AMERICAN COLLEGE OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

HIP AND GROIN DISORDERS GUIDELINE

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IMPACT

There are numerous disorders of the hip and groin, many of which will be covered in this chapter. However, robust prevalence, incidence, and cost estimates for hip disorders are largely unavailable except for osteoarthrosis (OA) and hip fractures. Osteoarthrosis affects 13.9% of adults over age 25, and 33.6% of adults over age 65. The prevalence of symptomatic hip OA is 4.4 per 100 adults over age 55.(1) A Danish study has estimated the 10-year incidence of hip OA requiring arthroplasty to be 0.9 to 1.0%.(2) Incidence rates increase with age. Of all arthritis-related procedures requiring hospitalization, 35% are due to hip and knee replacements. Job-related costs for OA overall are $3.4 to $13.2 billion per year with an average patient out-of-pocket direct expense of $2,600 per year. Twenty-five percent of those affected with OA cannot perform major activities of daily living.(1, 3, 4)

In the United States, hip fractures occur most commonly in adults 65 or older (90% as the result of a fall).(5, 6) However, a sizable minority involve occupational incidents such as motor vehicle accidents and falls from height. These latter types of injuries may lead to severe health problems, reduced quality of life, and premature death. Hospital admissions for hip fractures totaled 320,000 in 2004, and have been increasing; most of these admissions require approximately 1 week of hospitalization and 1 in 5 patients die within a year of their injury. Full recovery occurs in 25% of patients. Nursing home care is necessary for 40%. Cane or walker use is required longer term for 50% of hip fracture patients. The average cost of a hip fracture is $26,912 per patient. Women account for 76% of the incidence with rates increasing exponentially with age for both genders.(5, 6)

OVERVIEW OF MANAGEMENT OF HIP AND GROIN DISORDERS

The following hip and groin disorders are covered in this Guideline. Other prominent disorders, including lumbar radiculopathy and lumbar spinal stenosis especially for posterior and lateral hip pain, are not reviewed here in detail (see Low Back Disorders chapter for discussion of these disorders), but should be considered in the differential diagnosis of hip pain and hip symptoms. Additional diagnostic considerations include inguinal hernias, femoral hernias, atherosclerotic abnormalities, aneurysms, avulsion fractures (especially sartorius, rectus femoris), femoral mononeuritis, coxa saltans, tumor, cancer, crystal arthropathies (e.g., gout, pseudogout, hydroxyapatite), and infections including septic arthritis.

AVASCULAR NECROSIS

See Osteonecrosis.

EPIDIDYMO-ORCHITIS

The vast majority of cases of epididymitis or combined epididymito-orchitis have infectious origins.(7-18) More than 80% of cases in patients under ages 35 or 45 reportedly have Chlamydia trachomitis infections.(8, 19) Older patients tend to have gram-negative rod infections (7, 16) as do those who have had vasectomies and other urological procedures, a history of prostatitis, or who have engaged in anal intercourse.(8, 20, 21) A few cases have been attributed to amiodarone.(22, 23)

There is a small, but not insignificant minority of patients who report a history of a heavy lift or strain that precipitated the symptoms,(24-27) thus giving rise to the possibility that this entity may sometimes be an occupational disease or injury(28-32) outside of the obvious setting of direct work-related trauma.(33) Proposed mechanisms are reflux of urine in the course of the strain(27, 29, 34-36) or elicitation of symptoms from a latent infection.(24) In occupationally oriented medical clinics, patients whose jobs require heavy exertion appear to present more frequently with this diagnosis, whereas those with unequivocally non-occupational etiologies present less frequently.(24, 29)

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FEMOROACETABULAR IMPINGEMENT

Femoroacetabular impingement (FAI), which occurs when there is abnormal abutment between the femur and acetabulum, is thought to have many causes.(37) It has recently received increased attention as a structural entity reportedly associated with early arthritis of the hip.(38) FAI is associated with predisposing factors including altered femoral neck morphology (such as due to slipped capital femoral epiphysis), anteverted femoral neck, femoral neck nonunion, developmental hip dysplasia, Legg-Calves-Perthes disease, osteonecrosis, a “pistol grip” femoral neck, and coxa vara. It is also associated with acetabular morphologic variants, such as retroverted acetabulum, and deep acetabular socket (coxa profunda and protrusion). Impingement can occur as a result of femoral sided impingement (cam impingement), acetabular rim impingement (pincer impingement), or most commonly a combination of both.

Cam lesions on the femoral head-neck region lead to shear forces of the non-spherical portion of the femoral head against the acetabulum resulting in a characteristic pattern of anterosuperior cartilage loss over the femoral head and corresponding dome, as well as labral tears.(39) Labral tears associated with cam impingement are more commonly labral-chondral separation lesions affecting the transition zone cartilage and leaving the labral tissue in fairly good condition. The chondral damage tends to begin with softening, then debonding and delamination of the articular cartilage from the underlying acetabular bone. These chondral lesions are located in the anterosuperior region of the acetabulum and extend deeper into the acetabulum than chondral lesions due to pincer impingement.

The second category of femoroacetabular impingement is the “pincer” type lesion which is a result of repeated contact stresses of a normal femoral neck against an abnormal anterior acetabular rim as a result of “over coverage.” This situation results in degeneration, ossification, and tears of the anterosuperior labrum, as well as the characteristic posteroinferior “contre-coup” pattern of cartilage loss over the femoral head and corresponding acetabulum.(39) In this setting, the acetabular labrum fails first, which leads to degeneration and eventual ossification. This worsens the over coverage. Overall, the pincer type lesion has chondral damage that is limited to near the rim, but occurs more globally around the circumference of the acetabulum compared to the deep chondral injury associated with cam impingement.

