status I–II patients with advanced osteoarthritis of the hip scheduled for primary unilateral hip arthroplasty	Mean age: 67.2 years; 21 males, 32 females.	Group 1 (n=27) was given local anesthesia and then had a spinal needle enter the L4-L5 space and had 0.1 mg of morphine administered with 1 mL saline over 15 sec vs group 2 (n=26) was given local anesthesia and then a psoas block was done to give 1.5 mA, 2Hz, and 0.1 msec perpendicularly. 25 mL ropivacaine	Every 30 min for 2 hrs, then every 6 hours until 48 hrs.	Group 1 used less morphine in PACU 1.07 vs 4.38mg, during first 24 hr 0.56 vs 9.42mg, and during first 48 hr 1.67 vs 12.5md ($p<0.05$). More patients received morphine during first 24 hr in group 2 ($p<0.05$).	"0.1 mg intrathecal morphine administration provides better postoperative analgesia than single-shot psoas compartment block after primary hip arthroplasty for analgesia."	Data suggests 0.1 mg intrathecal morphine better than psoas compartment block after primary hip arthroplasty for analgesia.

						was given when there was negative blood aspiration.				
Garner 2017 (score= 5.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship. No COI.	N=46 patients who underwent hip arthroscopy	Mean age: 32.5 years; 25 males, 21 females	LAI Group: Received local anesthetic infiltration for pain management (n=20) vs FICB Group: Received fascia ilica compartment block for pain management (n=26) All patients received paracetamol 1g and diclogenac 75mg, as well as IV morphine	1, 3, 6, and 24 hours after procedure	The study was terminated early because of patient recruitment introducing bias in the primary outcome measure. Severity of pain in the FICB was higher during the first hour post-op in comparison with LAI (p=0.02). FICB was associated with more adverse effects, such as nausea and vomiting (no p-value given).	"LAI provided a better analgesia after arthroscopic surgery of the hip in comparison with FICB and was also associated with reduced consumption of opioids and a lower rate of side effects."	Study terminated early due to patient recruitment biasing the primary outcome measure. Short term follow-up (24 hours). Data suggest LAI was better than FICB and was associated with less adverse events and decreased opioid consumption.
Johnson 1992 (score= 5.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Medical Faculty, Linköping University, Linköping, Sweden, the County	N=30 patients undergoing major hip surgery	Mean age: 69.3 years; 17 males, 13 females	IT bupivacaine (20 mg) vs. IT bupivacaine + IT morphine (0.3 mg) vs. IT bupivacaine (20mg) + IT morphine (0.3mg) + IV	8, 12, 24 hours	"There was no statistical difference in ventilation between the three groups pre-operatively, 8 and 24h."	"Naloxone infusion seemed to reduce the risk of developing respiratory depression from the use of postoperative opioids. Furthermore, one third of the elderly had a poor response to hypoxemia before surgery."	Study suggests intrathecal morphine had no effect on ventilatory function in population that 1/3 had hypoxemia prior to surgery.

			Council of Öhergötland, Sweden, and the Meda AB, Göteborg, Sweden. No mention of COI.			naloxone infusion				
Wang 2014 (score= 5.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by National Institute of Health, Bethesda. No mention of COI.	N=62 patients scheduled for total hip arthroplasty with spinal anesthesia.	No mention of mean age or gender.	Group 1: Receive d13.5 mg hyperbaric bupivacaine with spinal saline (n=8) vs Group 2: 13.5 mg hyperbaric bupivacaine with 2 mg preservative-free ketorolac (n=49)	2 days, 8 weeks, and 6 months	2 patients in Group 1 compared with 2 patients in 2 patients in Group 2 experienced hypersensitivity near surgical wound (p-value not given).	"Our results suggest single spinal dose of ketorolac does not substantially reduce acute surgical pain, and is thus unlikely to reduce the risk of persistent incisional pain."	Sparse methods. Unequal group sizes (8 vs 49). Data suggest lack of efficacy but baseline data missing.
Reay 1989 (score= 5.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=60 patients undergoing total hip or total knee replacement	Mean age: 67.4 years; no mention of sex.	Intrathecal bupivacaine + diamorphine 0.25mg or 0.5mg vs. bupivacaine anesthesia	4, 8, 12, 24 hours	Duration of analgesia measured by time from injection to first administration of post-operative analgesic significantly greater in both intrathecal diamorphine groups ($p < 0.001$), but not different between the two diamorphine groups. Analgesic requirements in first 24 hours were significantly different between control and both	"Small intrathecal doses of diamorphine provide good postoperative analgesia for periods up to 24 h and that 0.25mg is as effective as 0.5 mg. Although there was no evidence of late respiratory depression, the frequency of adverse effects, in particular urinary retention, nausea	Baseline differences present, method details sparse.

								intervention groups (p, 0.001), but not between diamorphine groups.	and vomiting, was high in both groups receiving intrathecal diamorphine."	
Fredrickson 2015 (score= 4.5)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	Sponsored by Auckland Medical Research Foundation. One or more of the authors benefited personally or professionally from this project.	N=50 patients undergoing hip replacement	Mean age: 62.8 years; 21 males, 29 females	Group 1: Received spinal anesthesia (n=23) vs. Group 2: Received continuous lumbar plexus blockade (n=27)	24 hours post-procedure.	Block placement time was shorter for the spinal group, 5 vs 7 minutes (p=0.01). Worst pain on movement/ mobilization during not statistically significant between groups (p-value not given). Patients in the lumbar plexus block group were given more rescue morphine than spinal group (median 4mg vs 0mg; p<0.001). Median pain score was 5/10 in lumbar plexus block group compared with 0/10 in spinal group (p<0.001).	"[C]ompared to continuous lumbar plexus blockade, spinal anaesthesia incorporating adjunctive intrathecal morphine did not result in statistically significant difference in worst pain on movement/ mobilization during the first 24 hours, although it was associated with better analgesia in the post-anaesthesia care unit"	Short trial. Data suggest spinal anaesthesia combine with adjunctive intrathecal morphine was better than continuous lumbar plexus block
Celik 2013 (score= 4.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=60 patients scheduled to undergo hip surgery	Mean age: 57 years; 37 males, 23 females	Group 1: Received spinal anesthesia with 0.5% bupivacaine 12.5mg and fentanyl 10µg, total 2.6 ml (n=30) vs Group 2 Received spinal anesthesia with 0.5% levobupivacaine 12.5mg and fentanyl	5-10 minute intervals for 60 min post-op	Times to motor block development was shorter in Group 1 at 5 minutes (p=0.001), 10 minutes (p=0.007) and 15 minutes (p=0.009). Motor block was observed in 29 patients in Group 1 and 19 patients in Group 2 at 5 min (p<0.01). After 15 min, full motor block developed in all patients in Group 1 and 4 patients in Group 2 (p<0.001).	"We consider that levobupivacaine may be a good alternative to bupivacaine, particularly in surgical procedures where less motor block development is desired."	Short follow-up time. Data suggest comparable efficacy but levobupivacaine may be preferable in surgeries where less motor block development is preferred.

						10µg, total 2.6 ml (n=30)				
Niemi 1994 (score= 4.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=55 patients scheduled to undergo hip arthroplasty	Mean age: 68.5 years; 12 males, 28 females	Continuous intrathecal morphine (8.3µg/hour) vs. epidural catheter (200µg/hour +0.25 % bupivacaine 4ml/hour) for hip arthroplasty	24 hours	Spinal vs. epidural: need for additional opioids – number of patients: 9/20 vs. 4/20; number of doses: 17 vs. 5; time to first IM oxycodone (mean, minute): 716±SD 271 vs. 1082±SD 377.	"The combined spinal-epidural technique for post-operative pain relief was technically more often successful than a continuous spinal catheter technique after hip arthroplasty. Because of technical problems and the frequent occurrence of side effects, spinal opioid therapy via intrathecal catheters cannot be recommended for pain control after hip arthroplasty."	There were high rates of technical problems not reported in other studies.

Evidence for the Use of Tropisetron for Control of Adverse Effects of Spinal Opioid Anesthesia

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Pitkanen 1993 (score= 7.0)	Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty	RCT	No mention of sponsorship or COI.	N=54 patients undergoing hip or knee surgery	Mean age: 68.1 years; 15 males, 39 females	Tropisetron 5mg (5-HT3-receptor antagonist) vs. saline placebo in patients undergoing intrathecal bupivacaine (0.5%)/ morphine (0.3mg) block	24 hours	No significant differences found between number of patients experiencing nausea/ vomiting for tropisetron (17/11) vs. saline (20/13). No significant differences in	"Tropisetron has no effect on postoperative nausea, emesis, or pain control in patients who underwent spinal anesthesia with bupivacaine and morphine."	Negative study.

						for lower extremity surgery		pain relief or consumption of analgesic medications between the two groups.		

Evidence for the use of Spinal – Naloxone for Control of Respiratory Depression

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Naloxone, respiratory insufficiency, respiratory depression narcan, evzio, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 42 articles in PubMed, 546 in Scopus, 374 in CINAHL, 19 in Cochrane Library, 14700 in Google Scholar, and 0 from other sources. Zero articles met the inclusion criteria.

Evidence for the use of Nicardipine to Induce Hypotension

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: nicardipine, hypotension, hypertension, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 174 articles in PubMed, 91 in Scopus, 40 in CINAHL, 7 in Cochrane Library, 11900 in Google Scholar, and 2 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 3 articles considered for inclusion, 1 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for the Use of Nicardipine

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Bernard 1991 (score= 5.0)	Treatment of Adverse Anesthesia Effects	RCT	Sponsored by University of Nantes Institutional Grant Program. No mention of COI.	N=24 patients undergoing total hip arthroplasty	Mean age: 66.5 years; 12 males, 12 females	Deliberate hypotension with nicardipine (n=12) vs. nitroprusside during hip replacement surgery (n=12)	No mention of follow-up.	Nicardipine vs. nitroprusside mean±SEM: blood loss (ml):415±70 vs. 428±120. Average time to reach hypotension was 7 minutes.	"Nicardipine can be used to induce deliberate hypotension during total hip arthroplasty but results in cumulative effects that persist after the discontinuation of infusion, with a possibility of postoperative hypotension."	Nicardipine not an ideal agent to control arterial blood pressure.

Evidence for Use Tai Chi:

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Tai Chi, Tai Ji; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 7 articles in PubMed, 318 in Scopus, 5 in CINAHL, 1 in Cochrane Library, 229 in Google Scholar, and 15 from other sources. We considered for inclusion 3 from PubMed, 4 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 4 from other sources. Of the 13 articles considered for inclusion, 5 randomized trials and 6 systematic studies met the inclusion criteria.

Evidence for use of Gait Training:
A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: gait training, gait rehabilitation; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 9 articles in PubMed, 14in Scopus, 0 in CINAHL, 0 in Cochrane Library, 2490 in Google Scholar, and 8 from other sources. We considered for inclusion 4 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 8 from other sources. Of the 15 articles considered for inclusion, 12 randomized trials and 2 systematic studies met the inclusion criteria.

Evidence for use of Canes and Crutches

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: ambulatory devices, canes, shoe insoles, crutches, braces, orthotics; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthrosis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 327 in Scopus, 7 in CINAHL, 57 in Cochrane Library, 68 in Google Scholar, and 7 from other sources. We considered for inclusion 0 from PubMed, 8 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 7 from other sources. Of the 17 articles considered for inclusion, 0 randomized trials and 17 systematic studies met the inclusion criteria.

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Appendix 3 – Low Quality Studies

Post-Operative Exercise

Graham 1968 (score=2.5)										Suggests early weight bearing may be superior.
Abrami 1964 (score=2.0)										Few details. Outcome measure is crude, which likely reduces power.
Tsauo 2005 (score=2.0)										Small sample size and sparse details. Suggests home PT superior to education.

Baker 1991 (score=0.5)										Methods sparse; unclear if RCT; quasi-randomization. Intervention not described in detail. Analyses of strength included 12 of 18 subjects. Unclear if other analyses partial or complete. If an RCT, suggests treadmill superior to conventional training.
Binder 2003 (score=0.5)										Abstract suggests intensive exercise program may be superior.
Lauridsen 2002 (score=0.5)										Suggests compliance problems may be important.

FAI: Surgery

Van Houcke 2017 (score=3.5)	Navigated Cam Resection									Small sample. Data suggest navigated cam resection for FAI is effective but this procedure has higher radiation exposure and prolonged positioning time.

Hamstring and Hip Flexor Strains: PATS

Author Year (Score):	*Category:*	*Study type:*	*Conflict of Interest:*	*Sample size:*	*Age/Sex:*	*Comparison:*	*Follow-up:*	*Results:*	*Conclusion:*	*Comments:*
Engebretsen 2008 (score=3.5)										Prevention study of soccer players and applicability to other patients unclear. Multiple injuries and exercises combined with inadequate reporting of any one weak. Thus validity and utility for any one outcome unclear. Compliance so low (19-29%) that results appear without meaning.
Hartig 1999 (score=3.5)										Randomization by company. Baseline differences in hamstring flexibility (intervention more flexible 41.7±8.3 vs. 45.9±6.5, p <0.001), indicate randomiza-tion failure, potential fatal study flaw.

Laudner 2016 (score=3.5)	Stretching									Data suggest both stretching groups improved ROM compared to controls.
Askling 2003 (score=3.5)	Hamstring Training (eccentric)									Data suggest strength training with eccentric overload had fewer hamstring injuries with increased strength and speed.
Gabbe 2006 (score=3.0)	Eccentric Exercise									High dropout (lack of participation) rate. Data suggest eccentric exercise can prevent hamstring injuries in Australian football players and is better than stretching exercise.
Rey (score=3.0)	Nordic Exercise									Data suggest a 10-week Nordic hamstring training routine developed eccentric hamstring strength.

Cibulka (score=2.5)	Mobilizing exercise									Very small sample. Data suggest those with hamstring muscle strains treated by correcting SJ dysfunction have a greater increase in peak torque.

Engebretsen 2008 (score=3.5)										Prevention study of soccer players and applicability to other patients unclear. Multiple injuries and exercises combined with inadequate reporting of any one weak. Thus validity and utility for any one outcome unclear. Compliance so low (19-29%) that results appear without meaning.
Light 2010 (score=3.5)										Data suggest use of US as a standalone diagnostic test for groin hernias is not effective but has value when used in conjunction with clinical data.
Palumbo 2014 (score=3.5)										Data suggest US may be beneficial to identify occult hernias after an accurate clinical examination

Franneby 2007 (score=3.5)										Data suggest the IPQ may be useful after groin repair in assessing chronic groin pain
Drew 2016 (score=3.5)										Data suggest 0-degree adduction test resisted at the ankles is best for detecting musculus AL-related groin pain
Groin Strain: Exercise Therapy										
Hölmich 2010 (score=3.5)										Usual care bias, cluster randomization. Data suggest a trend forwards preventing group injury in the interventional group.
Engebretsen 2008 (score=3.5)										Prevention study of soccer players and applicability to other patients unclear. Multiple injuries and exercises combined with inadequate reporting of any one weak. Thus validity and utility for any one outcome unclear. Compliance so low (19-29%) that

										results appear without meaning.
Jensen 2012 (score=3.5)										Small sample. Data suggest 8 weeks of eccentric strengthening resulted in significant hip-adduction strength.

Regional Blocks

Graham 2008 (score=3.5)										Open label trial with sparse participant characteristics. Short term follow-up (8 hours). Data suggest comparable efficacy.
Becchi 2008 (score=3.5)										48 hour follow-up. Data suggest interventional group required less pain medication and had lower pain scores compared to controls.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Dolasetron										
Eberhart 2004 (score= 7.5)	Droperidol/ Dolasetron	RCT	No mention of sponsorship. No COI.	N=240 patients undergoing vitreoretinal surgery	Mean age: 63.0 years; 146 males, 158 females	Dolasetron Group: received 1 syringe with 12.5 mg of dalestron diluted to 10 ml and 1 syringe with 10 ml of saline (n=80) vs Droperidol Group: received 1 syringe containing 10µg/kg droperidol diluted to 10 ml and 1 syringe with 10 ml of saline (n=80) vs Comination Group: received 1 syringe with 10µgkg^{-1} droperidol and 1 syringe with 12.5 mg Dolasetron both diluted to 10 ml (n=80) vs Placebo: received 2 syringes containing 10ml of saline (n=80)	24 hours	Severity of PONV differed between the groups ($p<0.0001$). Antiemetic efficacy was better in combination group compared with dolasetron alone at reducing severity of PONV ($p=0.003$). Droperidol and combination group reduced number of patients with PONV compared to placebo ($p=0.0006$, $p<0.0001$, respectively). Least incidence of PONV in the combination group (18.4%) compared to dolasetron group (39.5%) and the droperidol group (28.4%).	"[L]ow-dose droperidol (10 µg · kg^{-+1}) can still be recommended, due to its favorable effectiveness in preventing PONV after vitreoretinal surgery. Dolasetron (12.5 mg) is not an equivalent substitute for droperidol but can be used for supplementation in high-risk patients."	Data suggest low dose droperidol reduced post-operative N&V post vitectomy compared to both dolasetron and placebo.
Graczyk 1997 (score= 7.0)	Dolasetron	RCT	Sponsored by Hoechst Marion Roussel. No Mention of COI.	N = 635 female patients scheduled for outpatient laparosc	Mean age: 32 ± 7 years; 0 males, 635 females.	Received 12.5mg of dolasetron mesylate salt, with dolasetron base of 9.3mg (n=159) vs	Follow up continuous over the first 24 hours	The proportion of complete responders was greater than 50% for each does of dolasetron and 30.6% with the placebo ($p<0.0003$). Approximately 45% of patients given dolasetron	"Dolasetron was an effective and well tolerated preventative treatment for PONV resulting from laparoscopic gynecologic surgery."	Data suggest dolasetron superior to placebo in the prevention of pony and there was little differences observed between efficacy of the 3 dolasetron doses.

				opic gynecologic surgery		Received 25mg of dolasetron mesylate salt, with dolasetron base of 18.5mg (n=157) vs Received 50mg of dolasetron mesylate salt, with dolasetron base of 37mg (n=162) vs Received placebo saline solution (n=157) *All dolasetron dosages and placebo were given as a single IV dose approximately 15 minutes before the cessation of anesthesia for a minimum of 30 seconds		required or requested escape antiemetic medication compared with approximately 70% placebo patients over 24 hours (p<0.0003). Dolasetron-treated patients had lower median VAS scores compared with placebo-treated patients (p<0.0357). Patient satisfaction with dolasetron was greater than with the placebo (p=0.0131).		
Kovac 1997 (score= 7.0)	Dolasetron	RCT	Sponsored by Hoechst Marion Roussel. No mention of COI.	N = 620 patients scheduled to undergo outpatient surgery *surgery procedure types	Mean age: years; 106 males, 514 females.	Received 12.5mg of dolasetron (n=130) vs Received 25mg of dolasetron (n=119) vs Received 50mg of dolasetron (n=124) vs	Follow up continuous over the first 24 hours	Complete response rates for all dolasetron doses was 35% in 12.5mg group, 28% in 25mg group, 29% in 50mg group, 29% in 100mg group, and 11% in placebo group (P<0.05). More patients in the 25mg (12%) and 100mg (13%) groups experienced no nausea (5%) (p<0.05).	"[A] 12.5mg dose of intravenous dolasetron, a new serotonin-receptor blocker, was significantly more effective than placebo in treating establisted postoperative nausea and vomiting (PONV)"	Data suggest that even at the lowest dose (12.5mg), dolasetron was significantly better than placebo for the treatment of PONV.

				primarily included gynecologic, orthopedic, eyes/nose/ throat, and breast		Received 100mg of dolasetron (n=126) vs Received placebo saline solution (n=121) *all dosages were administered intravenously & supplied in identical 10-mL ampules				
Korttila 1997 (score= 6.0)	Dolasetron/Ondansetron	RCT	Sponsored by Hoechst Marion Roussel. No mention of COI.	N = 514 patients undergoing surgical procedures with general anesthesia	Mean age: 43 years; 30 males, 484 females	Received placebo saline solution (n=128) vs Received 25mg of Dolasetron (n=127) vs Received 50mg of Dolasetron (n=129) vs Received 4mg of Ondansetron (n=130) *all dosages administered as single IV treatment	Follow up continuous over the 24 hours post operation.	36% of placebo patients received rescue medication compared with 29% of dolasetron 25mg (p=0.026) and 19% of dolasetron 50mg (p=0.002) and 24% in ondansetron group (p=0.034). Rate of complete response was 49% for placebo and 71% for 50mg of dolasetron (p<0.001). Complete response was 51% for dolasetron 25mg (p=0.001) and 64% for ondansetron (p=0.298).	"When given at induction of anesthesia, 50mg intravenous dolasetron is equivalent to 4mg ondansetron and superior to 25mg dolasetron and placebo for the prevention of PONV. All treatments were safely administered and well tolerated."	Also in ondansetron 27% of participants received rescue medication Single IV treatment to 3 groups. Data suggest 50mg dolasetron equivalent to 4mg ondansetron and both are better than 25mg dolasetron and placebo for PONV prevention.
Diemunsch 1997	Dolasetron	RCT	No mention of sponsors	N = 337 adult patients undergoi	Mean age: 40 ± 11 years; 18 males,	Received 12.5mg of dolasetron (n=66) vs	Continuous follow up over 24 hours	Complete responses were achieved by 24.2% in the 12.5mg group, 27.7% in the 25mg group, 37.3% in	"Single doses of dolasetron mesilate iv, given after the first episode of PONV, were both effective and safe in	Data suggest a single IV does of dolasetron significantly reduces PONV and all doses of dolasetron were better than placebo.

(score= 5.5)			hip or COI.	ng surgery with general anesthesia	319 females.	Received 25mg of dolasetron (n=65) vs Received 50mg of dolasetron (n=67) vs Received 100mg of dolasetron (n=68) vs Received placebo saline solution (n=71) *all dosages and placebo administered intravenously		the 50mg group, and 25% of 100mg group, and 11.3% in the placebo group (p<0.05). When compared with patients who received the placebo, patients who received 12, 25, 50mg of dolasetron had longer times to the first use of antiemetic medication (p<0.05). Likelihood of being nauseated was 45.1% in placebo group and 32.5% among patients who received dolasetron (p=0.06).	this adult patient population."	
Granisetron										
Taylor 1997 (score= 8.5)	Granisetron	RCT	No mention of sponsors hip or COI.	N = 519 ASA physical status I, II and III patients experiencing postoperative vomiting or severe nausea within 4 hours of the end of surgery.	Mean age: 47.5 years; 55 males, 464 females.	Patients received medication in syringes with 5.0ml of 0.9% sodium chloride solution and one of the following: 0.1 mg granisetron group (N = 128) vs 1.0 mg granisetron group (N = 133) vs 3.0 mg granisetron group (N = 125) vs no addition placebo group (N = 133)	Follow up at 30 minutes, 1, 2, 6 and 24 hours after administration of study drug.	Percent of patients with no vomiting after 6 hours was 53.1% in the 0.1 group, 57.9% in the 1.0 mg group, 60.0% in the 3.0 mg group and 26.3 in the placebo group showing a linear trend in efficacy for the granisetron dose (P<0.001).	"Granisetron was significantly more effective than placebo in all groups. Further studies in specific subgroups may be warranted."	Data suggest all doses of IV granisetron better than placebo and a statistically significant dose response linear relationship was observed in the granisetron groups.

Wilson 1996 (score= 7.5)	Granisetron	RCT	No mention of sponsorship or COI.	N = 527 ASA class I-III patients that were undergoing elective open cholecystectomy, open gynaecological procedures, or vaginal hysterectomy.	Mean age: 47.4 years; 20 males, 507 females.	Patients received an IV injection over 30 seconds with the same amount of fluid with granisetron doses: 0.1 mg granisetron group (N = 132) vs 1.0 mg granisetron group (N = 134) vs 1.0 mg granisetron group (N = 128) vs 0 mg granisetron placebo group (N = 133)	Follow up at 1, 2, 6 and 24 hours after operation.	Total control of nausea and vomiting at 0-6 hours was 31.6% for the placebo vs 63.4 for the 1.0 mg group (p<0.001 vs placebo) and 54.7 for the 3.0 mg group (p<0.001 vs placebo).	"In conclusion, granisetron proved effective in theprevention of PONV. Our data do not suggest that increasing the dose from 1.0 mg to 3.0 confers any additional benefit; a dose-response plateau appeared to have been reached. We conclude, therefore, that 1.0 mg is the optimum dose."	Data suggest 1.0 mg IV granisetron was effective in decreasing PONV and reducing the number of rescue medications given postoperatively.
Fujii 2004 (score= 7.0)	Granisetron/ Ramosetron	RCT	No sponsorship or COI.	N = 90 ASA physical status I female patients undergoing general anesthesia for breast surgery.	Mean age: 52.7 years; 0 males, 90 females	At the end of surgery patients intravenously received 3 mg granisetron (N = 30) vs 0.3 mg ramosetron (N = 30) vs placebo (N = 30) identical syringes were prepared for each drug. Identity of the placebo was not given.	Follow up continuous by nurses over the 48 hours post operation.	Percent of patients with emetic symptoms 0-24 hours after anesthesia was 47% in the placebo group vs 17% in the granisetron group (p=0.013 vs placebo) and 10% in the ramosetron group (p=0.002 vs placebo). At 24-48 hours, emetic symptoms were seen in 27% of the granisetron group vs 7% in the ramosetron group (p=0.039)	"In conclusion, ramosetron is more effective than granisetron for preventing PONV within a 48-hour postanesthetic period in women undergoing general anesthesia for breast surgery."	Data suggest ramosetron better than granisetron for prevention of PONV.
Lee 2002 (score= 6.5)	Granisetron/ Ramosetron	RCT	No mention of sponsors	N = 113 ASA physical status I or II	Mean age: 39.6 years; 9 males,	At the end of surgery patients intravenously received 20 µg/kg granisetron (N = 30)	Follow up over the 24 hours after surgery every	Overall PONV during the 24 hours occurred in 61% of placebo patients vs 30.6% of Granisetron patients (p=0.008). No	"Only granisetron 20 µg/kg was superior to placebo for the prevention of PONV after thyroidectomy."	Data suggest granisetron 20 µg/kg superior to ramosetron and placebo for reducing incidence of PONV.

			hip or COI.	patients undergoing general anesthesia for elective thyroidectomy.	104 females	vs 4 µg/kg ramosetron (N = 30) vs placebo of no additive (N = 30) All three were diluted with NS to 10 ml.	30 minutes and 6 hours.	other significant within or between group differences were found.		
Naguib 1996 (score= 6.0)	Ondansetron / Tropisetron/ Granisetron/ Metoclopramide	RCT	No mention of sponsors hip or COI.	N=132 patients	Mean age: 37.4 years; 24 males, 108 females.	Ondansetron group: patients received 4 mg of ondansetron intravenously (n=29) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=25) vs. Granisetron group: patients received 3 mg of granisetron intravenously (n=25) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously (n=24) vs. Placebo group: patients received NS IV (n=29).	Follow up at 1, 4, 9, 12, 18, and 24 hours after recovery from anesthesia.	65.6% patients in ondansetron group, 52% in granisetron, 48% in tropisetron, 29.2% in metoclopramide, and 27.6% in placebo were absent from emesis 24 hours after surgery. Ondansetron prophylactic antiemetic treatment showed lower incidence of postoperative nausea and vomiting than that in placebo and metoclopramide groups (p=0.02). On the other hand, Ondansetron group indicated longer first rescue antiemetic recovery times than that in metoclopramide and placebo groups (p<0.01).	"Ondansetron, when given prophylactically resulted in a significantly lower incidence of PONV than metoclopramide and placebo. Metoclopramide was ineffective"	Data suggest use of prophylactic ondansetron resulted in a significant reduction of PONV episodes, Metoclopramide was ineffective.
Metaxari 2011 (score= 6.0)	Ondansetron / Granisetron/ Tropisetron	RCT	No mention of sponsors hip. The authors	N=245 female patients experienced partial or total	Mean age: 46.7 years; 0 male, 245 females,	Placebo group: patients received 0.9% of NS intravenously (n=62) vs. Ondansetron group: patients received 4	Follow up at baseline on admission to the PACU and the following 1, 6, 12, and 18 hours	The incidence of postoperative nausea and vomiting in placebo group (44%) was higher in Post-anesthesia care unit (PACU) than that in granisetron group (24%),	"Among the female patients of this study undergoing thyroid surgery, granisetron 3 mg provided the best prophylaxis from PONV. Ondansetron 4 mg was	Data suggest granisetron better than ondansetron as effects lasted longer than 6 horus and study suggests tropisetron ineffective.

			declared no COI.	thyroide ctomy.		mg of ondansetron intravenously (n=61) vs. Granisetron group: patients received 3 mg of granisetron intravenously (n=61) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=61).		and ondansetron group (32%), but lower than tropisetron group (50%), and the difference between granisetron and tropisetron groups was significant (p=0.0081, odds ratio=0.31, 95%CI=0.13 to 0.73). 12 to 18 hours after surgery, the incidence of nausea dropped to 34% in placebo, 2% in granisetron, 14% in ondansetron, 17% in tropisetron group; and the difference between granisetron and placebo was significant (p=0.0001).	equally effective, but its action lasted only 6 h, whereas tropisetron 5 mg was found ineffective."	
Ondansetron										
Joo 2016 (score= 8.5)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship. No COI.	N = 89 patients who were ASA physical status I and II undergoing strabismus surgery with general anesthesia.	Mean age: 34.6 years; 41 males, 48 females.	Group one was given 2 mL normal saline as a placebo (n=31), group two was given 4 mg ondansetron (n=26), and group three was given 0.3 mg ramosetron (n=32) through an IV post-op.	Follow up at 2, 24, and 48 hours post-op.	The incidence in nausea at 2 hrs was 9.4% in ramosetron group, 34.6% in ondansetron, and 45.2% in placebo group ($p<0.05$). The incidence in nausea at 24 hrs was 3.1% in ramosetron group, 19.2% in ondansetron, and 22.6% in placebo group ($p<0.05$). Patients given ramosetron had a verbal rating scale for satisfaction of 8.11 at 2 hrs and 8.50 at 24 hrs vs placebo group that had 6.84 at 2 hrs and 7.25 at 24 hrs vs ondansetron group that had 7.28 at 2	"[…] the incidence of postoperative nausea was high until 24 h after strabismus surgery. Therefore, prevention of postoperative nausea during the 24 h after strabismus surgery is crucial. Ramosetron had an antiemetic efficacy greater than that of ondansetron or placebo during the first 24 h after strabismus surgery in adult patients."	Data suggests ramosetron is superior to ondansetron for preventing PONV in strabismus surgery patients.

								hrs and 7.27 at 24 hrs (p<0.05).		
Tang 1998 (score= 8.0)	Ondansetron	RCT	Sponsored by grant from Glaxo Wellcome Inc. and the Ambulatory Anesthesia Research Foundation of Dallas. No mention of COI.	N=164 females undergoing laparoscopic procedures	Mean age: 37.7 years; 0 males, 164 females	Group A: received saline in both syringes (n=39) vs Group B: received ondansetron 2 mg in both syringes (split-dose)(n=38) vs Group C: received ondansetron 4 mg in syringe1 and saline in syringe 2 (n=39) vs Group D: received saline before induction and ondansetron 4 mg at the end of surgery (n=40)	24 hours	Incidence of nausea at 24 hours was 88% in group A, 81% in group B, 79% in group C, and 46% in group D. Incidence of vomiting at 24 hours was 50% for group A, 38% for group B, 43% for group C, and 15% for group D. Group D experienced the lower incidence of nausea and compared to placebo.	"In summary, ondansetron 4 mg IV administered at the end of surgery is more effective in preventing PONV in the PACU, as well as in the postdischarge period, than ondansetron administered as a single dose before the induction of anesthesia or as a split dose at the induction and the end of surgery. When ondansetron is administered at the end of surgery, it seems to improve the patients' quality of life after outpatient laparoscopic surgery."	Data suggest timing the administration of ondansetron 4mg IV just before the conclusion of surgery is best in preventing PONV.
Vallejo 2012 (score= 8.0)	Ondansetron/Aprepitant	RCT	Sponsored by Merck Healthcare, Whitehouse Station, N.J., Department of Anesthesiology, Magee-Womens Hospital, Pitts-burgh,	N=150 ambulatory plastic surgery patients	Mean age: 44.5 years; 10 males, 140 females	Group A: received 40 mg of oral aprepitant plus 4 mg of intravenous ondansetron (given 2 hours prior to surgery (n=75) vs Group B: received oral placebo plus intravenous 4 mg of ondansetron(n=75)	1-48 hours	Incidence of vomiting was 29.7% for group B compared to 9.3% in group A (p=0.003, relative risk=31.3%, 95% CI 14.3-69.0). Nausea scores were lower in group A (median=5) compared to group B (median=8) (p=0.014).	"Aprepitant decreases postoperative vomiting and nausea severity and is a useful drug when used in combination with other antiemetics for prevention of postoperative nausea and vomiting. In patients undergoing plastic surgery procedures in which vomiting might be deleterious for surgical outcome, the addition of aprepitant would be especially useful."	Data suggest the addition of aprepitant to ondansetron.

			Pa. No COI.							
Kovac 1999 (score= 8.0)	Ondansetron	RCT	Sponsored by Glaxo Wellcome, Inc., Research Triangle Park, NC. No mention of COI.	N=2199 patients to undergo outpatient surgical procedures	Mean age: 36.1 years; 640 males, 1559 females	Ondansetron: received 4 mg ondansetron preoperatively and 4 mg postoperatively (n=214) vs Placebo: received 4 mg ondansetron preoperatively and placebo saline postoperatively (n=214)	2, 24 hours	Of the 2199 patients, only 428 patients experienced PONV. Incidence of complete response (no emesis, no rescue meds, no study withdrawal) was 34% in ondansetron group compared to 43% in placebo group (p=0.342).	"[P]atients for whom preoperative prophylaxis with ondansetron 4 mg IV is not successful in preventing the occurrence of emetic symptoms, administration of a repeat IV dose of ondansetron 4 mg postoperatively does not appear to offer additional control of PONV."	Data suggest if original dosing of ondansetron 4 mg IV is unsuccessful in reducing PONV, a subsequent dose does not provide efficacy.
Egerton - Warburton 2014 (score= 8.0)	Ondansetron / metoclopramide	RCT	Sponsored by the Australasian college of emergency medicine Morson Taylor award and the Southern health emerging researcher fellowship. No COI.	N = 258 emergency department patients with undifferentiated nausea and vomiting	Median age: 42 years; 89 males, 169 females.	Ondansetron group: patients received 12 ml of syringes contained 4 mg ondansetron intravenously (n=87) vs. Metoclopramide group: patients received 22 ml of syringes contained 20 mg metoclopramide intravenously (n=88) vs. Placebo group: patients received 12 ml of syringes contained 0.9% of saline solution (n=83).	Follow up at baseline and 30 minutes	The difference of primary outcome in this study visual analog scale (VAS) rating in ondansetron group was 27 mm (95%CI=22 to 33 mm), and that in metoclopramide group was 28 mm (95%CI=22 to 34 mm), and that in placebo group was 23 mm (95%CI=16 to 30 mm). The difference among the three groups was not statistically significant (p>0.05).	"There was a trend toward greater reductions in VAS ratings and a lesser requirement for rescue medication in the antiemetic drug groups, but differences from the placebo group did not reach significance."	Data suggest lack of efficacy of both study drugs compared to placebo but a trend towards less rescue medication being needed.
Grover 2009	Ondansetron	RCT	No mention	N=103 patients	Mean age: 42.3	I-ondansetron group: patients	No mention of follow-up.	The intravenous and oral ondansetron groups	"There was no significant difference between oral and	Data suggest comparable efficacy between both IV and oral

(score= 8.0)			of sponsors hip or COI.	experien ced general anaesthe sia.	years; 22 males, 81 females.	received 4 mg of ondansetron intravenously (n=33) vs. O-ondansetron group: patients received 8 mg of ondansetron orally (n=34) vs. Placebo group: patients received disintegrating placebo tablets orally (n=36).		indicated less incidence of vomiting or nausea after surgery than placebo groups (p<0.05), but no significant difference was found between intravenous and oral ondansetron groups. In addition, the two intervention groups indicated higher overall patients satisfaction scores than that in placebo group (p=0.01).	intravenous groups. In conclusion, orally disintegrating ondansetron was as efficacious as intravenous ondansetron in the peri-operative phase and may be a viable option for prophylaxis of emesis in day care surgery."	ondansetron for preventing PONV.
Moens 1997 (score= 7.5)	Ondan setron	RCT	No mention of sponsors hip or COI.	N=208 patients who had major gynecolo gical or elective abdomin al surgery	Mean age: 47±14.6 years; 64 males, 142 females	Ondansetron: received 4 mg intravenous ondansetron (n=104) vs Placebo: received placebo (n=102)	1-24 hours	Incidence of PONV was observed in 29% of ondansetron group compared to 42% in the placebo group (p=0.03). Maximum nausea score was lower in ondansetron group compared to placebo (1.5 vs 2.3, p=0.03).	"Ondansetron was well tolerated, with no side effect being reported as a significant problem."	Data suggest ondansetron is well tolerated and decreases episodes of PONV.
Barrett 2011 (score= 7.5)	Ondan setron /Meto clopra mide/ Prome thazin e	RCT	No mention of sponsors hip or COI.	N=163 patients presenti ng to the ED with undiffere ntiated nausea	Mean age: 32 years; 52 males, 111 females	Ondansetron: received 4 mg ondansetron in a 2 mL syringe (n=42) vs Metoclopramide: received 10 mg metoclopramide in 2 mL syringe (n=43) vs Promethazine: received 12.5 mg promethazine in 2 mL syringe so that the dose was actually 6.25 mg/mL (n=45) vs Placebo: received isotonic	30 minutes	No difference was detected between groups for antiemetic efficacy (Kruskal-Wallis Test, p=0.16). Median VAS score reduction compared to ondansetron group were -8mm (95% CI -18.5-3) for metoclopramide, -7mm (95% CI -21-5.5) for promethazine, and 6 mm (95% CI -7-20) for saline. More than 40% of patients showed need for additional antiemetics compared to 22% of	"Our study shows no evidence that ondansetron is superior to metoclopramide and promethazine in reducing nausea in ED adults. Early study termination may have limited detection of ondansetron's superior nausea reduction over saline."	Trial investigation of nausea only. Did not evaluate vomiting. Data suggest ondansetron not superior to either metoclopramide or promethazine.

						sodium chloride solution placebo (n=41)		patients in metoclopramide group.		
Jellish 1997 (score= 7.5)	Ondansetron / droperidol	RCT	Partially sponsored by Glaxo Wellcom Inc. in Research triangle park in North Carolina. No mention of COI.	N= 120 healthy or with mild disease patients who meet the anesthesiologists (ASA) physical status I and II.	Mean age: 42 years; 58 males, 62 females.	Group 1: patients received placebo (n=40) vs. Group 2: patients received 4 mg of ondansetron intravenously (n=40) vs. Group 3: patients received 25 mg of droperidol intravenously (n=40).	Follow up at 3, 5, 15, and 30 minutes as well as continuous follow up over the 24 hours post operation.	Frequency of incidences of vomiting over the 24 hours post recovery was 18% in the ondansetron group vs 32% in the placebo group ($p<0.05$). Droperidol was 25% ($p<0.05$ vs placebo), not statistically different than ondansetron ($p>0.05$).	"Ondansetron 4 mg Iv is as effective as droperidol and better than placebo in preventing nausea and vomiting in patients undergoing middle ear surgery."	Data suggest comparable efficacy with the benefit of ondansetron providing better relief of nausea with less reported sedative and dysphoric adverse effects.
Wilson 2001 (score= 7.5)	Metoclopramide/ ondansetron	RCT	No mention of sponsorship or COI.	N=232 patients experience laparoscopic cholecystectomy with general anesthesia.	Mean age: 43 years; 49 males, 183 females.	Metoclopramide group: patients received 30 ml syringe contained 10 mg intravenous metoclopramide 24 hours before surgery (n=72) vs. Ondansetron group: patients received 30 ml syringe contained 4mg intravenous ondansetron 24 hours before surgery (n=78) vs. Placebo group: patients received 30 ml syringe contained normal intravenous saline 24 hours before surgery (n=82).	Follow-up at baseline, 24 hours.	Patients in metoclopramide group indicated 32% incidence of nausea, patients in ondansetron group indicated 45%, and patients in placebo group indicated 44%. After anesthesia care, patients in metoclopramide group indicated 8% incidence of vomiting, patients in ondansetron group indicated 4%, and patients in placebo group showed 22% (Metoclopramide vs Placebo, $p=0.03$; Ondansetron vs Placebo, $p<0.01$) .	"Prophylactic administration of metoclopramide or ondansetron significantly reduces the incidence of postoperative vomiting for laparoscopic cholecystectomy, but neither drug was found to be significantly more effective than the other. Metoclopramide is a more cost-effective treatment."	Data suggest comparable efficacy compared to placebo.

Kim 2009 (score= 7.5)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship or COI.	N= 162 female patients undergoing elective gynecological surgery.	Mean age: 41.7 years; 0 males, 162 females.	Group one was given 0.3 mg ramosetron (n=54) vs group two given 8 mg ondansetron vs group three given saline via IV. All treatments were diluted to 4 mL and given 30min pre-op.	Continuous observation for 24hrs post-op	The incidence of nausea at 24 hrs was 50% in ramosetron group, 44% in ondansetron, and 69% in placebo group ($p<0.05$). The incidence of vomiting at 24 hrs was 17% in ramosetron group, 20% in ondansetron, and 44% in placebo group ($p<0.05$). The visual analogue scale score for nausea during 0-24 hrs was 28 for ramosetron group, 28 for ondansetron and 48 for placebo group ($p<0.05$). Rescue antiemetics were used for 15% of ramosetron group vs 41% of placebo group ($p<0.05$). No significant difference between ramosetron vs ondansetron.	"[…] ramosetron 0.3 mg i.v. and ondansetron 8 mg i.v. were equally effective in decreasing incidence of PONV and severity of nausea in high-risk female patients during the first 24 h after surgery."	Data suggests comparable efficiency between ramosetron 0.3mg IV and ondansetron 8mg IV.
Ryu 2010 (score= 7.5)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship or COI.	N= 120 patients who were ASA physical status I or II and undergoing Laparoscopic cholecystectomy (LC) with general	Mean age: 46.3 years; 59 males, 61 females.	Group O4 was given 4mg ondansetron (n=40), group O8 was given 8mg ondansetron (n=40), and group R was given 0.3mg ramosetron via IV at the end of the surgery.	Continuous observation for 48 hrs post-op.	At 2 hrs post-op, 80% of group O8 and group R had complete response vs 58% in group O4 ($p=0.04$). At 2-24 hrs post-op, 90% of group O8 and group R had complete response vs 76% in group O4 ($p=0.09$). At 24-48 hrs post-op, 98% of group O8 and group O4 had complete response vs 100% in group R ($p=0.36$). In the first 2 hrs, antiemetics were used in 20% of patients in O8 and R group vs 42.5% in O4 group ($p=0.04$).	"[…] ramosetron 0.3 mg was more effective than ondansetron 4 mg and as effective as ondansetron 8 mg for the prophylaxis of PONV in patients undergoing laparoscopic cholecystectomy."	Data suggests 0.3mg IV ramosetron is comparable in efficiency to 8mg ondansetron and both are better than 4mg ondansetron for prevention of PONV post LC.

				anesthesia.						
Bilgin 2010 (score= 7.0)	Ondansetron /Metoclopramide/ Dexamethasone	RCT	Sponsored by Department of Anesthesiology and Reanimation (Turkey). No mention of COI.	N=160 patients undergoing elective gynecological surgery	Mean age: 43.2 years; 0 males, 160 females	Group D: received IV 8 mg dexamethasone (n=40) vs Group O: received 4 mg ondansetron IV (n=40) vs Group M: received 10 mg metoclopramide (n=40) vs Group P: received 0.9% saline (n=40)	Follow up at 0-24 hours	Incidence of PONV was 5% in group D, 0% in group O, 5% in group M, and 5% in group P. More patients required rescue antiemetics in placebo group compared to other groups ($p<0.05$).	"Prophylactic IV dexamethasone 8 mg significantly reduces the incidence of PONV in patients undergoing gyneco-logic surgery. At this dosage, dexamethasone is as effective as ondansetron 4 mg, and metoclopramide 10 mg, and is more effective than placebo."	Data suggest comparable efficacy between all 3 study drugs compared to placebo.
Paech 1995 (score= 7.0)	Ondansetron / droperidol	RCT	Sponsored by women's and infants' health-King Edward memorial hospital foundation. No mention of COI.	N=259 female patients experienced abdominal gynecological surgery.	Mean age: 48.7 years; 0 male, 259 females.	Group O: patients received 8 mg of ondansetron intravenously during the surgery (n=83) vs. Group D: patients received 2.5 mg of droperidol intravenously during the surgery (n=89) vs. Group P: patients received saline placebo intravenously (n=87).	Follow up continuous over the 24 hours post operation with specific follow up at 6 and 24 hours.	Ondansetron and droperidol groups indicated effectiveness to prevent vomiting after surgery, compared to placebo group (Odds ratio=0.4; 95%CI=0.2 to 0.9). The incidence of vomiting in droperidol group was the lowest (25%), and that in ondansetron group was the second lowest (30%), and that in placebo group was 44% ($p<0.05$).	"Although, compared to placebo, both droperidol and ondansetron administered intraoperatively reduced vomiting after major abdominal gynaecological surgery, the incidence during the first 24 postoperative hours was very high in all groups."	Data suggest comparable efficacy between ondansetron and droperidol for reducing PONV.
Jellish 1998 (score= 7.0)	Ondansetron / droperidol	RCT	Partially sponsored by Glaxo Welcome Inc. No mention of COI.	N= 120 healthy or with mild disease patients who meet the anesthes	Mean age: 42 years; 58 males, 62 females.	Placebo group: patients received placebo (n=40) vs. Ondansetron group: patients received 4 mg of ondansetron intravenously (n=40) vs. Droperidol group:	Follow up at 3, 5, 15, and 30 minutes as well as continuous follow up over the 24 hours post operation.	66% patients in ondansetron group, 36% in droperidol group, and 33% in placebo group showed nausea after surgery, and the difference of incidence of nausea among the groups was not significant	"Ondansetron 4 mg intravenously is as effective as droperidol and better than saline solution in preventing nausea and vomiting in patients undergoing otologic surgery. No cost advantage as determined by lower use	Data suggest comparable efficacy between ondansetron and droperidol.

				iologists (ASA) physical status I and II.		patients received 25 mg of droperidol intravenously (n=40).		(p>0.05). The incidence of vomiting also showed no significant difference among the three groups: 16% in ondansetron group vs. 9% in droperidol group vs. 20% in placebo group.	of rescue antiemetics or shorter postanesthesia care unit times was noted after ondansetron therapy."	
Kovac 1996 (score= 7.0)	Ondansetron	RCT	Sponsored by Glaxo Research Institute, Glaxo-Wellcome, Inc., Research Triangle Park, NC. No mention of COI.	N=468 males undergoing ambulatory surgery	Mean age: 37 years; 468 males, 0 females	Ondansetron: received 4 mg ondansetron mixture with hydrochloride dehydrate 2mg/mL (n=226) vs Placebo: received citrate buffer (n=242)	24 hours	Patients with a complete response was greater for ondansetron group compared to placebo (p=0.05). Ondansetron group showed more patients without nausea compared to placebo (p<0.05). Rescue antiemetics were given to 19% of placebo compared to 11% in ondansetron.	"In conclusion, this study demonstrated that ondansentron 4 mg IV has antiemetic efficacy when given prophylactically to male outpatients. In addition, those patients experiencing PONV perceived its effects as having an equal or greater debilitating effect as the aftereffects of surgery."	Data suggest ondansetron significantly reduces PONV compared to placebo.
Khalil 1994 (score= 6.5)	Ondansetron	RCT	Sponsored by a grant from Glaxo Research Institute (Research Triangle Park, NC). No mention of COI.	N=589 females undergoing elective outpatient surgical procedures	Mean age: 32.8 years; 0 males, 589 females	Ondansetron 1mg: (n=145) vs Ondansetron 4 mg: (n=148) vs Ondansetron 8 mg: (n=144) vs Placebo: (n=152)	2-24 hours	Patients with complete responses were greater for ondansetron 4 mg and 8 mg compared to placebo. Patients in the 8 mg ondansetron group showed less nausea compared to placebo.	"This study indicates that ondansetron is a safe and effective prophylactic antiemetic for women who have outpatient surgery under nitrous oxide opioid-based general anesthesia."	Data suggest either the 4 mg or the 8 mg ondansetron treated patients were more likely to experience a complete response (no emesis) compared to placebo.
Singla 2010 (score= 6.5)	Ondansetron /Casopitant	RCT	Sponsored by GlaxoSmithKline, Research	N=702 pre or post-menopausal	Mean age: 38.9±8.23 years; 0 males,	Group 1: received ondansetron 4 mg and 0 mg casopitant (n=140) vs Group 2: received	24 hours	A complete response was achieved by 37.9% of group 1, 55.7% of group 2, 60% of group 3, and 57.1% of group 4	"Compared with ondansetron alone, the casopitant and ondansetron combination results in superior emesis prevention	Data suggest addition of casopitant augments effects of ondansetron on PONV.

			Triangle Park, NC, and Endo Pharmaceuticals, Chadds Ford, PA. No COI.	patients undergoing gynecologic surgical procesure or laparoscopic cholescystectomy	702 females	ondansetron 4 mg and 50 mg casopitant (n=140) vs Group 3: received ondansetron 4 mg and 100 mg casopitant (n=140) vs Group 4: received ondansetron 4 mg and 150 mg casopitant (n=140) vs Group 5: received 0 mg ondansetron and 150 mg casopitant (n=142)		compared to 40% in group 5. All dose levels achieved efficacy, so smallest dose showed greater complete response 59.3% compared to ondansetron alone 40%. Group 5 showed 50% complete response.	during the first 24 h postoperatively in female patients with known risk factors for postoperative nausea and vomiting."	
Kovac 1992 (score= 6.5)	Ondansetron	RCT	No mention of sponsorship or COI.	N=580 female patients experienced gynecological laparoscopy.	Mean age: 30.4 years; 0 male, 580 females.	Ondan group 1: patients received 1 mg of ondansetron intravenously before anesthesia (n=139) vs. Onda group 2: patients received 4 mg of ondansetron intravenously before anesthesia (n=152) vs. Onda group 3: patients received 8 mg of ondansetron intravenously before anesthesia (n=147) vs. Placebo group: patients received citrate buffer as placebo	Follow up at baseline (30 min before drug administration), 1 min after drug administration, 10, 20, 30, 60, and 120 min post anesthesia and continuous follow up over the 24 hours post anesthesia.	More patients who took 4 mg (40% patients) or 8 mg (60% patients) of ondansetron groups showed no symptoms of nausea than the other two groups (27% patients in placebo group, 30% in 1 mg ondansetron group) ($p<0.05$). 4 mg of ondansetron was recommended as the optimal dose to prevent nausea or vomiting.	"Ondansetron 4 mg was found to be the optimal prophylactic i.v. dose for female outpatients over the entire 24 hpostoperative period. Higher doses may offer an added benefit in some patients, such as those with a history of nausea and vomiting following general anaesthesia."	Data suggest ondansetron at any dose was more effective than placebo with the 4 mg IV dose being thought to be optimal.

						before anesthesia (n=142).				
Morris 1998 (score= 6.5)	Ondansetron / metoclopramide	RCT	No mention of sponsorship or COI.	N=1074 female patients experienced vaginal hysterectomy or gynecological surgery under general anaesthesia.	Mean age: 46 years; 0 male, 1074 females.	Ondansetron group: patients received 4 mg of ondansetron intravenously before anesthesia (n=468) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously before anesthesia (n=462) vs. Placebo group: patients received normal citrate buffered saline before anesthesia (n=117).	Follow up continuous over the 24 hours post operation.	44% patients in ondansetron group, 37% in metoclopramide group, 25% in placebo indicated no episodes of emesis, and the difference was significant (p<0.001). Less patients in ondansetron group requested rescue antiemetics, compared to patients in placebo and metoclopramide groups (p<0.001).	"In summary, this study supports published findings that ondansetron is a well-tolerated agent and is a more effective antiemetic for preventing post-operative nausea and emesis than placebo"	Data suggest ondansetron better than metoclopramide for effectively reducing episodes of PONV.
Alexander 1997 (score= 6.5)	Ondansetron / metoclopramide	RCT	No mention of sponsorship or COI.	N=124 ASA 1 and 2 patients received major lower limb orthopedic surgery.	Mean age: 56 years; 48 males, 76 females.	Placebo group: patients received placebo orally 1 hour before laparoscopy (n=40) vs. Metoclopramide group: patients received 10 mg of metoclopramide orally 1 hour before the surgery (n=42) vs. Ondansetron group: patients received 8 mg of ondansetron orally 1 hour before the surgery (n=42).	Follow up at 4, 8, 12, 16, 20, and 24 hours.	The three groups indicated no significant difference for the incidence of nausea (p=0.77). 12% patients in ondansetron group, 31% in metoclopramide group, and 25% in placebo group indicated nausea and vomiting before the surgery, and the difference was significant (p=0.035).	"We conclude that oral premedication with ondansetron 8 mg was superior to metoclopramide 10 mg and placebo in preventing postoperative nausea and vomiting following major orthopaedic surgery in patients given epidural opioid analgesia."	Data suggest 8 mg ondasetron is better than 10 mg metoclopramide and both better than placebo for reducing PONV. Also, the use of rescue medications was lower in the ondansetron group.
Chen 1998	Ondansetron /	RCT	No mention of	N=78 patients experien	Mean age: 62.5 years; 29	Ondansetron group: patients received 4 mg of ondansetron	Follow up at 14 predefined time intervals	Patients in ondansetron group (81%) indicated greater incidence of	"Prochlorperazine is associated with superior	Data suggest prochlorperazine better than ondansetron for control of PONV.

(score=6.5)	Prochlorperazine		sponsorship or COI.	ced hip or knee replacement surgery.	males, 49 females.	hydrochloride intravenously (n=37) vs. Prochlorperazine group: patients received 10 mg of prochlorperazine intravenously (n=41).	over the 48 hours post operation.	nausea than patients in prochlorperazine group (56%), and the difference was significant (Odds ratio=3.4; 95%CI=1.2 to 9.4; p=0.04). The ondansetron group (49%) also showed higher incidence of vomiting than prochlorperazine group (32%) (Odds ratio=2.0; 95%CI=0.8 to 5.0).	Efficacy and significant cost savings compared with ondansetron for the prevention of PONV in patients undergoing total hip and total knee replacement procedures."	
Wu 2000 (score=6.5)	Ondansetron / Droperidol	RCT	Sponsored by St. Michael's hospital health science research center in Toronto, Canada. No mention of COI.	N=160 female patients experienced laparoscopy.	Mean age: 32. 8 years; 0 male, 160 females.	Placebo group: patients received saline intravenously before surgery (n=38) vs. Droperidol group: patients received 1.25 mg of droperidol intravenously (n=38) vs. Ondansetron group: patients received 4 mg of ondansetron intravenously (n=37) vs. Combo group: patients received 1.25 mg of droperidol and 4 mg of ondansetron intravenously (n=39).	Follow-up at baseline, 30, 90, 150, and 210 minutes as well as 24 hours post operation.	Compared with placebo group, droperidol group was more effective to prevent postoperative nausea and vomiting (PONV) (p=0.006), same did ondansetron group (p=0.028) and combination group (p<0.001). No significant difference was found among the three treatment groups (p=0.093).	"The results of this study suggest that the combination of 4 mg ondansetron and 1.25 mg droperidol is more efficacious as a prophylactic anti-emetic than either agent alone during the 24 hr post-surgery. This additive effect may be due to the different mechanisms of action of ondansetron and droperidol."	Data suggest combining droperidol to ondansetron results in an addictive effective resulting in better PONV control.
Maestre 1997 (score=6.5)	Droperidol/ Ondansetron /Meto	RCT	No mention of sponsors	N=264 patients undergoing elective,	Mean age: 29.5 years; 119 males,	Control: received saline vs Metoclopramide: received 10 mg metoclopramide vs	12, 24 hours	Incidence of emetic episodes was 6% for all groups. Relative risk of PONV was 1.8 (95% CI 0.5-	"In conclusion, this study suggest that preoperative administration of metoclopramide, droperidol and two different doses of	Data suggest lack of efficacy for all drugs as none were better than placebo for preventing PONV after ambulatory surgery.

	chloprpamide		hip or COI.	outpatient surgery	144 females	Droperidol: received 1.25 mg vs Ondansetron: received 4 mg vs Ondansetron: received 2 mg. All groups were mixed with 0.9% sodium chloride solution to a final volume of 100 mL.		6.6) for ondansetron 4 mg group.	ondansetron are not superior to placebo for preventing PONV. Until more information becomes available, the key to judicious use of a prophylactic antiemetic should be the preoperative identification of patients who are at high risk of PONV."	
Kreisler 2000 (score= 6.5)	Droperidol/ Ondansetron /Promethazine	RCT	No mention of sponsorship or COI.	N=150 patients undergoing general anesthesia	Mean age: 48.3 years; 6 males, 25 females	Part 1: Droperidol: received 0.625 mg of droperidol IV (n=74) vs Placebo: received 0.625 mg saline (n=76)	24 hours	Greater number of patients suffered from vomiting and retching in the placebo group (p=0.008). Incidence of PONV was 6.8% in droperidol group compared to 40.8% in placebo (p<0.001). Delayed PONV was experienced by 22% of droperidol group compared to 32% in placebo (p=0.232).	"Droperidol, ondansetron, and promethazine were equally effective in treating established PONV, without significant differences in side effects or time to postanesthesia care unit discharge."	Data suggest comparable efficacy between droperidol, ondansetron and promethazine for PONV.
McKenzie 1993 (score= 6.5)	Ondansetron	RCT	Sponsored by Glaxo Inc., Research Triangle Park, NC. No mention of COI.	N=580 female patients undergoing gynecologic surgical procedures	Mean age: 30.4 years; 0 males, 580 females	Placebo: received 8 mL saline (n=139) vs Ondansetron 1: received 1 mg ondansetron hydrochloride dehydrate (2mg/mL-total 20mL through IV) (n=133) vs Ondansetron 4: received 4 mg (2mg/mL-total 20mL through IV) ondansetron	Follow up over the first 24 hours	Antiemetic efficacy was achieved in 62% of ondansetron 1, 76% in ondansetron 4, 77% in ondansetron 8 compared to 46% in placebo. Ondansetron 4 and 8 mg were more effective than placebo.	"In summary ondansetron given intravenously to prevent postoperative nausea and emesis was highly effective in both 4- and 8-mg doses in women having ambulatory surgery."	Pilot study. Data suggest ondansetron 8 mg IV consisting of two doses eight hours apart was superior to placebo regardless of prior history of prior exposure to general anesthesia and for PONV.

						(n=136) vs Ondansetron 8: received 8 mg (2mg/mL-total 20mL through IV) ondansetron (n=136)				
Rodrigo 1994 (score= 6.5)	Ondansetron	RCT	No mention of sponsorship or COI.	N=77 patients undergoing minor oral surgery	Mean age: 25 years; 32 males, 45 females	Ondansetron: received 4 mg in 2 mL (n=38) vs Placebo: received 2 mL saline (n=39)	Follow up at 1, 4, and 24 hours	Of the ondansetron group, 8 had nausea compared to 19 in the placebo group (X^2=6.47; p<0.05). Ondansetron group showed less vomiting compared to placebo (X^2=7.1 vs X^2=4.11; p<0.05). No patients in ondansetron group had rescue antiemetics compared to 6 in placebo (X^2=6.34; p<0.05).	"Nausea and vomiting in the first 24 hours was significantly less in the ondansetron group."	Data suggest ondansetron is significantly better than placebo in reducing the incidence of PONV.
Helmy 1999 (score= 6.5)	Ondansetron /Droperidol/ Metoclopramide	RCT	No mention of sponsorship or COI.	N=160 patients scheduled for laparoscopic cholecystectomy under total intravenous anesthesia	Mean age: 40 years; 35 males, 125 females	Ondansetron: received IV 4 mg ondansetron (n=40) vs Droperidol: received IV 1.25 mg droperidol (n=40) vs Metoclopramide: received IV 10 mg metoclopramide (n=40) vs Placebo: received single intravenous dose of general anesthesia (n=40)	Follow up at 1 hour, 4 hours, 24 hours	Incidence of nausea was lower in ondansetron (7.5%) compared to the other 3 groups (27.5% in both droperidol and metoclopramide, 42.5% in placebo; p<0.05). Incidence of vomiting was lower in the ondansetron group (7.5%) compared to 25% in droperidol, 22.5% in metoclopramide, and 47.5% in placebo (p<0.05).	"It is concluded that pre-anaesthetic intravenous ondansetron (4 mg) is superior to droperidol (1.25mg), metoclopramide (10 mg) and placebo as a prophylactic anti-emetic in patients undergoing laparoscopic cholecystectomy under TIVA, especially during the first 4 h. The prophylactic use of anti-emetic treatment is recommended in this setting."	Data suggest comparable efficacy between ondansetron, droperidol and metoclopramide compared to placebo in the first 4 hours post-operatively, but ondansetron was superior to all other groups for the period of 24 hours post-op.
McKenzie 1993	Ondansetron	RCT	Sponsored by Glaxo	N=544 females undergoi	Mean age: 30.4 years; 0	Ondansetron 1: received 1 mg ondansetron	Follow up over first 24 hours	The ondansetron groups showed 3-10% of patients having emesis after	"In summary, ondansetron given intravenously to prevent postoperative	Data suggest all ondansetron doses significantly more effective in decreasing PONV but the 4 mg

(score= 6.5)			Inc., Research Triangle Park, North Carolina. No mention of COI.	ng gynecological surgical procedures	males, 544 females	hydrochloride dehydrate (n=139) vs Ondansetron 4: received 4 mg ondansetron hydrochloride dehydrate (n=152) vs Ondansetron 8: received 8 mg ondansetron hydrochloride dehydrate (n=147) vs Placebo: received 8 mL saline to final volume of 20 mL (n=142)		discharge compared to 23% of placebo patients. Ondansetron 4- and 8-mg doses were more effective than placebo over the 24 hour period (p=0.017, p<0.001, respectively).	nausea and emesis was highly effective in both 4- and 8-mg doses in women having ambulatory surgery."	and 8 mg ondansetron doses well best.
Helmers 1993 (score= 6.5)	Ondansetron	RCT	Sponsored by Glaxo Group Research Limited, Greenford, Middlesex, United Kingdom. No mention of COI.	N=923 females requiring gynaecological surgery	Mean age: 42.7 years; 0 males, 923 females	Ondansetron 1: received 1 mg ondansetron hydrochloride dehydrate diluted to 20 mL in isotonic saline with citrate buffer (n=231) vs Ondansetron 8: received 8 mg ondansetron hydrochloride dehydrate diluted to 20 mL in isotonic saline with citrate buffer (n=228) vs Ondansetron 16: received 16 mg ondansetron hydrochloride dehydrate diluted to 20 mL in isotonic saline with citrate buffer (n=229) vs	Follow up at 1, 4, and 24 hours	Emesis was observed in 28% of ondansetron 1 group, 44% of ondansetron 8 group (p≤0.001), and 39% in ondansetron 16 mg (p<0.05) compared to 29% in placebo group. Nausea was observed in 26% of ondansetron 1 group, 31% in ondansetron 8 group (p<0.05), and 28% in ondansetron 16 group (p<0.05) compared to 20% in placebo group.	"In conclusion, patients undergoing gynaecological surgery are at high risk of experiencing postoperative emesis and nausea. The present study has shown that a greater proportion of these patients in both the 8 mg and 16 mg treatment groups experienced no emesis and no nausea than in the placebo group. In addition, the higher dose of ondansetron 16 mg, was not more effective than the 8 mg dose."	Data suggest both the 8 mg as well as the 16 mg dosages of ondansetron were effective in reducing PONV although no additional benefit was observed from the 16 mg ondansetron.

						Placebo: received isotonic saline with citrate buffer (n=235)				
Claybon 1994 (score= 6.5)	Ondansetron	RCT	No mention of sponsorship or COI.	N=2812 patients undergoing various outpatient surgical procedures	Mean age: 33 years; 422 males, 2390 females	Placebo: (n=129) vs Ondansetron 1: received 1 mg ondansetron (n=130) vs Ondansetron 4: received 4 mg ondansetron (n=119) vs Ondansetron 8: received 8 mg ondansetron (n=122)	Follow up from 0-2 hours, 2-24 hours	Ondansetron groups appeared more effective than placebo (p<0.05). Incidence of PONV was 39% in females and 27% in males. For females patients more patients in ondansetron 4 mg group had a complete response compared to ondansetron 1 mg (p=0.052). No significance was observed between ondansetron groups and placebo for male complete response (p=0.06).	"Overall, ondansetron 4mg is the optimal dose for the treatment of PONV and is well tolerated. Ondansetron 4 mg administered intravenously has the same systemic availability as 4 mg administered intramuscularly and the intramuscular route is less painful than with placebo."	Data suggest ondansetron, administered at any dose was superior to placebo for prevention of PONV. Data suggest 4 mg ondansetron was best dose.
Cholwill 1999 (score= 6.5)	Cyclizine/Ondansetron	RCT	No mention of sponsorship or COI.	N = 180 ASA I or II women undergoing day-case gynaecological laparoscopy.	Mean age: 31.1 years; 0 males, 180 women	Ondansetron group: Ondansetron 4mg IV (n=60) vs Cyclizine 50 mg IV (n=57) vs Placebo group: NS IV (n=58). all received this before induction of anesthesia	Follow up at 24 hours.	Moderate or severe nausea was reduced in both ondansetron and cyclizine (P=0.02 and P=0.001) when compared with saline. Requirement for escape antiemetic was also reduced in both ondansetron and cyclizine (P=0.04 and P<0.001). Patients with ondansetron and cyclizine suffered no PONV more when compared with placebo (31% and 33% vs 12%; P=0.02 and P<0.01).	"We would recommend that cyclizine should be considered for first-line antiemetic therapy for DL but that ondansetron may be an equally valid choice where a greater amount of tissue trauma is anticipated, such as with LS."	Data suggest comparable efficacy between both medications with fewer rescue medications required in the cyclizine group.
Fortney 1998 (score= 6.5)	Ondansetron /	RCT	Sponsored by Glaxo Wellcom	N=2061 outpatients experien	Mean age: 35.2 years; 244 males,	Placebo group: patients received normal saline less than 20 minutes	Follow up at baseline on admission to the	2 hours after surgery, higher number of patients in ondansetron (29%), droperidol group1 (29%)	"In summary, we showed ondansetron 4 mg, droperidol 0.625 mg, and droperidol 1.25 mg to be	Data suggest comparable efficacy and patient satisfaction between ondansetron and droperidol for prevention of PONV.

	Droperidol		e Inc. No mention of COI.	ced surgical procedure.	1817 females.	before anesthesia (n=518) vs. Droperidol group 1: patients received 0.625 mg of droperidol less than 20 minutes before anesthesia (n=518) vs. Droperidol group 2: patients received 1.25 mg of droperidol less than 20 minutes before anesthesia (n=510) vs. Ondansetron group: patients received 4 mg of ondansetron less than 20 minutes before anesthesia (n=515).	postanesthesia care unit (PACU), and the following 30, 60, 90, and 120 minutes. Addition follow up at 24 hours post discharge.	and droperidol group 2 (43%) indicated complete absence of nausea and vomiting, compared with placebo group (23%) (p<0.005). 24 hours after surgery, treatment groups still indicated higher proportion of patients who were absent from nausea, compared with placebo group (p<0.05); however, the differences among the three treatment groups was not significant (p>0.05).	superior to placebo for the relief of PONV in a study involving more than 2000 adults outpatients at high risk of PONV."	
Koivuranta 1997 (score= 6.5)	Ondansetron / Droperidol	RCT	Sponsored by Emil Aaltonen foundation of Finland. No mention of COI.	N=439 female patients experienced gynecological laparoscopy.	Mean age: 41.4 years; 0 male, 439 females.	Ondansetron group: patients received 8 mg of ondansetron intravenously during anesthesia (n=195) vs. Droperidol group: patients received 1.25 mg of droperidol intravenously during anesthesia (n=193) vs. Placebo group: patients received 10 ml of 0.9% sodium chloride solution intravenously	Follow up at 2 in the recovery room and 24 hours on the ward.	The incidence of nausea in placebo group (67%) was higher than that in ondansetron group (48%) and droperidol group (50%), and the difference was significant (p=0.02). Ondansetron group (18%) indicated lower incidence of vomiting than that in droperidol group (26%) (p=0.05) and placebo group (37%) (p=0.004).	"The efficacy of prophylactic ondansetron and droperidol in reducing postoperative nausea associated with laparoscopic surgery in female inpatients was similar, but ondansetron appeared to be slightly more efficient than droperidol in preventing vomiting."	Data suggest both drugs better than placebo but ondansetron best for PONV control.

						during anesthesia (n=51).				
Du Pen 1992 (score= 6.0)	Ondansetron	RCT	Sponsored by Glaxo Inc., Research Triangle Park, NC, USA. No mention of COI.	N=500 surgical patients	Mean age: 33.0 years; 447 males, 53 females	Placebo: (n=129) vs Ondansetron 1: received 1 mg ondansetron (n=130) vs Ondansetron 4: received 4 mg ondansetron (n=119) vs Ondansetron 8: received 8 mg ondansetron (n=122)	Follow up at 2, 24 hours	Complete response for each group after 2 hours was 57% in ondansetron 1 mg, 61% for ondansetron 4 mg, and 57% in ondansetron 8 mg compared to 30% in the placebo group. Complete response after 24 hours was 41% in ondansetron 1 mg group, 47% in ondansetron 4 mg group, and 47% in ondansetron 8 mg group compared to placebo in 15%. Mean nausea scores after 24 hours ranged from 1.4-1.7 for ondansetron groups compared to placebo 2.9.	"All doses of ondansetron were well tolerated. No clinically significant increases in laboratory parameters or alterations in haemodynamic stability occurred in the ondansetron groups compared to placebo. "	Data suggest all doses of ondansetron (1 mg, 4 mg, or 8 mg), all superior to placebo for preventing PONV.
Sung 1993 (score= 6.0)	Ondansetron	RCT	Sponsored by Glaxo, Inc., Research Triangle Park, NC. No mention of COI.	N=180 patients undergoing laparoscopic procedures	Mean age: 31.5 years; 0 males, 180 females	Ondansetron: received 8 mg ondansetron IV (n=89) vs Placebo: received IV saline (n=91)	Follow up from 0-24 hours	Of the ondansetron group, 62% patients showed a complete response compared to 40% of patients in the placebo group (p=0.005). Degree of nausea was lower in the ondansetron group compared to placebo.	"Ondansetron, infused IV before anesthesia induction, appears to be safe and effective when used in the prevention of postoperative nausea and emesis."	Pilot study. Data suggest ondansetron better than placebo for prevention of PONV.
Bodner 1991 (score= 6.0)	Ondansetron	RCT	Sponsored in part by a grant to the Division of Clinical Research	N=155 female outpatients scheduled to undergo diagnostic	Mean age: 31.0 years; 0 males, 71 females	Ondansetron: received 8 mg ondansetron IV (n=35) vs Saline: received placebo (n=36)	Follow up from 2-24 hours	Efficacy was achieved by 49% of ondansetron group compared to 8% of placebo. Of the ondansetron group 43% required rescue antiemetic compared to 86% of placebo group.	"In conclusion, ondansetron is an antiemetic drug that appears to be safe for treating acute postoperative nausea and vomiting. As ondansetron (8 mg IV) was only partially effective in treating postoperative emetic sequelae, further	Female population only and age of ondansetron patients younger than placebo group. Data suggest ondansetron significantly decreased nausea and vomiting over placebo. Additionally, ondansetron treated patients required half as much rescue medication.

			by Glaxo, Inc., Five Moore Drive, Research Triangle Park, NC. No mention of COI.	laparoscopy or laparoscopic tubal ligation					studies are needed to determine the optimal dose of ondansetron for both the treatment and prevention of emetic sequelae in the outpatient setting."	
Tang 1996 (score= 6.0)	Droperidol/ Ondansetron	RCT	No mention of sponsorship or COI.	N=161 females undergoing outpatient gynecologic surgery	Mean age: 29 years; 0 males, 161 females	Placebo: received saline (n=40) vs Droperidol 0.625: received 0.625 mg of droperidol (n=41) vs Droperidol 1.25: received 1.25 mg droperidol (n=40) vs Ondansetron: received 4 mg ondansetron (n=40)	Follow up over the first 24 hours	Incidence of emesis was lower in both droperidol and ondansetron groups compared to placebo ($p<0.05$). Incidence of nausea was only different between ondansetron and placebo ($p<0.05$).	"In summary, this study has demonstrated that droperidol 0.625 mg IV is as effective as ondansetron 4 mg IV in the prophylaxis of PONV in women undergoing outpatient gynecologic surgery."	Data suggest comparable efficacy between droperidol and ondansetron but droperidol is more cost effective at time of this article.
Choi, 2010 (score= 6.0)	Ramosetron/ Ondansetron	RCT	Sponsored by Asian Medical Center. No mention of COI.	N= 279 patients undergoing cardiac surgery who had continuous infusion of treatment with a PCA pump.	Mean age: 58.5 years; 169 males, 120 females.	Group P had 2 mL saline given post-op and 6 mL saline added to patient-controlled analgesia (PCA) pump (n=70) vs group O had 4 mg ondansetron given post-op and 12 mg ondansetron added to PCA pump (n=71) vs group R1 had 0.3 mg ramosetron given post-op and 6 mL saline added to PCA pump (n=70) vs group R2 had 0.3 mg ramosetron	Continuous observation for 48hrs post-op.	Incidence for PONV was 71% for group P, 46% for group O, 54% for group R1, and 35% for group R2 ($p<0.001$). Incidence of nausea was 46% for group O ($p=0.003$), 54% for group R1 ($p=0.036$), and 35% for group R2 ($p<0.001$) vs 71% for group P. Percentage of patients receiving rescue antiemetics was 34% in group O ($p=0.022$) and 29% in group R2 ($p=0.005$) vs 53% in group P.	"[…] a continuous infusion of ondansetron or ramosetron combined with PCA following a bolus dose at the end of surgery is an effective means of reducing the incidence of PONV during the first 48 h after cardiac surgery."	Data suggest adding ondansetron or ramosetron added to PCA decreases episodes of PONV.

						given post-op and 0.6 mg ramosetron added to PCA pump (n=68).				
Suen 1994 (score= 5.5)	Ondansetron	RCT	Sponsored by Glaxo Laboratories. No mention of COI.	N=210 female patients undergoing laparoscopic sterilization or diagnostic laparoscopy	Mean age: 34.7 years; 0 males, 204 females	Ondansetron: received 4 mg ondansetron in a total 10 mL volume with normal saline (n=102) vs Placebo: received normal saline 10 mL (n=102)	Follow up from 5-24 hours	Ondansetron showed fewer emetic episodes compared to placebo ($p<0.01$). Incidence of nausea was lower in ondansetron (median=1.6) compared to placebo (median=3.1) ($p<0.05$). Complete antiemetic response was achieved in 52% of ondansetron group compared to 27% in the placebo group.	"Ondansetron 4 mg was more effective than placebo in preventing postoperative nausea and vomiting throughout the 24 h after minor laparoscopic surgery."	Sparse details on randomization. Data suggest ondansetron 4 mg superior to placebo for preventing PONV.
Naguib 1996 (score= 6.0)	Ondansetron / Tropisetron/ Granisetron/ Metoclopramide	RCT	No mention of sponsorship or COI.	N=132 patients	Mean age: 37.4 years; 24 males, 108 females.	Ondansetron group: patients received 4 mg of ondansetron intravenously (n=29) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=25) vs. Granisetron group: patients received 3 mg of granisetron intravenously (n=25) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously (n=24) vs. Placebo group: patients	Follow up at 1, 4, 9, 12, 18, and 24 hours after recovery from anesthesia.	65.6% patients in ondansetron group, 52% in granisetron, 48% in tropisetron, 29.2% in metoclopramide, and 27.6% in placebo were absent from emesis 24 hours after surgery. Ondansetron prophylactic antiemetic treatment showed lower incidence of postoperative nausea and vomiting than that in placebo and metoclopramide groups ($p=0.02$). On the other hand, Ondansetron group indicated longer first rescue antiemetic recovery times than that in metoclopramide and placebo groups ($p<0.01$).	"Ondansetron, when given prophylactically resulted in a significantly lower incidence of PONV than metoclopramide and placebo. Metoclopramide was ineffective"	Data suggest use of prophylactic ondansetron resulted in a significant reduction of PONV episodes, Metoclopramide was ineffective.

						received 0.9% normal saline intravenously (n=29).				
Metaxari 2011 (score= 6.0)	Ondansetron / Granisetron/ Tropisetron	RCT	No mention of sponsorship. The authors declared no COI.	N=245 female patients experienced partial or total thyroidectomy.	Mean age: 46.7 years; 0 male, 245 females,	Placebo group: patients received 0.9% of normal saline intravenously (n=62) vs. Ondansetron group: patients received 4 mg of ondansetron intravenously (n=61) vs. Granisetron group: patients received 3 mg of granisetron intravenously (n=61) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=61).	Follow up at baseline on admission to the PACU and the following 1, 6, 12, and 18 hours	The incidence of postoperative nausea and vomiting in placebo group (44%) was higher in Post-anesthesia care unit (PACU) than that in granisetron group (24%), and ondansetron group (32%), but lower than tropisetron group (50%), and the difference between granisetron and tropisetron groups was significant (p=0.0081, odds ratio=0.31, 95%CI=0.13 to 0.73). 12 to 18 hours after surgery, the incidence of nausea dropped to 34% in placebo, 2% in granisetron, 14% in ondansetron, 17% in tropisetron group; and the difference between granisetron and placebo was significant (p=0.0001).	"Among the female patients of this study undergoing thyroid surgery, granisetron 3 mg provided the best prophylaxis from PONV. Ondansetron 4 mg was equally effective, but its action lasted only 6 h, whereas tropisetron 5 mg was found ineffective."	Data suggest granisetron better than ondansetron as effects lasted longer than 6 horus and study suggests tropisetron ineffective.
Gan 1994 (score= 6.0)	Droperidol/ Ondansetron	RCT	No mention of sponsorship or COI.	N=120 patients undergoing hip and knee replacements and femoral	Mean age: 59.0 years; 53 males, 67 females	Droperidol: received 25-mL bag of normal saline containing 1.25 mg of droperidol after surgery completion (n=38) vs Ondansetron: received 25-mL bag	24 hours	Symptom free patients were 32.5% of placebo, 53% after droperidol, and 62% after ondansetron. Lower incidence of vomiting was observed with ondansetron and droperidol compared to placebo (p<0.01).	"In this study, we demonstrated that there was no significant difference between prophylactic ondansetron and droperidol in the incidence of postoperative nausea (21% *vs* 29%, respectively) and	Data suggest comparable efficacy for PONV in total hip and total knee patients between ondansetron and droperidol compared to placebo.

				resections		of normal saline containing 4 mg of ondansetron after surgery completion (n=42) vs Placebo: received 25-mL bag of normal saline after surgery completion (n=40)		Incidence of nausea was 23% in placebo, 29% in droperidol, and 21% in ondansetron. Incidence of rescue antiemetic was 38% in placebo, 34% in droperidol, and 17% in ondansetron.	vomiting (17 *vs* 18%, respectively)."	
Choi 2010 (score= 6.0)	Ramosetron/ Ondansetron	RCT	Sponsored by Asian Medical Center. No mention of COI.	N= 279 patients undergoing cardiac surgery who had continuous infusion of treatment with a PCA pump.	Mean age: 58.5 years; 169 males, 120 females.	Group P had 2 mL saline given post-op and 6 mL saline added to patient-controlled analgesia (PCA) pump (n=70) vs group O had 4 mg ondansetron given post-op and 12 mg ondansetron added to PCA pump (n=71) vs group R1 had 0.3 mg ramosetron given post-op and 6 mL saline added to PCA pump (n=70) vs group R2 had 0.3 mg ramosetron given post-op and 0.6 mg ramosetron added to PCA pump (n=68).	Continuous observation for 48hrs post-op.	Incidence for PONV was 71% for group P, 46% for group O, 54% for group R1, and 35% for group R2 ($p<0.001$). Incidence of nausea was 46% for group O ($p=0.003$), 54% for group R1 ($p=0.036$), and 35% for group R2 ($p<0.001$) vs 71% for group P. Percentage of patients receiving rescue antiemetics was 34% in group O ($p=0.022$) and 29% in group R2 ($p=0.005$) vs 53% in group P.	"[…] a continuous infusion of ondansetron or ramosetron combined with PCA following a bolus dose at the end of surgery is an effective means of reducing the incidence of PONV during the first 48 h after cardiac surgery."	Data suggest adding ondansetron or ramosetron added to PCA decreases episodes of PONV.
Bestas 2007 (score= 6.0)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship or COI.	N = 90 ASA physical status I or II patients scheduled for	Mean age: 40.4 years; 21 males, 69 femfales	At the end of surgery patients intravenously received 40 µg/kg granisetron (N = 30) vs 100 µg/kg ondansetron (N = 30) vs placebo of no	Follow up at baseline, 1, 2, 4, 8, 12, and 24 hours post operation.	Percent of patients that needed rescue antiemetics in the 24 hour period was 60% in the placebo group vs 30% in the ondansetron group ($p<0.01$ vs placebo) and 20% in the granisetron	"Patients administered ondansetron 100 1Jg/kg or granisetron 40 1Jg/kg 20 to 30 minutes before the end of LC had significantly higher PONV	Data suggest comparable efficacy between ondasetron and granisetron for prevention of PONV

				elective laparoscopic cholecystectomy.		additive (N = 30) All three were diluted with normal saline (0.9% NaCl) to a volume of 100 ml.		group (p<0.01 vs placebo). No significant between group differences for granisetron vs ondansetron	control during the 24-hour postoperative observation period than patients receiving placebo. However, there were no significant differences between the active treatment groups in the incidence of PONV, patient satisfaction, or AEs"	
Paxton 1995 (score= 6.0)	Metoclopramide/ ondansetron / droperidol	RCT	No mention of sponsorship or COI.	N=118 patients underwent gynaecological laparoscopy.	Mean age: 31.5 years; no mention of sex.	Ondansetron group: patients received 4 mg ondansetron (n=32) vs. Droperidol group: patients received 1 mg droperidol (n=29) vs. Metoclopramide group: patients received 10 mg metoclopramide (n=29) vs. Placebo group: patients received 1 mg placebo (n=28).	Follow up at 1, 2, 4, 6, 12, 24, and 48 hours post operation.	25% patients in ondasetron group, 86% in droperidol group, 59% in metoclopramide group, 96% in placebo group had nausea. 18% patients in ondansetron group, 48% in droperidol group, 41% in metoclopramide, and 48% in placebo group had vomiting.	"In conclusion, a direct comparison of ondansetron 4 mg with metoclopramide 10 mg and droperidol 1 mg showed it to be superior for prophylaxis against PONV."	Data suggest ondansetron was significantly better than metoclopramide or droperidol as well as placebo for both nausea and vomiting post laparoscopy. Additionally, the number of patients requiring "rescue meds" much lower in ondansetron group.
Korttila 1997 (score = 6.0)	Dolasetron/Ondansetron	RCT	Sponsored by Hoechst Marion Roussel. No mention of COI.	N = 514 patients undergoing surgical procedures with general anesthesia	Mean age: 43 years; 30 males, 484 females	Received placebo saline solution (n=128) vs Received 25mg of Dolasetron (n=127) vs Received 50mg of Dolasetron (n=129) vs Received 4mg of Ondansetron (n=130)	Follow up continuous over the 24 hours post operation.	36% of placebo patients received rescue medication compared with 29% of dolasetron 25mg (p=0.026) and 19% of dolasetron 50mg (p=0.002) and 24% in ondansetron group (p=0.034). Rate of complete response was 49% for placebo and 71% for 50mg of dolasetron (p<0.001). Complete response was 51% for dolasetron 25mg	"When given at induction of anesthesia, 50mg intravenous dolasetron is equivalent to 4mg ondansetron and superior to 25mg dolasetron and placebo for the prevention of PONV. All treatments were safely administered and well tolerated."	Also in ondansetron 27% of participants received rescue medication Single IV treatment to 3 groups. Data suggest 50mg dolasetron equivalent to 4mg ondansetron and both are better than 25mg dolasetron and placebo for PONV prevention.

						*all dosages administered as single IV treatment		(p=0.001) and 64% for ondansetron (p=0.298).		
Desilva 1995 (score= 5.5)	Ondansetron / Droperidol/ Metoclopramide	RCT	Sponsored by Beth Israel anesthesia foundation. No mention of COI.	N=360 patients experienced total abdominal hysterectomy (TAH).	Mean age: 46.4 years; no mention of sex.	Group O: patients received 4 mg of ondansetron intravenously (n=58) vs. Group D: patients received 1.25 mg of droperidol intravenously (n=55) vs. Group P: patients received 5 mg of perphenazine intravenously (n=57) vs. Group M: patients received 10 mg of metoclopramide intravenously (n=58) vs. Placebo group: patients received normal saline (n=58).	Follow up at baseline, 5, 10, and 15 mins as well as ever 30 mins for 4 hrs post operation.	Patients in ondansetron and metoclopramide groups indicated no significant difference for their nausea score, compared with placebo group (p>0.05). The number of patients free of SES in the Ondansetron group was 37% (p<0.05 vs placebo), 42% in the Droperidol group (p<0.0005 vs placebo), 40% in the Perphenazine group (p<0.05 vs placebo) and 29% in the Metoclopramide group (p>0.05)	"Although ondansetron, droperidol, and perphenazine were effective in providing antiemetic prophylaxis, only IV perphenazine was free of side effects. Hence, we conclude that perphenazine is the best choice for antiemetic prophylaxis after TAH."	Data suggest comparable efficacy between ondansetron, droperidol and perphenazine for PONV. Metoclopramide found ineffective.
Polati 1997 (score= 5.5)	Ondansetron / Metoclopramide	RCT	No mention of sponsorship or COI.	N=175 experienced nausea and vomiting after gynecological	Mean age: 35 years; no mention of sex.	Ondansetron group: patients received 4 mg of ondansetron intravenously (n=58) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously	Follow-up at baseline, 12, 24, 36, and 48 hours.	Ondansetron group indicated higher effectiveness in improving vomiting or nausea than metoclopramide and placebo groups (p<0.001). 55.2% patients in ondansetron group, 29.8% in metoclopramide group, and 11.7% in placebo	"In conclusion, ondansetron 4 mg is more effective than metoclopramide 10 mg and placebo in the treatment of established PONV."	Data suggest a single dose of 4 mg ondansetron is better than metoclopramide 10 mg for managing PONV.

				laparoscopy.		(n=57) vs. Placebo group: patients received 20 ml normal saline (n=60).		group indicated effective treatment to prevent recurrence of postoperative nausea and vomiting (p=0.003).		
van den Berg 1996 (score= 5.5)	Ondansetron / Prochlorperazine	RCT	No mention of sponsorship or COI.	N=148 patients received balanced inhalational anesthesia.	Mean age: 29.7 years; 79 males, 69 females.	Placebo group: patients received 1 to 2 ml of saline intravenously (n=37) vs. im-P group: patients received 0.2 mg of prochlorperazine intramuscularly (n=37) vs. iv-P group: patients received 0.1 mg of prochlorperazine intravenously (n=37) vs. Ondansetron group: patients received 0.06 mg of ondansetron intravenously (n=37)	Follow up continuous over the 24 hours post operation.	The nausea and vomiting combination in placebo group dropped to 53% and the difference was significant ($p<0.0005$), and that in im-prochlorperazine group dropped to 16% with significant change ($p<0.0005$), and that in iv-ondansetron group dropped to 19% with significant change ($p<0.0005$), and that in iv-prochlorperazine group dropped to 30% ($p<0.05$). The frequency of patients absent from postoperative nausea and vomiting was increased in placebo group to 27%, 57% in im-prochlorperazine group ($p<0.01$), 62% in iv-ondansetron group ($p<0.005$), and 43% in iv-prochlorperazine group with no significant change ($p>0.05$).	"Prophylactic prochlorperazine 0.2 $mg.kg^{-1}$ im and ondansetron 0.06 rag. kg -t iv are similarly efficacious in reducing nausea with vomiting after tympanoplasty, while prochlorperazine 0.1 rag. Kg^{-1} iv is less efficacious."	Data suggest IM prochlorperazine 0.2 mg and ondansetron 0.06 mg/kg are comparable but IV prochlorperazine is ineffective.
Sandhu 1999 (score= 5.5)	Ondansetron / Dimenhydrinate	RCT	No mention of sponsorship or COI.	N=87 female patients experienced gynecolo	Mean age: 32.7 years; 0 male, 87 females.	Placebo group: patients received placebo intravenously immediately after anesthesia (n=38)	Follow up at baseline post operation, 1 and 2 hrs post PACU admission	The incidence of postoperative nausea and vomiting was similar among the three groups: placebo group=21% vs. dimenhydrinate	"PONV is a multifactorial problem, which may not have a singular therapeutic solution. PONV is an important complication and is distressing to our patients.	Data suggest lack of efficacy.

				gical laparoscopy.		vs. Dimenhydrinate group: patients received 50 mg of dimenhydrinate intravenously immediately after anesthesia (n=33) vs. Ondansetron group: patients received 8 mg of ondansetron intravenously immediately after anesthesia (n=29).	and the next day.	group=17% vs. ondansetron group=10%; and the difference was not significant (p>0.05). Patients in dimenhydrinate group were delayed for their immediate recovery from anesthesia, and showed lower score on digit symbol substitution test (p<0.05).	Prior work has examined the efficacy of prophylactic antiemetic therapy."	
Malins 1994 (score= 5.0)	Ondansetron / Metoclopramide	RCT	No mention of sponsorship or COI.	N=153 female patients experienced gynecological laparoscopy for sterilization.	Mean age: 32.7 years; 0 male, 153 females.	Group O: patients received 4 mg of ondansetron orally 1 hour before surgery (n=50) vs. group M: patients received 10 mg of metoclopramide orally 1 hour before surgery (n=50) vs. Placebo group: patients received placebo orally 1 hour before surgery (n=50).	Follow up when ready to leave the recovery room, on returning to the ward, and when ready for discharge from the hospital. Follow up about the 48 hours post operation in a take home questionnaire.	Less patients in ondansetron group (n=13) indicated emetic symptoms of vomiting or nausea 48 hours after surgery than that in placebo group (n=25), and the difference was significant (p<0.05, 95%CI= 5.6 to 42.4%). After leaving hospital, 40 patients in ondansetron group showed absence of nausea, compared to 33 in metoclopramide group and 30 in placebo group; the difference was significant (p<0.05, 95%CI=0.3 to 35%)	"Emetic symptoms (nausea or vomiting) occurred in 26% of patients who received ondansetron, 42% of those who received metoclopramide and 50% of those given placebo."	Data suggest ondansetron is approximately twice as effective as metoclopramide for decreasing PONV.
Alexander 1995 (score= 4.5)	Ondansetron	RCT	Partially sponsored by Glaxo. No mention of COI.	N=145 patients who meet American Society of	Mean age: 44.9 years; 50 males, 77 females.	Group S: patients received syringe contained saline and 60 mg morphine after the surgery (n=41) vs. group D: patients	Follow up at baseline post operation and then every 4 hours for 24 hours.	72% patients in ondansetron group, 45% in droperidol group and 20% in saline group indicated no symptom of nausea and vomiting, and	"We conclude that ondansetron is superior to droperidol when used with patient-controlled analgesia and causes less sedation."	Data suggest PONV decreased in both ondansetron and droperidol groups but ondansetron had less sedative effects.

				Anesthesiologists 1 (normal healthy) and 2 (mild systemic morbid) experienced major orthopedic surgery.		received syringe contained 1.25 mg droperidol intravenously and 60 mg morphine after the surgery (n=43) vs. group O: patients received syringe contained 4 mg ondansetron intravenously and 60 mg morphine after the surgery (n=43).		the difference was significant (p<0.0001). Ondansetron group showed less patients (n=2) with moderate to severe symptoms, compared to droperidol group (n=8) and saline group (n=7), and the difference was significant (p<0.05).		
Palonosetron										
Chun 2013 (score= 8.0)	Palonosetron	RCT	No mention of sponsorship. No COI.	N = 204 healthy inpatients with an ASA physical status of I–II, who were going under elective surgery	Mean age: 43 years; 119 males, 85 females	The palonosetron group: received 0.075mg IV of palonosetron (n=102) vs Placebo group: received 1.5ml of NS IV (n=102). All patients received midazolam 3-5mg i.m. 30 minutes before surgery.	Follow up at 1, 6, 24, 48 and 72 hours	When compared with the palonosetron group and the placebo group, there was a lower incidence of postoperative nausea and vomiting (PONV) during 0-24h (33% vs 47%) and 0-72h (33% vs 52%) (P<0.05), but not during 24-72h. There was also a lower incidence of nausea in the palonosetron group than the placebo group during 0-24h and 0-72h (P<0.05).	"Palonosetron 0.075 mg i.v. effectively reduced the incidence of PONV during the first 72 h after operation, with most of the reduction occurring in the first 24 h."	Data suggest 0.075mg of IV palonosetron is effective in reducing PONV up to 72 hours post-operatively, especially in the first 24 hours.
Candiotti 2008 (score= 7.5)	Palonosetron	RCT	Sponsored by Helsinn Healthcare SA and	N = 574 patients undergoing either outpatient abdomin	Mean age: 35.9 years; 51 males, 523 females	Palonosetron 0.025mg group: received 0.025mg of palonosetron via I.V along with enough saline to bring the total	Follow up at 2, 6, 24, 48, and 72 hours.	Complete Response (CR) increased as the doses of palonosetron increased. Patients who received palonosetron 0.075 mg during the 0-6h,	"In patients undergoing elective gynecological or abdominal laparoscopic surgery, a single 0.075 mg IV dose of palonosetron significantly improved the CR	Data suggest single dose of 0.075mg IV palonsetron significantly decreased episodes of PONV as well as reducing the need for rescue medications. There was also an observed dose-

			supported by MGI PHARMA INC. No mention of COI.	al or gynecological laparoscopic surgery with a history of PONV or motion sickness, and nonsmoking status.		volume to 2mL (n=136) vs Palonosetron 0.050 mg group: received 0.050 mg of palonosetron via I.V along with enough saline to bring the total volume to 2mL (n=137) vs Palonosetron 0.075 mg group: received 0.075 mg of palonosetron via I.V along with enough saline to bring the total volume to 2mL (n=138) vs Placebo group: received a single IV dose of normal saline as a 2mL bolus (n=135). All was administrated as a 10-s IV bolus before induction of anesthesia		6- 72h, and 0- 72h had CR rates of 49% (*P*= 0.042), 45% (*P*= 0.064) and 39% (*P*= 0.010), when compared to the placebo.	rate, decreased nausea severity and reduced the interference with patients' postoperative functioning due to PONV."	response trend in palonosetron patients.
Kovac 2008 (score= N/A)	Palonosetron	Secondary Analysis of Candiotti 2008	Sponsored by Helsinn Healthcare SA and by MGI PHARMA. No mention of COI.	N = 544 patients with one or more risk factors of postoperative nausea and vomiting (PONV).	Mean age: 35.9 years; 51 males, 523 females	Palonosetron 0.025mg group: received 0.025mg of palonosetron via I.V along with enough saline to bring the total volume to 2mL (n=136) vs Palonosetron 0.050 mg group: received 0.050 mg of palonosetron via I.V	Follow up at 2, 6, 24, 48, and 72 hours.	Complete Response (CR) rates for 0–24h were 46% for palonosetron 0.025mg (P=0.073), 47% for palonosetron 0.050mg (P=0.069), 56% for palonosetron .075mg (P=0.001), and 36% for placebo. CR rates for 24-72h were 56% for palonosetron 0.025mg (P=0.511), 61% for	"In the inpatient surgical setting, a single 0.075-mg IV dose of palonosetron significantly reduced emesis, intensity of nausea and the use of rescue antiemetics in addition to delaying the time to emesis and treatment failure, particularly during the first 24 h after surgery. The lower 0.025 mg and 0.050 mg doses of palonosetron	Data suggest a single dose of 0.075mg IV palonosetron significantly decreased PONV.

						along with enough saline to bring the total volume to 2mL (n=137) vs Palonosetron 0.075 mg group: received 0.075 mg of palonosetron via I.V along with enough saline to bring the total volume to 2mL (n=138) vs Placebo group: received a single IV dose of normal saline as a 2mL bolus (n=135). All was administrated as a 10-s IV bolus before induction of anesthesia		palonosetron 0.050mg (P=0.151), 70% for palonosetron .075mg (P=0.002), and 52% for placebo. During 0-24h, palonosetron 0.075mg had less intense nausea (P<0.001), delayed median time to emesis (P=0.002), and treatment failure (P=0.004) than placebo.	tended not to be significantly different from placebo."	
Ramosetron										
Joo 2016 (score= 8.5)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship. No COI.	N = 89 patients who were ASA physical status I and II undergoing strabismus surgery with general anesthesia.	Mean age: 34.6 years; 41 males, 48 females.	Group one was given 2 mL normal saline as a placebo (n=31), group two was given 4 mg ondansetron (n=26), and group three was given 0.3 mg ramosetron (n=32) through an IV post-op.	Follow up at 2, 24, and 48 hours post-op.	The incidence in nausea at 2 hrs was 9.4% in ramosetron group, 34.6% in ondansetron, and 45.2% in placebo group (p<0.05). The incidence in nausea at 24 hrs was 3.1% in ramosetron group, 19.2% in ondansetron, and 22.6% in placebo group (p<0.05). Patients given ramosetron had a verbal rating scale for satisfaction of 8.11 at 2 hrs and 8.50 at 24 hrs vs placebo group that had 6.84 at 2 hrs and 7.25 at 24 hrs vs ondansetron	"[…] the incidence of postoperative nausea was high until 24 h after strabismus surgery. Therefore, prevention of postoperative nausea during the 24 h after strabismus surgery is crucial. Ramosetron had an antiemetic efficacy greater than that of ondansetron or placebo during the first 24 h after strabismus surgery in adult patients."	Data suggests ramosetron is superior to ondansetron for preventing PONV in strabismus surgery patients.

								group that had 7.28 at 2 hrs and 7.27 at 24 hrs (p<0.05).		
Ryu 2010 (score= 7.5)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship or COI.	N= 120 patients who were ASA physical status I or II and undergoing Laparoscopic cholecystectomy (LC) with general anesthesia.	Mean age: 46.3 years; 59 males, 61 females.	Group O4 was given 4mg ondansetron (n=40), group O8 was given 8mg ondansetron (n=40), and group R was given 0.3mg ramosetron via IV at the end of the surgery.	Continuous observation for 48 hrs post-op.	At 2 hrs post-op, 80% of group O8 and group R had complete response vs 58% in group O4 (p=0.04). At 2-24 hrs post-op, 90% of group O8 and group R had complete response vs 76% in group O4 (p=0.09). At 24-48 hrs post-op, 98% of group O8 and group O4 had complete response vs 100% in group R (p=0.36). In the first 2 hrs, antiemetics were used in 20% of patients in O8 and R group vs 42.5% in O4 group (p=0.04).	"[…] ramosetron 0.3 mg was more effective than ondansetron 4 mg and as effective as ondansetron 8 mg for the prophylaxis of PONV in patients undergoing laparoscopic cholecystectomy."	Data suggests 0.3mg IV ramosetron is comparable in efficiency to 8mg ondansetron and both are better than 4mg ondansetron for prevention of PONV post LC.
Kim 2009 (score= 7.5)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship or COI.	N= 162 female patients undergoing elective gynecological surgery.	Mean age: 41.7 years; 0 males, 162 females.	Group one was given 0.3 mg ramosetron (n=54) vs group two given 8 mg ondansetron vs group three given saline via IV. All treatments were diluted to 4 mL and given 30min pre-op.	Continuous observation for 24hrs post-op	The incidence of nausea at 24 hrs was 50% in ramosetron group, 44% in ondansetron, and 69% in placebo group (p<0.05). The incidence of vomiting at 24 hrs was 17% in ramosetron group, 20% in ondansetron, and 44% in placebo group (p<0.05). The visual analogue scale score for nausea during 0-24 hrs was 28 for ramosetron group, 28 for ondansetron and 48 for placebo group (p<0.05). Rescue antiemetics were used for 15% of ramosetron group vs 41%	"[…] ramosetron 0.3 mg i.v. and ondansetron 8 mg i.v. were equally effective in decreasing incidence of PONV and severity of nausea in high-risk female patients during the first 24 h after surgery."	Data suggests comparable efficiency between ramosetron 0.3mg IV and ondansetron 8mg IV.

								of placebo group (p<0.05). No significant difference between ramosetron vs ondansetron.		
Fujii 2004 (score= 7.0)	Granisetron/ Ramosetron	RCT	No sponsorship or COI.	N = 90 ASA physical status I female patients undergoing general anesthesia for breast surgery.	Mean age: 52.7 years; 0 males, 90 females	At the end of surgery patients intravenously received 3 mg granisetron (N = 30) vs 0.3 mg ramosetron (N = 30) vs placebo (N = 30) identical syringes were prepared for each drug. Identity of the placebo was not given.	Follow up continuous by nurses over the 48 hours post operation.	Percent of patients with emetic symptoms 0-24 hours after anesthesia was 47% in the placebo group vs 17% in the granisetron group (p=0.013 vs placebo) and 10% in the ramosetron group (p=0.002 vs placebo). At 24-48 hours, emetic symptoms were seen in 27% of the granisetron group vs 7% in the ramosetron group (p=0.039)	"In conclusion, ramosetron is more effective than granisetron for preventing PONV within a 48-hour postanesthetic period in women undergoing general anesthesia for breast surgery."	Data suggest ramosetron better than granisetron for prevention of PONV.
Fujii 2000 (score= 7.0)	Ramosetron	RCT	No mention of sponsorship or COI.	N= 120 patients who were ASA physical status I or II and undergoing abdominal hysterectomy, vaginal hysterectomy, or salpingo-oophorectomy.	Mean age: 44.3 years; 0 males, 120 females.	Group one was given placebo (n=30) vs group two given 0.15 mg ramosetron (n=30) vs group three given 0.3 mg ramosetron (n=30) vs group four given 0.6 mg ramosetron (n=30) via IV after procedure.	Continuous observation for 48hrs post-op.	During 0-3 hrs post-op, there was a complete response of 40% for placebo, 47% for 0.15 mg ramosetron, 87% for 0.3 mg ramosetron, and 90% for 0.6 mg ramosetron. During 24-48 hrs post-op, there was a complete response of 50% for placebo, 53% for 0.15 mg ramosetron, 90% for 0.3 mg ramosetron, and 93% for 0.6 mg ramosetron. During the first 48 hrs post op, more patients with 0.3 and 0.6 mg ramosetron had complete response (p<0.05). No significant difference between 0.15 mg	"[…] ramosetron 0.3 mg appears to be the minimal effective dose for preventing PONV in patients undergoing major gynecological surgery. A double dose of 0.6 mg does not add any therapeutic advantage compared with ramosetron 0.3 mg."	Data suggests 0.3mg of IV ramosetron is the minimal effective dose for preventing PONV.

								ramosetron vs placebo. Intensity of nausea was lower in 0.3 mg and 0.6 mg ramosetron vs placebo (p<0.05). Patients who received 0.3 mg and 0.6 mg ramosetron had satisfaction scores of 8.5 and 9, respectively vs a 3.5 score for the placebo group (p<0.05).		
Lee 2002 (score= 6.5)	Granisetron/ Ramosetron	RCT	No mention of sponsorship or COI.	N = 113 ASA physical status I or II patients undergoing general anesthesia for elective thyroidectomy.	Mean age: 39.6 years; 9 males, 104 females	At the end of surgery patients intravenously received 20 µg/kg granisetron (N = 30) vs 4 µg/kg ramosetron (N = 30) vs placebo of no additive (N = 30) All three were diluted with normal saline (0.9% NaCl) to a volume of 10 ml.	Follow up over the 24 hours after surgery every 30 minutes and 6 hours.	Overall PONV during the 24 hours occurred in 61% of placebo patients vs 30.6% of Granisetron patients (p=0.008). No other significant within or between group differences were found.	"Only granisetron 20 µg/kg was superior to placebo for the prevention of PONV after thyroidectomy."	Data suggest granisetron 20 µg/kg superior to ramosetron and placebo for reducing incidence of PONV.
Bestas 2007 (score= 6.0)	Ramosetron/ Ondansetron	RCT	No mention of sponsorship or COI.	N = 90 ASA physical status I or II patients scheduled for elective laparoscopic cholecystectomy.	Mean age: 40.4 years; 21 males, 69 females	At the end of surgery patients intravenously received 40 µg/kg granisetron (N = 30) vs 100 µg/kg ondansetron (N = 30) vs placebo of no additive (N = 30) All three were diluted with normal saline (0.9% NaCl) to a volume of 100 ml.	Follow up at baseline, 1, 2, 4, 8, 12, and 24 hours post operation.	Percent of patients that needed rescue antiemetics in the 24 hour period was 60% in the placebo group vs 30% in the ondansetron group (p<0.01 vs placebo) and 20% in the granisetron group (p<0.01 vs placebo). No significant between group differences for granisetron vs ondansetron	"Patients administered ondansetron 100 1Jg/kg or granisetron 40 1Jg/kg 20 to 30 minutes before the end of LC had significantly higher PONV control during the 24-hour postoperative observation period than patients receiving placebo. However, there were no significant differences between the active treatment groups in the incidence of PONV, patient satisfaction, or AEs"	Data suggest comparable efficacy between ondasetron and granisetron for prevention of PONV

Choi 2010 (score= 6.0)	Ramosetron/ Ondansetron	RCT	Sponsored by Asian Medical Center. No mention of COI.	N= 279 patients undergoing cardiac surgery who had continuous infusion of treatment with a PCA pump.	Mean age: 58.5 years; 169 males, 120 females.	Group P had 2 mL saline given post-op and 6 mL saline added to patient-controlled analgesia (PCA) pump (n=70) vs group O had 4 mg ondansetron given post-op and 12 mg ondansetron added to PCA pump (n=71) vs group R1 had 0.3 mg ramosetron given post-op and 6 mL saline added to PCA pump (n=70) vs group R2 had 0.3 mg ramosetron given post-op and 0.6 mg ramosetron added to PCA pump (n=68).	Continuous observation for 48hrs post-op.	Incidence for PONV was 71% for group P, 46% for group O, 54% for group R1, and 35% for group R2 (p<0.001). Incidence of nausea was 46% for group O (p=0.003), 54% for group R1 (p=0.036), and 35% for group R2 (p<0.001) vs 71% for group P. Percentage of patients receiving rescue antiemetics was 34% in group O (p=0.022) and 29% in group R2 (p=0.005) vs 53% in group P.	"[…] a continuous infusion of ondansetron or ramosetron combined with PCA following a bolus dose at the end of surgery is an effective means of reducing the incidence of PONV during the first 48 h after cardiac surgery."	Data suggest adding ondansetron or ramosetron added to PCA decreases episodes of PONV.
Choi, 2010 (score= 6.0)	Ramosetron/ Ondansetron	RCT	Sponsored by Asian Medical Center. No mention of COI.	N= 279 patients undergoing cardiac surgery who had continuous infusion of treatment with a PCA pump.	Mean age: 58.5 years; 169 males, 120 females.	Group P had 2 mL saline given post-op and 6 mL saline added to patient-controlled analgesia (PCA) pump (n=70) vs group O had 4 mg ondansetron given post-op and 12 mg ondansetron added to PCA pump (n=71) vs group R1 had 0.3 mg ramosetron given post-op and 6 mL saline added to PCA pump (n=70) vs	Continuous observation for 48hrs post-op.	Incidence for PONV was 71% for group P, 46% for group O, 54% for group R1, and 35% for group R2 (p<0.001). Incidence of nausea was 46% for group O (p=0.003), 54% for group R1 (p=0.036), and 35% for group R2 (p<0.001) vs 71% for group P. Percentage of patients receiving rescue antiemetics was 34% in group O (p=0.022) and 29% in group R2 (p=0.005) vs 53% in group P.	"[…] a continuous infusion of ondansetron or ramosetron combined with PCA following a bolus dose at the end of surgery is an effective means of reducing the incidence of PONV during the first 48 h after cardiac surgery."	Data suggest adding ondansetron or ramosetron added to PCA decreases episodes of PONV.

						group R2 had 0.3 mg ramosetron given post-op and 0.6 mg ramosetron added to PCA pump (n=68).				
Lee 2009 (score= 5.5)	Ramosetron	RCT	Sponsored by Gil Medical Center, Incheon, Korea. No mention of COI.	N= 120 patients who were ASA physical status I or II and undergoing laparoscopy with general anesthesia.	Mean age: 41 years; 0 males, 120 females.	The control group was given a cup with 10 mL saline and syringe with 2 mL saline (n=40) vs IV group was given a cup with 10 mL saline and syringe with 0.3 mg ramosetron in IV (n=40) vs PO group was given 0.1 mg ramosetron dissolved in 10 mL saline and syringe with 2 mL saline (n=40).	Continuous observation for 24hrs post-op.	During the first 1 h, the incidence of complete response was 65% for control group, 90% for IV group, and 87.5% for PO group. The incidence of nausea was 12.5% for IV group (p=0.099) and 15% in PO group (p=0.18) vs 30% in control group.	"[…] prophylactic oral ramosetron 0.1 mg may be considered in patients with a high risk of developing PONV, such as patients undergoing gynecological laparoscopy, because it is simple, less expensive, and equally effective in terms of patient satisfaction compared to IV ramosetron 0.3 mg."	Data suggest comparable efficacy between oral and IV ramosetron.
Tropisetron										
Kaufmann 1994 (score= 7.5)	Droperidol/ Metoclopramide/ Tropisetron	RCT	No mention of sponsorship or COI.	N=286 patients undergoing elective surgery	Mean age: 56.7 years; 130 males, 156 females	Group 1: received placebo of only morphine from the PCA device (n=67) vs Group 2: received antiemetic mixed with morphine in the PCA syringe of metoclopramide (n=71) vs Group 3: received antiemetic mixed with morphine in the PCA syringe of droperidol (n=70) vs	3, 18 hours, then 6 hours from thereafter	Incidence of postoperative nausea and vomiting (PONV) was 54% for group 1, 40% for group 2, 17% in group 3 (p<0.0001), and 33% in group 4 (p=0.02). Droperidol reduced incidence (p<0.001) and severity (p<0.01) of PONV for 36 hours.	"In summary, combining droperidol and morphine for PCA after major orthopedic surgery effectively reduced both the incidence and severity of PONV."	Data suggest both droperidol and tropisetron are effective antiemetics but tropisetron requires more than one does for efficacy.

						Group 4: received only morphine from the PCA device (n=78)				
Alon 1998 (score= 7.0)	Tropisetron	RCT	Sponsored by Sandoz Pharma Ltd. No mention of COI.	N= 314 patients who were ASA physical status I and II with postoperative nausea lasting over 10 min and vomiting within 2 h post op.	Mean age: 42 years; 25 males, 289 females.	Patients were given either 5mL of saline as the placebo (n=77) or varying doses of tropisetron: 0.5 mL of tropisetron diluted with saline up to 5 mL (n=77), 2 mL of tropisetron diluted with saline up to 5 mL (n=80), or 5 (n=80) mL of tropisetron through an IV. Treatments were given after patients experienced postoperative nausea and vomiting (PONV).	Follow up during 24 hour post-op period.	Absence of emetic episodes were 29% in placebo group, 40% in 0.5mg tropisetron group, 46% in 2mg tropisetron group, and 48% in 5mg tropisetron group. Absence of rescue antiemetics were 32% in placebo group, 55% in 0.5mg tropisetron group, 55% in 2mg tropisetron group, and 56% in 5mg tropisetron group. Absence of nausea was 45% with patients taking 2mg tropisetron and 46% with patients taking 5mg tropisetron compared with 34% taking a placebo ($p<0.05$).	"[…]tropisetron administered to treat established PONV significantly reduced the recurrence of vomiting and need for rescue antiemetics. It also reduced the recurrence or persistence of nausea, but this reduction was significant only in the subgroup of patients included for nausea."	Data suggests a single dose of IV tropisetron significantly reduced PONV and all doses were superior to placebo. Headache was noted in 13 patients in the 5 mg group.
Purhonen 1997 (score= 7.0)	Tropisetron/ Droperidol	RCT	No mention of sponsorship or COI.	N = 146 female patients who were ASA physical status I - III and were undergoing an elective gynecologic	Mean age: 50.3 years; 0 males, 146 females.	Patients were given 0.15-0.2 mg/kg of peroral diazepam 1 h before surgery. The patients were divided into three groups to receive 100 mL saline containing either 5 mg tropisetron (n=48), 1.25 mg droperidol (n=49), or only saline (n=49) through an IV 15 minutes post-op.	Follow up at 2, 6, 24, and 48 hours post-op.	44% of patients taking tropisetron needed to take metoclopramide vs 69% of patients in the placebo group ($p<0.05$). 8%, 22%, and 29% of patients vomited on day one of post-op when given tropisetron, droperidol, and placebo, respectively ($p<0.05$). 13 patients in the tropisetron group had a cough vs 5 patients in the placebo	"We conclude that 5 mg of IV tropisetron is well tolerated and reduces the incidence and intensity of postoperative vomiting, but not nausea and retching, after gynecologic incontinence operation performed under general anesthesia. Droperidol 1.25 mg IV is comparable to placebo in preventing PONV, and patients experience more adverse effects."	Data suggests lack of efficiency.

				incontinence operation.				group during 6-24 hours post-op ($p<0.05$).		
Madenoglu 2003 (score= 7.0)	Tropisetron	RCT	No mention of sponsorship or COI.	N= 60 patients who were ASA physical status I - III undergoing craniotomy for resection of various supratentorial tumors.	Mean age: 44 years; 29 males, 31 females.	Patients in tropisetron group (n=33) were given 2 mg of tropisetron diluted with 0.9% saline to 5 mL while placebo group (n=32) was given 5 mL of saline through an IV when dural closure was beginning. Only 60 patients completed the study.	Follow up during 24 hour post-op period.	There was a 30% nausea incidence in tropisetron group vs 46.7% in placebo group ($p>0.05$). There was 60% emetic episodes in placebo group and 26.7% in tropisetron group ($p<0.05$). Rescue treatments were given to 60% of placebo group and 26.7% of tropisetron group ($p<0.05$) in 24 h period.	"[…] intravenous administration of tropisetron (2 mg) at the time of dural closure was effective in reducing the overall incidence and frequency of emetic episodes among adult patients undergoing elective craniotomy for supratentorial tumor resection."	Data suggests 2 mg of IV tropisetron is effective for decreasing PONV.
Ali-Melkkila 1996 (score= 6.5)	Tropisetron/ Metoclopramide	RCT	No mention of sponsorship or COI.	N= 120 patients undergoing ophthalmic surgery with general anesthesia.	Mean age: 45.4 years; 70 males, 50 females.	All patients were given 5 mg of diazepam orally 90 before operation. After anesthesia: group one was given 0.1 mg/kg tropisetron (n=40), group two was given 0.25 $mg.kg^{-1}$ metoclopramide (n=40), and group three was given saline (n=40) through an IV injection at the end of anesthesia.	Follow up during 24 hour post-op period.	27% of patients in tropisetron group experienced nausea vs 52% in placebo group ($p<0.01$). 35% of patients experienced nausea in metoclopramide group vs placebo ($p<0.05$). 15% of patients with metoclopramide vomited vs 30% in placebo group ($p<0.05$).	"[…] our results would argue against the use of tropisetron as the first choice antiemetic agent in the prevention of postoperative nausea and vomiting in ophthalmic patients."	Data suggest metoclopramide is best for decreasing PONV as tropisetron was effective for reducing only nausea.

Naguib 1996 (score= 6.0)	Ondansetron / Tropisetron/ Granisetron/ Metoclopramide	RCT	No mention of sponsorship or COI.	N=132 patients	Mean age: 37.4 years; 24 males, 108 females.	Ondansetron group: patients received 4 mg of ondansetron intravenously (n=29) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=25) vs. Granisetron group: patients received 3 mg of granisetron intravenously (n=25) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously (n=24) vs. Placebo group: patients received 0.9% normal saline intravenously (n=29).	Follow up at 1, 4, 9, 12, 18, and 24 hours after recovery from anesthesia.	65.6% patients in ondansetron group, 52% in granisetron, 48% in tropisetron, 29.2% in metoclopramide, and 27.6% in placebo were absent from emesis 24 hours after surgery. Ondansetron prophylactic antiemetic treatment showed lower incidence of postoperative nausea and vomiting than that in placebo and metoclopramide groups (p=0.02). On the other hand, Ondansetron group indicated longer first rescue antiemetic recovery times than that in metoclopramide and placebo groups (p<0.01).	"Ondansetron, when given prophylactically resulted in a significantly lower incidence of PONV than metoclopramide and placebo. Metoclopramide was ineffective"	Data suggest use of prophylactic ondansetron resulted in a significant reduction of PONV episodes, Metoclopramide was ineffective.
Metaxari 2011 (score= 6.0)	Ondansetron / Granisetron/ Tropisetron	RCT	No mention of sponsorship. The authors declared no COI.	N=245 female patients experienced partial or total thyroidectomy.	Mean age: 46.7 years; 0 male, 245 females,	Placebo group: patients received 0.9% of normal saline intravenously (n=62) vs. Ondansetron group: patients received 4 mg of ondansetron intravenously (n=61) vs. Granisetron group: patients received 3 mg of granisetron intravenously	Follow up at baseline on admission to the PACU and the following 1, 6, 12, and 18 hours	The incidence of postoperative nausea and vomiting in placebo group (44%) was higher in Post-anesthesia care unit (PACU) than that in granisetron group (24%), and ondansetron group (32%), but lower than tropisetron group (50%), and the difference between granisetron and tropisetron groups was significant (p=0.0081,	"Among the female patients of this study undergoing thyroid surgery, granisetron 3 mg provided the best prophylaxis from PONV. Ondansetron 4 mg was equally effective, but its action lasted only 6 h, whereas tropisetron 5 mg was found ineffective."	Data suggest granisetron better than ondansetron as effects lasted longer than 6 horus and study suggests tropisetron ineffective.

						(n=61) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=61).		odds ratio=0.31, 95%CI=0.13 to 0.73). 12 to 18 hours after surgery, the incidence of nausea dropped to 34% in placebo, 2% in granisetron, 14% in ondansetron, 17% in tropisetron group; and the difference between granisetron and placebo was significant (p=0.0001).		
Droperidol										
Culebras 2003 (score= 7.5)	Droperidol	RCT	No mention of sponsorship. COI: Dr. Tramèr is a recipient of a PROSPER grant from the Swiss National Science Foundation.	N=340 patients having postoperative analgesia controlled device receiving morphine	No mention of mean age; 155 males, 174 females	Droperidol 5µg: received droperidol 5µg/mg morphine (0.5 mg added to 100 mg of morphine) (n=82) vs Droperidol 15 µg: received droperidol 15µg/mg morphine (1.5 mg added to 100 mg of morphine) (n=82) vs Droperidol 50 µg: received droperidol 50µg/mg morphine (5 mg added to 100 mg of morphine) (n=83) vs Controls: received morphine only (n=82)	No mention of follow-up.	Incidence of nausea was 48.8% for controls, 42.7% for droperidol 5µg, 32.9% for droperidol 15µg, and 21.7% for droperidol 50 µg. Incidence of vomiting was 24.4% for controls, 23.2% for droperidol 5µg, 22.0% for droperidol 15µg, and 12% for droperidol 50 µg. Incidence for emetic event was 52.4% for controls, 46.3% for droperidol 5µg, 34.1% for droperidol 15µg, and 25.3% for droperidol 50 µg.	"[W]e may assume that the optimal dose of droperidol, when added to a morphine PCA, is between 15 and 50 µg/mg of morphine (i.e., between 1.5 and 5 mg/100 mg of morphine). It may be that larger doses of droperidol would have a better antivomiting effect, but very likely at the price of even more sedation and perhaps further adverse drug effects."	Data suggest highest dose of droperidol (50µg) was best as an antiemetic.
Kaufmann 1994 (score= 7.5)	Droperidol/ Metoclopramide/	RCT	No mention of sponsorship or COI.	N=286 patients undergoing elective surgery	Mean age: 56.7 years; 130 males, 156 females	Group 1: received placebo of only morphine from the PCA device (n=67) vs Group 2: received antiemetic	3, 18 hours, then 6 hours from thereafter	Incidence of postoperative nausea and vomiting (PONV) was 54% for group 1, 40% for group 2, 17% in group 3 (p<0.0001), and 33% in	"In summary, combining droperidol and morphine for PCA after major orthopedic surgery effectively reduced both the incidence and severity of PONV."	Data suggest both droperidol and tropisetron are effective antiemetics but tropisetron requires more than one does for efficacy.

	Tropisetron					mixed with morphine in the PCA syringe of metoclopramide (n=71) vs Group 3: received antiemetic mixed with morphine in the PCA syringe of droperidol (n=70) vs Group 4: received only morphine from the PCA device (n=78)		group 4 (p=0.02). Droperidol reduced incidence (p<0.001) and severity (p<0.01) of PONV for 36 hours.		
Eberhart 2004 (score= 7.5)	Droperidol/ Dolasetron	RCT	No mention of sponsorship. No COI.	N=240 patients undergoing vitreoretinal surgery	Mean age: 63.0 years; 146 males, 158 females	Dolasetron Group: received 1 syringe with 12.5 mg of dalestron diluted to 10 ml and 1 syringe with 10 ml of saline (n=80) vs Droperidol Group: received 1 syringe containing 10μgkg^{-1} droperidol diluted to 10 ml and 1 syringe with 10 ml of saline (n=80) vs Comination Group: received 1 syringe with 10μgkg^{-1} droperidol and 1 syringe with 12.5 mg Dolasetron both diluted to 10 ml (n=80) vs Placebo: received 2 syringes containing 10ml of saline (n=80)	24 hours	Severity of PONV differed between the groups (p<0.0001). Antiemetic efficacy was better in the combination group compared with dolasetron alone at reducing severity of PONV (p=0.003). Droperidol and combination group reduced number of patients with PONV compared to placebo (p=0.0006, p<0.0001, respectively). Least incidence of PONV in the combination group (18.4%) compared to dolasetron group (39.5%) and the droperidol group (28.4%).	"In summary, low-dose droperidol (10 μg · kg^{-+1}) can still be recommended, due to its favorable effectiveness in preventing PONV after vitreoretinal surgery. Dolasetron (12.5 mg) is not an equivalent substitute for droperidol but can be used for supplementation in high-risk patients."	Data suggest low dose droperidol reduced post-operative N&V post vitectomy compared to both dolasetron and placebo.

Jellish 1997 (score= 7.5)	Ondansetron / droperidol	RCT	Partially sponsored by Glaxo Wellcom Inc. in Research triangle park in North Carolina. No mention of COI.	N= 120 healthy or with mild disease patients who meet the anesthesiologists (ASA) physical status I and II.	Mean age: 42 years; 58 males, 62 females.	Group 1: patients received placebo (n=40) vs. Group 2: patients received 4 mg of ondansetron intravenously (n=40) vs. Group 3: patients received 25 mg of droperidol intravenously (n=40).	Follow up at 3, 5, 15, and 30 minutes as well as continuous follow up over the 24 hours post operation.	Frequency of incidences of vomiting over the 24 hours post recovery was 18% in the ondansetron group vs 32% in the placebo group ($p<0.05$). Droperidol was 25% ($p<0.05$ vs placebo), not statistically different than ondansetron ($p>0.05$).	"Ondansetron 4 mg Iv is as effective as droperidol and better than placebo in preventing nausea and vomiting in patients undergoing middle ear surgery."	Data suggest comparable efficacy with the benefit of ondansetron providing better relief of nausea with less reported sedative and dysphoric adverse effects.
Eberhart 1999 (score= 7.0)	Droperidol/ Dimenhydrinate	RCT	No mention of sponsorship or COI.	N=140 male hospitalized patients undergoing nasal surgery	Mean age: 34.8 years; 140 males, 0 females	Placebo: received 100 mL saline (n=) vs Dimenhydrinate: received 1mg kg^{-1} diluted in 100 mL of saline (n=) vs Droperidol: received 15 µg kg^{-1} diluted in 100 mL of saline (n=) vs Combination Group: received droperidol 15 µg kg^{-1} and dimenhydrinate 1mg kg^{-1} diluted together in 100 mL of saline	2, 5, 8, 24 hours	Incidence without PONV was 63% in placebo group, 77% in dimenhydrinate group ($p=0.21$), 83% in the droperidol group ($p=0.07$), and 94% in the combination group ($p=0.0015$). Severity of PONV was reduced in droperidol group and in the combination group only. Severity of PONV was reduced in all groups compared to placebo ($p=0.0003$).	"We conclude that combining anti-emetic drugs having different sites of action results in an additional action that is superior to the effect of each drug alone."	Data suggest a combination of droperidol and dimenhydrinate is best for reducing the frequency of PONV compared to placebo or either drug alone.
Valanne 1985 (score= 7.0)	Droperidol	RCT	No mention of sponsorship or COI.	N=100 patients undergoing restorative dentistry and oral surgery	Mean age:27.5 years; 67 males, 32 females	Droperidol: received droperidol 0.014 mg/kg (n=49) vs Saline: received equivalent amount of saline (n=50)	1 hour, 6, 12 hours	Incidence of PONV was low (16% to 24%). After 6 hours of anaesthesia, more patients were nauseated in droperidol group compared to saline group.	"[A]lthough droperidol is a less effective antiemetic after outpatient than after inpatient enflurane anaesthesia, small doses of droperidol may be used for outpatients prone to vomiting to prevent delayed	Data suggest a small dose of droperidol may be effective to reduce PONV.

				under general anaesthesia					discharge from the clinic due to prolonged vomiting."	
Paech 1995 (score= 7.0)	Ondansetron / droperidol	RCT	Sponsored by women's and infants' health-King Edward memorial hospital foundation. No mention of COI.	N=259 female patients experienced abdominal gynecological surgery.	Mean age: 48.7 years; 0 male, 259 females.	Group O: patients received 8 mg of ondansetron intravenously during the surgery (n=83) vs. Group D: patients received 2.5 mg of droperidol intravenously during the surgery (n=89) vs. Group P: patients received saline placebo intravenously (n=87).	Follow up continuous over the 24 hours post operation with specific follow up at 6 and 24 hours.	Ondansetron and droperidol groups indicated effectiveness to prevent vomiting after surgery, compared to placebo group (Odds ratio=0.4; 95%CI=0.2 to 0.9). The incidence of vomiting in droperidol group was the lowest (25%), and that in ondansetron group was the second lowest (30%), and that in placebo group was 44% ($p<0.05$).	"Although, compared to placebo, both droperidol and ondansetron administered intraoperatively reduced vomiting after major abdominal gynaecological surgery, the incidence during the first 24 postoperative hours was very high in all groups."	Data suggest comparable efficacy between ondansetron and droperidol for reducing PONV.
Jellish 1998 (score= 7.0)	Ondansetron / droperidol	RCT	Partially sponsored by Glaxo Welcome Inc. No mention of COI.	N= 120 healthy or with mild disease patients who meet the anesthesiologists (ASA) physical status I and II.	Mean age: 42 years; 58 males, 62 females.	Placebo group: patients received placebo (n=40) vs. Ondansetron group: patients received 4 mg of ondansetron intravenously (n=40) vs. Droperidol group: patients received 25 mg of droperidol intravenously (n=40).	Follow up at 3, 5, 15, and 30 minutes as well as continuous follow up over the 24 hours post operation.	66% patients in ondansetron group, 36% in droperidol group, and 33% in placebo group showed nausea after surgery, and the difference of incidence of nausea among the groups was not significant ($p>0.05$). The incidence of vomiting also showed no significant difference among the three groups: 16% in ondansetron group vs. 9% in droperidol group vs. 20% in placebo group.	"Ondansetron 4 mg intravenously is as effective as droperidol and better than saline solution in preventing nausea and vomiting in patients undergoing otologic surgery. No cost advantage as determined by lower use of rescue antiemetics or shorter postanesthesia care unit times was noted after ondansetron therapy."	Data suggest comparable efficacy between ondansetron and droperidol.
Purhonen 1997 (score= 7.0)	Tropisetron	RCT	No mention of sponsors	N = 146 female patients undergoi	Mean age: 50.3 years; 0 males,	Patients were divided into three groups to receive 100 mL saline	Follow up at 2, 6, 24, and 48 hours post-op.	There was less patients needing to take metoclopramide that were given tropisetron	"We conclude that 5 mg of IV tropisetron is well tolerated and reduces the incidence and intensity of	Data suggests lack of efficiency.

			hip or COI.	ng an elective gynecologic incontinence operation.	146 females.	containing either tropisetron (n=48), droperidol (n=49), or only saline (n=49) 15 minutes post-op.		compared to the placebo group (p<0.05). 8%, 22%, and 29% of patients vomited on day one of post-op when given tropisetron, droperidol, and placebo, respectively (p<0.05). There was more patients who had a cough during 6-24 hours post-op in the tropisetron group vs placebo group (p<0.05).	postoperative vomiting, but not nausea and retching, after gynecologic incontinence operation performed under general anesthesia. Droperidol 1.25 mg IV is comparable to placebo in preventing PONV, and patients experience more adverse effects."	
Helmy 1999 (score= 6.5)	Ondansetron /Droperidol/ Metoclopramide	RCT	No mention of sponsorship or COI.	N=160 patients scheduled for laparoscopic cholecystectomy under total intravenous anesthesia	Mean age: 40 years; 35 males, 125 females	Ondansetron: received IV 4 mg ondansetron (n=40) vs Droperidol: received IV 1.25 mg droperidol (n=40) vs Metoclopramide: received IV 10 mg metoclopramide (n=40) vs Placebo: received single intravenous dose of general anesthesia (n=40)	Follow up at 1 hour, 4 hours, 24 hours	Incidence of nausea was lower in ondansetron (7.5%) compared to the other 3 groups (27.5% in both droperidol and metoclopramide, 42.5% in placebo; p<0.05). Incidence of vomiting was lower in the ondansetron group (7.5%) compared to 25% in droperidol, 22.5% in metoclopramide, and 47.5% in placebo (p<0.05).	"It is concluded that pre-anaesthetic intravenous ondansetron (4 mg) is superior to droperidol (1.25mg), metoclopramide (10 mg) and placebo as a prophylactic anti-emetic in patients undergoing laparoscopic cholecystectomy under TIVA, especially during the first 4 h. The prophylactic use of anti-emetic treatment is recommended in this setting."	Data suggest comparable efficacy between ondansetron, droperidol and metoclopramide compared to placebo in the first 4 hours post-operatively, but ondansetron was superior to all other groups for the period of 24 hours post-op.
Wu 2000 (score= 6.5)	Ondansetron / Droperidol	RCT	Sponsored by St. Michael's hospital health science research center in Toronto, Canada. No	N=160 female patients experienced laparoscopy.	Mean age: 32. 8 years; 0 male, 160 females.	Placebo group: patients received saline intravenously before surgery (n=38) vs. Droperidol group: patients received 1.25 mg of droperidol intravenously (n=38) vs. Ondansetron group:	Follow-up at baseline, 30, 90, 150, and 210 minutes as well as 24 hours post operation.	Compared with placebo group, droperidol group was more effective to prevent postoperative nausea and vomiting (PONV) (p=0.006), same did ondansetron group (p=0.028) and combination group (p<0.001). No significant difference was found among the three	"The results of this study suggest that the combination of 4 mg ondansetron and 1.25 mg droperidol is more efficacious as a prophylactic anti-emetic than either agent alone during the 24 hr post-surgery. This additive effect may be due to the different mechanisms of	Data suggest combining droperidol to ondansetron results in an addictive effective resulting in better PONV control.

			mention of COI.			patients received 4 mg of ondansetron intravenously (n=37) vs. Combo group: patients received 1.25 mg of droperidol and 4 mg of ondansetron intravenously (n=39).		treatment groups (p=0.093).	action of ondansetron and droperidol."	
Maestre 1997 (score= 6.5)	Droperidol/ Ondansetron /Metochlopramide	RCT	No mention of sponsorship or COI.	N=264 patients undergoing elective, outpatient surgery	Mean age: 29.5 years; 119 males, 144 females	Control: received saline vs Metoclopramide: received 10 mg metoclopramide vs Droperidol: received 1.25 mg vs Ondansetron: received 4 mg vs Ondansetron: received 2 mg. All groups were mixed with 0.9% sodium chloride solution to a final volume of 100 mL.	12, 24 hours	Incidence of emetic episodes was 6% for all groups. Relative risk of PONV was 1.8 (95% CI 0.5-6.6) for ondansetron 4 mg group.	"[P]reoperative administration of metoclopramide, droperidol and two different doses of ondansetron are not superior to placebo for preventing PONV. Until more information becomes available, the key to judicious use of a prophylactic antiemetic should be the preoperative identification of patients who are at high risk of PONV."	Data suggest lack of efficacy for all drugs as none were better than placebo for preventing PONV after ambulatory surgery.
Kreisler 2000 (score= 6.5)	Droperidol/ Ondansetron /Promethazine	RCT	No mention of sponsorship or COI.	N=150 patients undergoing general anesthesia	Mean age: 48.3 years; 6 males, 25 females	Part 1: Droperidol: received 0.625 mg of droperidol IV (n=74) vs Placebo: received 0.625 mg saline (n=76)	24 hours	Greater number of patients suffered from vomiting and retching in the placebo group (p=0.008). Incidence of PONV was 6.8% in droperidol group compared to 40.8% in placebo (p<0.001). Delayed PONV was experienced by 22% of droperidol group compared to 32% in placebo (p=0.232).	"Droperidol, ondansetron, and promethazine were equally effective in treating established PONV, without significant differences in side effects or time to postanesthesia care unit discharge."	Data suggest comparable efficacy between droperidol, ondansetron and promethazine for PONV.

Koivuranta 1997 (score= 6.5)	Ondansetron / Droperidol	RCT	Sponsored by Emil Aaltonen foundation of Finland. No mention of COI.	N=439 female patients experienced gynecological laparoscopy.	Mean age: 41.4 years; 0 male, 439 females.	Ondansetron group: patients received 8 mg of ondansetron intravenously during anesthesia (n=195) vs. Droperidol group: patients received 1.25 mg of droperidol intravenously during anesthesia (n=193) vs. Placebo group: patients received 10 ml of 0.9% sodium chloride solution intravenously during anesthesia (n=51).	Follow up at 2 in the recovery room and 24 hours on the ward.	The incidence of nausea in placebo group (67%) was higher than that in ondansetron group (48%) and droperidol group (50%), and the difference was significant (p=0.02). Ondansetron group (18%) indicated lower incidence of vomiting than that in droperidol group (26%) (p=0.05) and placebo group (37%) (p=0.004).	"The efficacy of prophylactic ondansetron and droperidol in reducing postoperative nausea associated with laparoscopic surgery in female inpatients was similar, but ondansetron appeared to be slightly more efficient than droperidol in preventing vomiting."	Data suggest both drugs better than placebo but ondansetron best for PONV control.
Fortney 1998 (score= 6.5)	Ondansetron / Droperidol	RCT	Sponsored by Glaxo Wellcome Inc. No mention of COI.	N=2061 outpatients experienced surgical procedure.	Mean age: 35.2 years; 244 males, 1817 females.	Placebo group: patients received normal saline less than 20 minutes before anesthesia (n=518) vs. Droperidol group 1: patients received 0.625 mg of droperidol less than 20 minutes before anesthesia (n=518) vs. Droperidol group 2: patients received 1.25 mg of droperidol less than 20 minutes before anesthesia (n=510) vs. Ondansetron group: patients	Follow up at baseline on admission to the postanesthesia care unit (PACU), and the following 30, 60, 90, and 120 minutes. Addition follow up at 24 hours post discharge.	2 hours after surgery, higher number of patients in ondansetron (29%), droperidol group1 (29%) and droperidol group 2 (43%) indicated complete absence of nausea and vomiting, compared with placebo group (23%) (p<0.005). 24 hours after surgery, treatment groups still indicated higher proportion of patients who were absent from nausea, compared with placebo group (p<0.05); however, the differences among the three treatment groups was not significant (p>0.05).	"In summary, we showed ondansetron 4 mg, droperidol 0.625 mg, and droperidol 1.25 mg to be superior to placebo for the relief of PONV in a study involving more than 2000 adults outpatients at high risk of PONV."	Data suggest comparable efficacy and patient satisfaction between ondansetron and droperidol for prevention of PONV.

						received 4 mg of ondansetron less than 20 minutes before anesthesia (n=515).				
Tang 1996 (score= 6.0)	Droperidol/ Ondansetron	RCT	No mention of sponsorship or COI.	N=161 females undergoing outpatient gynecologic surgery	Mean age: 29 years; 0 males, 161 females	Placebo: received saline (n=40) vs Droperidol 0.625: received 0.625 mg of droperidol (n=41) vs Droperidol 1.25: received 1.25 mg droperidol (n=40) vs Ondansetron: received 4 mg ondansetron (n=40)	Follow up over the first 24 hours	Incidence of emesis was lower in both droperidol and ondansetron groups compared to placebo ($p<0.05$). Incidence of nausea was only different between ondansetron and placebo ($p<0.05$).	"In summary, this study has demonstrated that droperidol 0.625 mg IV is as effective as ondansetron 4 mg IV in the prophylaxis of PONV in women undergoing outpatient gynecologic surgery."	Data suggest comparable efficacy between droperidol and ondansetron but droperidol is more cost effective at time of this article.
Paxton 1995 (score= 6.0)	Metoclopramide/ ondansetron / droperidol	RCT	No mention of sponsorship or COI.	N=118 patients underwent gynaecological laparoscopy.	Mean age: 31.5 years; no mention of sex.	Ondansetron group: patients received 4 mg ondansetron (n=32) vs. Droperidol group: patients received 1 mg droperidol (n=29) vs. Metoclopramide group: patients received 10 mg metoclopramide (n=29) vs. Placebo group: patients received 1 mg placebo (n=28).	Follow up at 1, 2, 4, 6, 12, 24, and 48 hours post operation.	25% patients in ondasetron group, 86% in droperidol group, 59% in metoclopramide group, 96% in placebo group had nausea. 18% patients in ondansetron group, 48% in droperidol group, 41% in metoclopramide, and 48% in placebo group had vomiting.	"In conclusion, a direct comparison of ondansetron 4 mg with metoclopramide 10 mg and droperidol 1 mg showed it to be superior for prophylaxis against PONV."	Data suggest ondansetron was significantly better than metoclopramide or droperidol as well as placebo for both nausea and vomiting post laparoscopy. Additionally, the number of patients requiring "rescue meds" much lower in ondansetron group.
Gan 1994 (score= 6.0)	Droperidol/ Ondansetron	RCT	No mention of sponsorship or COI.	N=120 patients undergoing hip and knee replacements and femoral	Mean age: 59.0 years; 53 males, 67 females	Droperidol: received 25-mL bag of normal saline containing 1.25 mg of droperidol after surgery completion (n=38) vs Ondansetron:	24 hours	Symptom free patients were 32.5% of placebo, 53% after droperidol, and 62% after ondansetron. Lower incidence of vomiting was observed with ondansetron and droperidol compared to	"In this study, we demonstrated that there was no significant difference between prophylactic ondansetron and droperidol in the incidence of postoperative nausea (21% *vs* 29%, respectively) and	Data suggest comparable efficacy for PONV in total hip and total knee patients between ondansetron and droperidol compared to placebo.

				resections		received 25-mL bag of normal saline containing 4 mg of ondansetron after surgery completion (n=42) vs Placebo: received 25-mL bag of normal saline after surgery completion (n=40)		placebo (p<0.01). Incidence of nausea was 23% in placebo, 29% in droperidol, and 21% in ondansetron. Incidence of rescue antiemetic was 38% in placebo, 34% in droperidol, and 17% in ondansetron.	vomiting (17 *vs* 18%, respectively)."	
Desilva 1995 (score= 5.5)	Ondansetron / Droperidol/ Metoclopramide	RCT	Sponsored by Beth Israel anesthesia foundation. No mention of COI.	N=360 patients experienced total abdominal hysterectomy (TAH).	Mean age: 46.4 years; no mention of sex.	Group O: patients received 4 mg of ondansetron intravenously (n=58) vs. Group D: patients received 1.25 mg of droperidol intravenously (n=55) vs. Group P: patients received 5 mg of perphenazine intravenously (n=57) vs. Group M: patients received 10 mg of metoclopramide intravenously (n=58) vs. Placebo group: patients received normal saline (n=58).	Follow up at baseline, 5, 10, and 15 mins as well as ever 30 mins for 4 hrs post operation.	Patients in ondansetron and metoclopramide groups indicated no significant difference for their nausea score, compared with placebo group (p>0.05). The number of patients free of SES in the Ondansetron group was 37% (p<0.05 vs placebo), 42% in the Droperidol group (p<0.0005 vs placebo), 40% in the Perphenazine group (p<0.05 vs placebo) and 29% in the Metoclopramide group (p>0.05)	"Although ondansetron, droperidol, and perphenazine were effective in providing antiemetic prophylaxis, only IV perphenazine was free of side effects. Hence, we conclude that perphenazine is the best choice for antiemetic prophylaxis after TAH."	Data suggest comparable efficacy between ondansetron, droperidol and perphenazine for PONV. Metoclopramide found ineffective.
Cozanitis 1996 (score= 5.5)	Droperidol/Ranitidine/Placebo	RCT	Sponsored partially by Glaxo (UK). No mention of COI.	N=180 Finnish patients undergoing abdominal	Mean age: 46.2 years; no mention of sex.	Ranitidine: received 300 mg orally on the night before surgery and again the following morning, 30 min before end of surgery received	Followed up in recovery room and in ward.	Ranitidine showed 75% of patients free from PONV, compared to 88% of patients in droperidol, and 65% of patients with placebo (p=0.0109). After patients were returned to ward, showed similar	"In conclusion, when compared with placebo, both ranitidine and droperidol reduced the incidence of PONV. During the immediate postoperative period,	Data suggest droperidol better than ranitidine and both better than placebo in prevention of PONV.

				hysterectomy		isotonic saline 0.3 mL IV (n=60) vs Droperidol: received placebo tablets night before surgery and on morning of surgery, 30 min before surgery ended, given droperidol 0.75 mg (0.3 mL) injected IV (n=60) vs Placebo: received placebo tablets on evening before surgery and morning before surgery, then given 0.3 mL saline injected IV (n=60) All patients received temazepam 20 mg night before surgery, and 10 mg diazepam on morning of surgery.		difference (p=0.007). Preventing PONV in recovery room was greater in droperidol compared to placebo (n=53 vs n=39, 3p=0.015). The results for rantidine compared to placebo was ineffective (n=45 vs n=39, p=0.319). When observed in the ward, ranitidine and droperidol were more effective than placebo (3p=0.010, 3p=0.003, respectively).	droperidol provided better control of PONV than did ranitidine. Both anti-emetics were more effective than placebo during the period when patients were back on the ward. The need for the rescue drug did not differ among the groups."	
Madej 1986 (score= 5.5)	Droperidol/ Domperidone/Metoclopramide	RCT	No mention of sponsorship or COI.	N=200 females undergoing major gynaecological surgery	Mean age: 39.2 years; 0 males, 197 females	Droperidol: (n=49) vs Metoclopramide: (n=48) vs Domperidone: (n=50) vs Placebo: (n=50)	6 hours	Incidence of emetic sequelae in placebo group was 58%. Droperidol group showed less PONV compared to placebo ($p<0.05$). Domperidone compared to placebo showed less PONV ($p<0.01$). Metoclopramide showed less PONV compared to placebo ($p<0.02$). Incidence of pain was not different	"It was concluded that the high incidence of emetic sequelae was sufficient to justify the use of prophylactic antiemetics. Droperidol 2.5 mg i.v. was effective, and produced no significant adverse effects."	Data suggest droperidol better than domperidone and metoclopramide in preventing PONV post major gynecological surgery.

								between groups compared with placebo.		
Prochlorperazine										
Chen 1998 (score= 6.5)	Ondansetron / Prochlorperazine	RCT	No mention of sponsors hip or COI.	N=78 patients experienced hip or knee replacement surgery.	Mean age: 62.5 years; 29 males, 49 females.	Ondansetron group: patients received 4 mg of ondansetron hydrochloride intravenously (n=37) vs. Prochlorperazine group: patients received 10 mg of prochlorperazine intravenously (n=41).	Follow up at 14 predefined time intervals over the 48 hours post operation.	Patients in ondansetron group (81%) indicated greater incidence of nausea than patients in prochlorperazine group (56%), and the difference was significant (Odds ratio=3.4; 95%CI=1.2 to 9.4; p=0.04). The ondansetron group (49%) also showed higher incidence of vomiting than prochlorperazine group (32%) (Odds ratio=2.0; 95%CI=0.8 to 5.0).	"Prochlorperazine is associated with superior Efficacy and significant cost savings compared with ondansetron for the prevention of PONV in patients undergoing total hip and total knee replacement procedures."	Data suggest prochlorperazine better than ondansetron for control of PONV.
van den Berg 1996 (score= 5.5)	Ondansetron / Prochlorperazine	RCT	No mention of sponsors hip or COI.	N=148 patients received balanced inhalational anesthesia.	Mean age: 29.7 years; 79 males, 69 females.	Placebo group: patients received 1 to 2 ml of saline intravenously (n=37) vs. im-P group: patients received 0.2 mg of prochlorperazine intramuscularly (n=37) vs. iv-P group: patients received 0.1 mg of prochlorperazine intravenously (n=37) vs. Ondansetron group: patients received 0.06 mg of ondansetron intravenously (n=37)	Follow up continuous over the 24 hours post operation.	The nausea and vomiting combination in placebo group dropped to 53% and the difference was significant (p<0.0005), and that in im-prochlorperazine group dropped to 16% with significant change (p<0.0005), and that in iv-ondansetron group dropped to 19% with significant change (p<0.0005), and that in iv-prochlorperazine group dropped to 30% (p<0.05). The frequency of patients absent from postoperative nausea and vomiting was increased in placebo group to 27%,	"Prophylactic prochlorperazine 0.2 mg.kg^{-1} im and ondansetron 0.06 rag. kg -t iv are similarly efficacious in reducing nausea with vomiting after tympanoplasty, while prochlorperazine 0.1 rag. Kg^{-1} iv is less efficacious."	Data suggest IM prochlorperazine 0.2 mg and ondansetron 0.06 mg/kg are comparable but IV prochlorperazine is ineffective.

								57% in im-prochlorperazine group (p<0.01), 62% in iv-ondansetron group (p<0.005), and 43% in iv-prochlorperazine group with no significant change (p>0.05).		
Cyclizine										
Cholwill 1999 (score= 6.5)	Cyclizine/Ondansetron	RCT	No mention of sponsorship or COI.	N = 180 ASA I or II women undergoing day-case gynaecological laparoscopy.	Mean age: 31.1 years; 0 males, 180 women	Ondansetron group: received 4 mg i.v. of ondansetron (n=60) vs Cyclizine group: received 50 mg i.v. (n=57) vs Placebo group: received 0.9% saline i.v. (n=58). all received this before induction of anesthesia	Follow up at 24 hours.	Moderate or severe nausea was reduced in both ondansetron and cyclizine (P=0.02 and P=0.001) when compared with saline. Requirement for escape antiemetic was also reduced in both ondansetron and cyclizine (P=0.04 and P<0.001). Patients with ondansetron and cyclizine suffered no PONV more when compared with placebo (31% and 33% vs 12%; P=0.02 and P<0.01).	"We would recommend that cyclizine should be considered for first-line antiemetic therapy for DL but that ondansetron may be an equally valid choice where a greater amount of tissue trauma is anticipated, such as with LS."	Data suggest comparable efficacy between both medications with fewer rescue medications required in the cyclizine group.
Dimenhydrinate										
Eberhart 1999 (score= 7.0)	Droperidol/ Dimenhydrinate	RCT	No mention of sponsorship or COI.	N=140 male hospitalized patients undergoing nasal surgery	Mean age: 34.8 years; 140 males, 0 females	Placebo: received 100 mL saline (n=) vs Dimenhydrinate: received 1mg kg^{-1} diluted in 100 mL of saline (n=) vs Droperidol: received 15 µg kg^{-1} diluted in 100 mL of saline (n=) vs Combination Group: received droperidol 15 µg kg^{-1} and dimenhydrinate	2, 5, 8, 24 hours	Incidence without PONV was 63% in placebo group, 77% in dimenhydrinate group (p=0.21), 83% in the droperidol group (p=0.07), and 94% in the combination group (p=0.0015). Severity of PONV was reduced in droperidol group and in the combination group only. Severity of PONV was reduced in all groups	"We conclude that combining anti-emetic drugs having different sites of action results in an additional action that is superior to the effect of each drug alone."	Data suggest a combination of droperidol and dimenhydrinate is best for reducing the frequency of PONV compared to placebo or either drug alone.

						1mg kg^{-1} diluted together in 100 mL of saline		compared to placebo (p=0.0003).		
Sandhu 1999 (score= 5.5)	Ondansetron / Dimenhydrinate	RCT	No mention of sponsorship or COI.	N=87 female patients experienced gynecological laparoscopy.	Mean age: 32.7 years; 0 male, 87 females.	Placebo group: patients received placebo intravenously immediately after anesthesia (n=38) vs. Dimenhydrinate group: patients received 50 mg of dimenhydrinate intravenously immediately after anesthesia (n=33) vs. Ondansetron group: patients received 8 mg of ondansetron intravenously immediately after anesthesia (n=29).	Follow up at baseline post operation, 1 and 2 hrs post PACU admission and the next day.	The incidence of postoperative nausea and vomiting was similar among the three groups: placebo group=21% vs. dimenhydrinate group=17% vs. ondansetron group=10%; and the difference was not significant (p>0.05). Patients in dimenhydrinate group were delayed for their immediate recovery from anesthesia, and showed lower score on digit symbol substitution test (p<0.05).	"PONV is a multifactorial problem, which may not have a singular therapeutic solution. PONV is an important complication and is distressing to our patients. Prior work has examined the efficacy of prophylactic antiemetic therapy."	Data suggest lack of efficacy.
Promethazine										
Barrett 2011 (score= 7.5)	Ondansetron /Metoclopramide/ Promethazine	RCT	No mention of sponsorship or COI.	N=163 patients presenting to the ED with undifferentiated nausea	Mean age: 32 years; 52 males, 111 females	Ondansetron: received 4 mg ondansetron in a 2 mL syringe (n=42) vs Metoclopramide: received 0 mg metoclopramide in 2 mL syringe (n=43) vs Promethazine: received 12.5 mg promethazine in 2 mL syringe so that the dose was actually 6.25 mg/mL (n=45) vs Placebo:	30 minutes	No difference was detected between groups for antiemetic efficacy (Kruskal-Wallis Test, p=0.16). Median VAS score reduction compared to ondansetron group were -8mm (95% CI -18.5-3) for metoclopramide, -7mm (95% CI -21-5.5) for promethazine, and 6 mm (95% CI -7-20) for saline. More than 40% of patients showed need for additional antiemetics	"Our study shows no evidence that ondansetron is superior to metoclopramide and promethazine in reducing nausea in ED adults. Early study termination may have limited detection of ondansetron's superior nausea reduction over saline."	Trial investigation of nausea only. Did not evaluate vomiting. Data suggest ondansetron not superior to either metoclopramide or promethazine.

						received isotonic sodium chloride solution placebo (n=41)		compared to 22% of patients in metoclopramide group.		
Kreisler 2000 (score= 6.5)	Droperidol/ Ondansetron /Promethazine	RCT	No mention of sponsorship or COI.	N=150 patients undergoing general anesthesia	Mean age: 48.3 years; 6 males, 25 females	Part 1: Droperidol: received 0.625 mg of droperidol IV (n=74) vs Placebo: received 0.625 mg saline (n=76)	24 hours	Greater number of patients suffered from vomiting and retching in the placebo group (p=0.008). Incidence of PONV was 6.8% in droperidol group compared to 40.8% in placebo (p<0.001). Delayed PONV was experienced by 22% of droperidol group compared to 32% in placebo (p=0.232).	"Droperidol, ondansetron, and promethazine were equally effective in treating established PONV, without significant differences in side effects or time to postanesthesia care unit discharge."	Data suggest comparable efficacy between droperidol, ondansetron and promethazine for PONV.
Shirdashtzadeh 2011 (score = 5.5)	Promethazine	RCT	No mention of COI or sponsorship.	N = 75 patients who underwent appendectomy surgically	Mean age: 24.6 years; 75 males, 0 females	Group 1: Received 0.05 mg/kg Midazolam intravenously (n = 25) vs Group 2: Received 1 mg/kg Promethazine intravenously (n = 25) vs Group 3: Received placebo saline solution intravenously (n = 25) *All medications were given to patients 5 minutes prior to surgery	Follow up continuous for 24 hours	Postoperative nausea and vomiting (PONV) occurrence during first 24 hours was 18.2% in Midazolam group, 0% in Promethazine group, and 96.2% in placebo group. P values not given.	"Our study suggests that midazolam can be used as multipurpose drugs in postoperative nausea and vomiting as a preoperative medication after appendectomy and treatment using midazolam for anti-emetic, prophylaxis provide a similar effect compared to promethazine in the present study."	Data suggest parenteral promethazine (Phenergan) better than placebo when used preoperatively for PONV post-appendectomy. Study also suggests midazolam comparable to promethazine (Phenergan).

Metoclopramide										
Egerton - Warburton 2014 (score= 8.0)	Ondansetron / metoclopramide	RCT	Sponsored by the Australasian college of emergency medicine Morson Taylor award and the Southern health emerging researcher fellowship. No COI.	N = 258 emergency department patients with undifferentiated nausea and vomiting	Median age: 42 years; 89 males, 169 females.	Ondansetron group: patients received 12 ml of syringes contained 4 mg ondansetron intravenously (n=87) vs. Metoclopramide group: patients received 22 ml of syringes contained 20 mg metoclopramide intravenously (n=88) vs. Placebo group: patients received 12 ml of syringes contained 0.9% of saline solution (n=83).	Follow up at baseline and 30 minutes	The difference of primary outcome in this study visual analog scale (VAS) rating in ondansetron group was 27 mm (95%CI=22 to 33 mm), and that in metoclopramide group was 28 mm (95%CI=22 to 34 mm), and that in placebo group was 23 mm (95%CI=16 to 30 mm). The difference among the three groups was not statistically significant (p>0.05).	"There was a trend toward greater reductions in VAS ratings and a lesser requirement for rescue medication in the antiemetic drug groups, but differences from the placebo group did not reach significance."	Data suggest lack of efficacy of both study drugs compared to placebo but a trend towards less rescue medication being needed.
Kaufmann 1994 (score= 7.5)	Droperidol/ Metoclopramide/ Tropisetron	RCT	No mention of sponsorship or COI.	N=286 patients undergoing elective surgery	Mean age: 56.7 years; 130 males, 156 females	Group 1: received placebo of only morphine from the PCA device (n=67) vs Group 2: received antiemetic mixed with morphine in the PCA syringe of metoclopramide (n=71) vs Group 3: received antiemetic mixed with morphine in the PCA syringe of droperidol (n=70) vs	3, 18 hours, then 6 hours from thereafter	Incidence of postoperative nausea and vomiting (PONV) was 54% for group 1, 40% for group 2, 17% in group 3 (p<0.0001), and 33% in group 4 (p=0.02). Droperidol reduced incidence (p<0.001) and severity (p<0.01) of PONV for 36 hours.	"In summary, combining droperidol and morphine for PCA after major orthopedic surgery effectively reduced both the incidence and severity of PONV."	Data suggest both droperidol and tropisetron are effective antiemetics but tropisetron requires more than one does for efficacy.

						Group 4: received only morphine from the PCA device (n=78)				
Wilson 2001 (score= 7.5)	Metoclopramide/ ondansetron	RCT	No mention of sponsorship or COI.	N=232 patients experience laparoscopic cholecystectomy with general anesthesia.	Mean age: 43 years; 49 males, 183 females.	Metoclopramide group: patients received 30 ml syringe contained 10 mg intravenous metoclopramide 24 hours before surgery (n=72) vs. Ondansetron group: patients received 30 ml syringe contained 4mg intravenous ondansetron 24 hours before surgery (n=78) vs. Placebo group: patients received 30 ml syringe contained normal intravenous saline 24 hours before surgery (n=82).	Follow-up at baseline, 24 hours.	Patients in metoclopramide group indicated 32% incidence of nausea, patients in ondansetron group indicated 45%, and patients in placebo group indicated 44%. After anesthesia care, patients in metoclopramide group indicated 8% incidence of vomiting, patients in ondansetron group indicated 4%, and patients in placebo group showed 22% (Metoclopramide vs Placebo, p=0.03; Ondansetron vs Placebo, p<0.01) .	"Prophylactic administration of metoclopramide or ondansetron significantly reduces the incidence of postoperative vomiting for laparoscopic cholecystectomy, but neither drug was found to be significantly more effective than the other. Metoclopramide is a more cost-effective treatment."	Data suggest comparable efficacy compared to placebo.
Bilgin 2010 (score= 7.0)	Ondansetron /Metoclopramide/ Dexamethasone	RCT	Sponsored by Department of Anesthesiology and Reanimation (Turkey). No mention of COI.	N=160 patients undergoing elective gynecological surgery	Mean age: 43.2 years; 0 males, 160 females	Group D: received IV 8 mg dexamethasone (n=40) vs Group O: received 4 mg ondansetron IV (n=40) vs Group M: received 10 mg metoclopramide (n=40) vs Group P: received 0.9% saline (n=40)	0-24 hours	Incidence of PONV was 5% in group D, 0% in group O, 5% in group M, and 5% in group P. More patients required rescue antiemetics in placebo group compared to other groups (p<0.05).	"Prophylactic IV dexamethasone 8 mg significantly reduces the incidence of PONV in patients undergoing gyneco-logic surgery. At this dosage, dexamethasone is as effective as ondansetron 4 mg, and metoclopramide 10 mg, and is more effective than placebo."	Data suggest comparable efficacy between all 3 study drugs compared to placebo.

Maestre 1997 (score= 6.5)	Droperidol/ Ondansetron /Metochlopramide	RCT	No mention of sponsorship or COI.	N=264 patients undergoing elective, outpatient surgery	Mean age: 29.5 years; 119 males, 144 females	Control: received saline vs Metoclopramide: received 10 mg metoclopramide vs Droperidol: received 1.25 mg vs Ondansetron: received 4 mg vs Ondansetron: received 2 mg. All groups were mixed with 0.9% sodium chloride solution to a final volume of 100 mL.	12, 24 hours	Incidence of emetic episodes was 6% for all groups. Relative risk of PONV was 1.8 (95% CI 0.5-6.6) for ondansetron 4 mg group.	"In conclusion, this study suggest that preoperative administration of metoclopramide, droperidol and two different doses of ondansetron are not superior to placebo for preventing PONV. Until more information becomes available, the key to judicious use of a prophylactic antiemetic should be the preoperative identification of patients who are at high risk of PONV."	Data suggest lack of efficacy for all drugs as none were better than placebo for preventing PONV after ambulatory surgery.
Ali-Melkkila, 1996 (score= 6.5)	Tropisetron/ Metoclopramide	RCT	No mention of sponsorship or COI.	N= 120 patients undergoing ophthalmic surgery with general anesthesia.	Mean age: 45.4 years; 70 males, 50 females.	All patients were given 5 mg of diazepam orally 90 before operation. After anesthesia: group one was given 0.1 $mg.kg^{-1}$ tropisetron (n=40), group two was given 0.25 $mg.kg^{-1}$ metoclopramide (n=40), and group three was given saline (n=40) through an IV injection at the end of anesthesia.	Follow up during 24 hour post-op period.	27% of patients in tropisetron group experienced nausea vs 52% in placebo group ($p<0.01$). 35% of patients experienced nausea in metoclopramide group vs placebo ($p<0.05$). 15% of patients with metoclopramide vomited vs 30% in placebo group ($p<0.05$).	"[…] our results would argue against the use of tropisetron as the first choice antiemetic agent in the prevention of postoperative nausea and vomiting in ophthalmic patients."	Data suggest metoclopramide is best for decreasing PONV as tropisetron was effective for reducing only nausea.
Eberhart 2000 (score= 6.5)	Metoclopramide	RCT	No mention of sponsorship or COI.	N=160 ASA 1-2 male patients undergoing	Mean age: 37.5 years; 160 males, 0 female.	Metoclopramide group: patients received 0.3 $mg.kg^{-1}$ of metoclopramide (n=40) vs. Dimenhydrinate	Follow up at 2, 5, 8, and 24 hours.	62.5% patients in placebo group, 72.5% in metoclopramide group (p=0.54), 75% in dimenhydrinate group (p=0.34), 85% in	"Dimenhydrinate and metoclopramide were ineffective in reducing the incidence and the severity of PONV. Their combination reduced the incidence of	Data suggest each of efficacy of earlier drug alone but the combination did decrease incidence of PONV.

				endonasal surgery.		group: patients received 1 $mg.kg^{-1}$ of dimenhydrinate (n=40) vs. Combo group: patients received 0.3 $mg.kg^{-1}$ of metoclopramide and 1 $mg.kg^{-1}$ of dimenhydrinate (n=40) vs. Placebo group: patients received normal saline (n=40).		combination group (p=0.025) were free from nausea and vomiting 6 hours after medication intervention.	PONV compared with placebo."	
Wallenborn 2006 (score= 6.5)	Metoclopramide	RCT	Sponsored by Merck KgaA in Germany. No COI.	N=3140 patients undergoing regional or balanced anesthesia intraoperatively.	Age range: >50 years; 1349 males, 1791 females.	Group A: patients received no metoclopramide (n=788) vs. group B: patients received 10 mg of metoclopramide intravenously 30 to 60 minutes before surgery (n=783) vs. group C: patients received 25 mg of metoclopramide intravenously 30 to 60 minutes before surgery (n=781) vs. group D: patients received 50 mg of metoclopramide intravenously 30 to 60 minutes before surgery (n=788).	Follow up over the first 24 hours after surgery.	23.1% patients without metoclopramide treatment, 20.6% patients took 10 mg metoclopramide, 17.2% patients took 25 mg metoclopramide, and 14.5% patients took 50 mg metoclopramide indicated nausea and vomiting after operation. Group C showed significant change in nausea or vomiting <12 hours after surgery (p<0.001) and adverse drug reaction (p<0.01), so does group D in change of nausea or vomiting <12 hours after surgery (p<0.001), 12-24 hours after surgery (p<0.01) and adverse drug (p<0.001).	"The addition of 50 mg metoclopramide to 8 mg dexamethasone (given intraoperatively) is an effective, safe, and cheap way to prevent postoperative nausea and vomiting."	Data suggest the combo of 8mg of dexamethasone to 50mg metoclopramide is effective for PONV although smaller doses of metoclopramide may be equally effective with fewer adverse events.
Morris 1998 (score= 6.5)	Ondansetron / metoc	RCT	No mention of sponsors	N=1074 female patients experien	Mean age: 46 years; 0 male,	Ondansetron group: patients received 4 mg of ondansetron intravenously 30	Follow up continuous during the 0-24 hour	44% patients in ondansetron group, 37% in metoclopramide group, 25% in placebo indicated	"In summary, this study supports published findings that ondansetron is a well-tolerated agent and is a	Data suggest ondansetron better than metoclopramide for effectively reducing episodes of PONV.

	lopramide		hip or COI.	ced vaginal hysterectomy or gynecological surgery under general anaesthesia.	1074 females.	seconds before anesthesia (n=468) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously 30 seconds before anesthesia (n=462) vs. Placebo group: patients received normal saline intravenously 30 seconds before anesthesia (n=117).	period after recovery from anesthesia.	no episodes of emesis, and the difference was significant (p<0.001). Less patients in ondansetron group (n=215/465; 46%) requested rescue antiemetics, compared to patients in placebo (n=247/462; 53%) and metoclopramide groups (n=79/117; 68%) (p<0.001).	more effective antiemetic for preventing post-operative nausea and emesis than placebo"	
Helmy 1999 (score=6.5)	Ondansetron /Droperidol/ Metoclopramide	RCT	No mention of sponsorship or COI.	N=160 patients scheduled for laparoscopic cholecystectomy under total intravenous anesthesia	Mean age: 40 years; 35 males, 125 females	Ondansetron: received IV 4 mg ondansetron (n=40) vs Droperidol: received IV 1.25 mg droperidol (n=40) vs Metoclopramide: received IV 10 mg metoclopramide (n=40) vs Placebo: received single intravenous dose of general anesthesia (n=40)	Follow up at 1 hour, 4 hours, 24 hours	Incidence of nausea was lower in ondansetron (7.5%) compared to the other 3 groups (27.5% in both droperidol and metoclopramide, 42.5% in placebo; p<0.05). Incidence of vomiting was lower in the ondansetron group (7.5%) compared to 25% in droperidol, 22.5% in metoclopramide, and 47.5% in placebo (p<0.05).	"It is concluded that pre-anaesthetic intravenous ondansetron (4 mg) is superior to droperidol (1.25mg), metoclopramide (10 mg) and placebo as a prophylactic anti-emetic in patients undergoing laparoscopic cholecystectomy under TIVA, especially during the first 4 h. The prophylactic use of anti-emetic treatment is recommended in this setting."	Data suggest comparable efficacy between ondansetron, droperidol and metoclopramide compared to placebo in the first 4 hours post-operatively, but ondansetron was superior to all other groups for the period of 24 hours post-op.
Alexander 1997 (score=6.5)	Ondansetron / metoclopramide	RCT	No mention of sponsorship or COI.	N=124 ASA 1 and 2 patients received major lower limb orthope	Mean age: 56 years; 48 males, 76 females.	Placebo group: patients received placebo orally 1 hour before laparoscopy (n=40) vs. Metoclopramide group: patients received 10 mg of metoclopramide	Follow up at 4, 8, 12, 16, 20, and 24 hours.	The three groups indicated no significant difference for the incidence of nausea (p=0.77). 12% patients in ondansetron group, 31% in metoclopramide group, and 25% in placebo group indicated nausea and	"We conclude that oral premedication with ondansetron 8 mg was superior to metoclopramide 10 mg and placebo in preventing postoperative nausea and vomiting following major orthopaedic	Data suggest 8 mg ondasetron is better than 10 mg metoclopramide and both better than placebo for reducing PONV. Also, the use of rescue medications was lower in the ondansetron group.

				dic surgery.		orally 1 hour before the surgery (n=42) vs. Ondansetron group: patients received 8 mg of ondansetron orally 1 hour before the surgery (n=42).		vomiting before the surgery, and the difference was significant (p=0.035).	surgery in patients given epidural opioid analgesia."	
Naguib 1996 (score= 6.0)	Ondansetron / Tropisetron/ Granisetron/ Metoclopramide	RCT	No mention of sponsorship or COI.	N=132 patients	Mean age: 37.4 years; 24 males, 108 females.	Ondansetron group: patients received 4 mg of ondansetron intravenously (n=29) vs. Tropisetron group: patients received 5 mg of tropisetron intravenously (n=25) vs. Granisetron group: patients received 3 mg of granisetron intravenously (n=25) vs. Metoclopramide group: patients received 10 mg of metoclopramide intravenously (n=24) vs. Placebo group: patients received 0.9% normal saline intravenously (n=29).	Follow up at 1, 4, 9, 12, 18, and 24 hours after recovery from anesthesia.	65.6% patients in ondansetron group, 52% in granisetron, 48% in tropisetron, 29.2% in metoclopramide, and 27.6% in placebo were absent from emesis 24 hours after surgery. Ondansetron prophylactic antiemetic treatment showed lower incidence of postoperative nausea and vomiting than that in placebo and metoclopramide groups (p=0.02). On the other hand, Ondansetron group indicated longer first rescue antiemetic recovery times than that in metoclopramide and placebo groups (p<0.01).	"Ondansetron, when given prophylactically resulted in a significantly lower incidence of PONV than metoclopramide and placebo. Metoclopramide was ineffective"	Data suggest use of prophylactic ondansetron resulted in a significant reduction of PONV episodes, Metoclopramide was ineffective.
Paxton 1995 (score= 6.0)	Metoclopramide/ ondansetron /	RCT	No mention of sponsorship or COI.	N=118 patients underwent gynaecological	Mean age: 31.5 years; no mention of sex.	Ondansetron group: patients received 4 mg ondansetron (n=32) vs. Droperidol group: patients received 1	Follow up at 1, 2, 4, 6, 12, 24, and 48 hours post operation.	25% patients in ondasetron group, 86% in droperidol group, 59% in metoclopramide group, 96% in placebo group had nausea. 18% patients in	"In conclusion, a direct comparison of ondansetron 4 mg with metoclopramide 10 mg and droperidol 1 mg showed it to be superior for prophylaxis against PONV."	Data suggest ondansetron was significantly better than metoclopramide or droperidol as well as placebo for both nausea and vomiting post laparoscopy. Additionally, the number of

	droperidol			laparoscopy.		mg droperidol (n=29) vs. Metoclopramide group: patients received 10 mg metoclopramide (n=29) vs. Placebo group: patients received 1 mg placebo (n=28).		ondansetron group, 48% in droperidol group, 41% in metoclopramide, and 48% in placebo group had vomiting.		patients requiring "rescue meds" much lower in ondansetron group.
Desilva 1995 (score= 5.5)	Ondansetron / Droperidol/ Metoclopramide	RCT	Sponsored by Beth Israel anesthesia foundation. No mention of COI.	N=360 patients experienced total abdominal hysterectomy (TAH).	Mean age: 46.4 years; no mention of sex.	Group O: patients received 4 mg of ondansetron intravenously (n=58) vs. Group D: patients received 1.25 mg of droperidol intravenously (n=55) vs. Group P: patients received 5 mg of perphenazine intravenously (n=57) vs. Group M: patients received 10 mg of metoclopramide intravenously (n=58) vs. Placebo group: patients received normal saline (n=58).	Follow up at baseline, 5, 10, and 15 mins as well as ever 30 mins for 4 hrs post operation.	Patients in ondansetron and metoclopramide groups indicated no significant difference for their nausea score, compared with placebo group ($p>0.05$). The number of patients free of SES in the Ondansetron group was 37% ($p<0.05$ vs placebo), 42% in the Droperidol group ($p<0.0005$ vs placebo), 40% in the Perphenazine group ($p<0.05$ vs placebo) and 29% in the Metoclopramide group ($p>0.05$)	"Although ondansetron, droperidol, and perphenazine were effective in providing antiemetic prophylaxis, only IV perphenazine was free of side effects. Hence, we conclude that perphenazine is the best choice for antiemetic prophylaxis after TAH."	Data suggest comparable efficacy between ondansetron, droperidol and perphenazine for PONV. Metoclopramide found ineffective.
Davidson 1979 (score= 5.5)	Metoclopramide	RCT	No mention of sponsorship or COI.	N=115 patients underwent laparotomy and were evaluate	Mean age: 50.9 years; 58 males, 57 females.	Metoclopramide group: patients received 10 mg of metoclopramide on the evening and next morning after surgery (n=58) vs. Placebo group:	Follow up during the first 60 hours.	Patients who had gastrointestinal entry, suture or anastomosis (n=19) had less nausea after surgery than that in placebo group (n=22) ($p<0.05$). Patients who had abdominal surgery	"Overall postoperative ileus was unaffected by metoclopramide with the exception of a statistically significant earlier return to solid food diet in patients not undergoing	Data suggest metoclopramide did reduce postoperative nausea and vomiting.

				d for metoclopramide effect on postoperative adynamic ileus.		patients received 10 mg of intramuscular sterile buffer solution on the evening and next morning after surgery (n=57).		(n=2) indicated less emesis than that in placebo group (n=8) (p=0.027).	gastrointestinal anastomosis."	
Dobkin 1968 (score= 5.5)	Metoclopramide	RCT	Sponsored by Merck Sharp & Dohme research laboratories. No mention of COI.	N=284 patients scheduled major upper abdominal operation.	Mean age: 49 years; 125 males, 159 females.	Metoclopramide group: patients received 20 mg of metoclopramide intravenously 30 minutes before anesthesia with 200-400 mg thiopental and 80-120 mg gallamine (n=96) vs. Trimethobenzamide group: patients received 300 mg of trimethobenzamide intravenously 30 minutes before anesthesia with 200-400 mg thiopental and 80-120 mg gallamine (n=94) vs. Placebo group: patients received lactose as placebo intravenously 30 minutes before anesthesia with 200-400 mg thiopental and 80-120 mg gallamine (n=94).	Follow up during the first 24 hours postoperatively.	26.6% patients in placebo group experienced vomiting after intervention; 23% patients in metoclopramide group also experienced vomiting; 25.5% patients in trimethobenzamide group had vomiting.	"It appears that neither of the anti-emetic compounds is effective in reducing the incidence of nausea and vomiting associated with the administration of methoxyflurane-nitrous-oxide anesthesia for major upper abdominal operations."	Data suggest lack of efficacy as neither study drug was better than placebo.

Malins 1994 (score= 5.0)	Ondansetron / Metoclopramide	RCT	No mention of sponsorship or COI.	N=153 female patients experienced gynecological laparoscopy for sterilization.	Mean age: 32.7 years; 0 male, 153 females.	Group O: patients received 4 mg of ondansetron orally 1 hour before surgery (n=50) vs. group M: patients received 10 mg of metoclopramide orally 1 hour before surgery (n=50) vs. Placebo group: patients received placebo orally 1 hour before surgery (n=50).	Follow up when ready to leave the recovery room, on returning to the ward, and when ready for discharge from the hospital. Follow up about the 48 hours post operation in a take home questionnaire.	Less patients in ondansetron group (n=13) indicated emetic symptoms of vomiting or nausea 48 hours after surgery than that in placebo group (n=25), and the difference was significant (p<0.05, 95%CI= 5.6 to 42.4%). After leaving hospital, 40 patients in ondansetron group showed absence of nausea, compared to 33 in metoclopramide group and 30 in placebo group; the difference was significant (p<0.05, 95%CI=0.3 to 35%)	"Emetic symptoms (nausea or vomiting) occurred in 26% of patients who received ondansetron, 42% of those who received metoclopramide and 50% of those given placebo."	Data suggest ondansetron is approximately twice as effective as metoclopramide for decreasing PONV.
Hüseyinoğlu 2016 (score= 3.5)	Metoclopramide									Data suggest comparable efficacy between both treatment groups compared to placebo.
Rolapitant or Aprepitant										
Gan 2011 (score= 9.0)	Rolapitant	RCT	Sponsored by Schering Plough, Inc. One or more of the authors have or will receive benefits for personal or	N = 619 female patients who underwent elective open abdominal surgery with general anesthesia	Mean age: 46.1 ± 11.2 years; 0 males, 619 females	Received placebo saline solution (n=103) vs Received Rolapitant 5mg (n=103) vs Received Rolapitant 20mg (n=102) vs Received Rolapitant 70mg (n=103)	Follow up at 24, 48, 72, 96, & 120 hours	At 24 hours after surgery, groups that received rolapitant 20mg (p<0.05), 70mg (p<0.01), and 200mg (p<0.01) had higher incidence of no emetic episodes in comparison with the placebo group. At 120 hours after surgery, the groups receiving 70mg (p<0.01) and 120mg (p<0.01) rolapitant has higher incidence of no emetic episodes. Odds	"Rolapitant is superior to placebo in reducing emetic episodes after surgery and reduces the incidence of comiting in a dose-dependent manner. No differences in side effect profile were observed between rolipitant and placebo."	Data suggest rolapitant superior to placebo in preventing post-operative nausea and vomiting in a dose dependent manner

			professional use.			vs Received Rolapitant 200mg (n=104) vs Received Ondansetron 4mg (n=103) *all dosages administered intravenously following surgical procedure; rescue medications available to patients were IV ondansetron 4mg and oral ondansetron up to 8mg		ratio of rolapitant 70mg and 200mg to placebo for primary outcomes were 2.87 (p<0.001) and 4.73 (p<0.001), respectively.		
Diemunsch 2007 (score= 8.5)	Aprepitant	RCT	Sponsored by Merck and Co., Inc. One or more of the authors have received or will receive benefits for personal or professional use.	N = 922 patients who underwent major abdominal surgery and received general anesthesia	Mean age: 46 years; 83 males, 839 females	Group 1: Received 40mg Aprepitant (A40) orally before surgery (n=307) vs Group 2: Received 125mg Aprepitant orally before surgery(A125) (n=313) vs Group 3: Received 4mg Ondansetron intravenously before surgery (O4) (n=302)	Follow up at 24, & 48 hours	Complete response was achieved in 64% of A40 group, 63% in A125, and 55% in O4 group. Percentage of patients with no vomiting over 24 hours was 84% in A40 group, 86% in A125 group, compared with 71% in O4 group. The odds ratio for A40 vs O4 was 2.1 (p<0.001) and 2.5 for A125 vs O4 (p<0.001).	"Aprepitant was non-inferior to ondansetron in achieving complete response for 24 h after surgery. Aprepitant was significantly more effective than ondansetron for preventing vomiting at 24 and 48 h after surgery, and in reducing nausea severity in the first 48 h after surgery. Aprepitant was generally well tolerated."	Data suggest comparable efficacy between aprepitant and ondansetron for post-op nausea and vomiting prevention.

Vallejo 2012 (score= 8.0)	Ondansetron /Aprepitant	RCT	Sponsored by Merck Healthcare, Whitehouse Station, N.J., Department of Anesthesiology, Magee-Womens Hospital, Pitts-burgh, Pa. No COI.	N=150 ambulatory plastic surgery patients	Mean age: 44.5 years; 10 males, 140 females	Group A: received 40 mg of oral aprepitant plus 4 mg of intravenous ondansetron (given 2 hours prior to surgery (n=75) vs Group B: received oral placebo plus intravenous 4 mg of ondansetron(n=75)	Follow up at 1-48 hours	Incidence of vomiting was 29.7% for group B compared to 9.3% in group A (p=0.003, relative risk=31.3%, 95% CI 14.3-69.0). Nausea scores were lower in group A (median=5) compared to group B (median=8) (p=0.014).	"Aprepitant decreases postoperative vomiting and nausea severity and is a useful drug when used in combination with other antiemetics for prevention of postoperative nausea and vomiting. In patients undergoing plastic surgery procedures in which vomiting might be deleterious for surgical outcome, the addition of aprepitant would be especially useful."	Data suggest the addition of aprepitant to ondansetron.
Sinha 2014 (score= 8.0)	Aprepitant	RCT	Sponsored by Merck & Co., Inc. No COI.	N = 124 morbidly obese patients undergoing laparoscopic bariatric surgery	Mean age: 43 ± 12 years; 43 males, 81 females	Group A: Received 80 mg of aprepitant (n=64) Group P: Received placebo saline solution (n=60) *aprepitant and placebo administered intravenously; all patients also received intravenous ondansetron (4mg)	Follow up at 30 min, 1, 2, 6, 24, 48, & 72 hours	Incidence of vomiting at 72 hours 3% in group A and 15% in group P (p=0.021). Odds ratio for vomiting in group P compared to group A was 5.47 times (p=0.026). Average time to first vomiting was delayed in group A in comparison with group P (p=0.019). Complete response was seen in 42.18% of group A and 36.67% of group P (p=0.51).	"In morbidly obese patients undergoing laparoscopic bariatric surgery, addition of aprepitant to ondansetron can significantly delay vomiting episodes simultaneously lowering the incidence of postoperative vomiting."	Data suggest addition of aprepitant to ondansetron decreased frequency of post-operative vomiting.

Jung 2013 (score= 6.0)	Aprepitant	RCT	No mention of sponsorship or COI.	N = 120 patients undergoing laparoscopic hysterectomy surgery	Mean age: 46 years; 0 males, 120 females	Group 1: Received 80mg Aprepitant orally via tablets dissolved in water (A80) (n=40) vs Group 2: Received 125mg Aprepitant orally via tablets dissolved in water (A125) (n=40) vs Group 3: Control group received 10ml saline solution orally (n=40)	Continuous follow up for 48 hours	Complete response in the first 2 hours was 65% in A80 group (p=0.025) and 65% in A125 group (p=0.025) compared with 38% in placebo group. Complete response in the first 48 hours was 56% in A80 group (p=0.007) and 63% in A125 group (p=0.003) compared with 28% in placebo group.	"Aprepitant 80mg orally was effective in lowering the incidence of PONV in the first 48 h after anesthesia in patients receiving fentanyl-based PCA after gynecological laparoscopy."	Data suggest aprepitant (80mg po) was beneficial for lowering PONV during the first 48 hours post anesthesia in those patients on fentanyl-based PCA after gynecological lap. surgery.
Scopolamine										
Bailey 1990 (score= 4.0)	Scopolamine	RCT	Sponsored by Ciba Geigy pharmaceuticals, and Stanley research foundation. No mention of COI.	N=138 ASA physical status 1 or 2 patients experienced outpatient laparoscopy.	Mean age: 32 years; 0 males, 138 females.	Scopolamine group: patients received 1.5 mg scopolamine in a 0.2 mm thick unit with 5µg per hour delivery for 3 days (n=70) vs. Placebo group: patients received the same procedure as the scopolamine group but with no scopolamine involved (n=68).	Follow up hourly after surgery until discharge.	Repeated vomiting episodes in placebo group were more frequent than that in scopolamine group (41% vs. 23%; p=0.0213). The discharge time in the hospital reduced average of 4 ± 1.3 hours in scopolamine group and 4.5 ± 1.5 hours in placebo group (p=0.0487).	"The authors conclude that transdermal scopolamine is a safe and effective antiemetic for outpatients undergoing laparoscopy."	Data suggest transdermal scopolamine is effective for use in outpatient laparoscopic surgery to decrease PONV compliance difficult to assess as at least 25%of study population breached protocol.