Patients with femoroacetabular impingement commonly present with anterior groin pain, hip pain, and pain with hip flexion and internal rotation. The typical patient is middle aged and younger than the usual patient with degenerative joint disease. The typical cam lesion patient is a young adult male in his 20s, while the average pincer patient is an active female in her 40s.(39) Pain and symptoms are normally activity related. On physical exam, patients commonly exhibit decreased internal rotation and adduction with the hip flexed to 90 degrees. Examination reveals a positive impingement test where there is pain with passively adducting and gradually internal rotating the flexed hip. Common treatments include avoidance of aggravating exposures and positions, medications, exercise, and surgery. As noted, femoroacetabular impingement is theorized to increase the risk for hip osteoarthrosis.(38-48) Treatment has included avoidance of postures, especially squatting that provokes symptoms. Surgery is often proposed as a treatment as it is thought to delay or prevent development of osteoarthrosis.

GREATER TROCHANTERIC BURSITIS

Bursae are sacks with a small amount of fluid that are usually located between structures that move. They provide a structure to reduce friction between the two moving body parts (e.g., between muscle and bone or between bone and overlying skin). Bursitis occurs when the bursae become inflamed and irritated. Trochanteric bursitis is a theoretical condition, as there is little evidence it exists. However, it is theorized to involve an irritated bursa in the lateral hip, and it has also been reported that many patients have pathology in the gluteus medius tendon.(49) Causal mechanisms are somewhat unclear, but are thought to include direct trauma over the trochanter, such as falling on the lateral hip joint or repetitive overuse movement patterns. Unaccustomed use, such as putting pressure over the trochanter, is thought to be a risk factor; routine use is of unknown risk. Greater trochanteric bursitis has most

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commonly been treated with NSAIDs, a glucocorticosteroid injection, and physical or occupational therapy.

GREATER TROCHANTERIC PAIN SYNDROME (ALSO LATERAL HIP PAIN)
This entity is being used to describe patients with pain in the lateral hip joint. Some practitioners use this diagnostic entity in preference to other terms as the precise diagnosis may be unclear at times, or one label (e.g., greater trochanteric bursitis) may fail to completely describe a patient with other abnormalities.

GROIN STRAINS (AND "EPIDIDYMITIS")
A strain is believed to usually consist of a disruption of a myotendinous junction. A groin strain most classically involves the adductor muscles of the thigh. A complete muscular tear may occur. However, structures within the groin include the lower rectus abdominis musculature, inguinal region, symphysis pubis, upper portions of the adductor muscles of the thigh, and the genitalia and scrotum. Some cases of a lower abdominal muscle strain (usually in the inguinal area) include a clinical case of epididymitis even without an apparent infectious component. Strains that do not promptly resolve are most commonly treated by removing the patient from high-force activities. For more severely affected cases, treatment includes NSAIDs and therapy.

GLUTEUS MEDIUS TENDON TEARS
The most common location for gluteus medius tendon tears is along the middle facet. There may be extension of the tear toward fibers of the gluteus minimus insertion on the anterior facet. Oftentimes, these are high-grade partial thickness tears starting on the undersurface of the tendon. Therefore, a thorough evaluation is required to identify the site of the tear. Treatment includes NSAIDs, observation, physical or occupational therapy, and surgical repairs.

LUMBAR RADICULOPATHY AND LUMBAR STENOSIS
Lumbar radiculopathy and stenosis are two common disorders that present as hip pain. They constitute prominent disorders in the differential diagnosis of hip pain (see Low Back Disorders for discussion of these disorders).

OSTEOARTHROSIS INCLUDING DEGENERATIVE JOINT DISEASE ("OSTEOARTHRITIS" AND "DEGENERATIVE ARTHRITIS")
Hip degenerative joint disease (DJD) is most commonly caused by osteoarthrosis (OA). While osteoarthritis is the more common name for this entity, osteoarthrosis is more technically precise as there is no classic inflammation. Other arthritic disorders that cause degenerative joint disease prominently include inflammatory autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus, and psoriasis) and crystal diseases (e.g., gout, pseudogout, apatites). As these latter disorders are non-occupational, they are not included in this discussion.

Other than intervertebral discs, joints in the body are typically synovial fluid filled, synovium lined, ligamentously encapsulated joints that allow for low friction movement between adjacent bones. OA, an age-related degenerative change in the joint particularly affecting the cartilage on the articular surface, leads to thinning of that cartilage. Pain on movement and stiffness develop. OA may develop in only one joint after a significant traumatic injury (e.g., fracture), in which case it is often delayed by many years. If this injury was occupational, then the subsequent osteoarthrosis is also considered, at least in part, occupational.

The common pathway for hip OA includes such destruction of the joint that it may be indistinguishable on x-ray. Thus, a correct interpretation of an x-ray may include degenerative joint disease, but not osteoarthritis. OA of the hips has been reported to occur as frequently in men as women. The reason for this difference compared with other joints where women are at a greater risk is unknown. Some studies have found that slipped capital femoral epiphyses are responsible for most cases of hip OA.(50) However, that finding has not been universal, although it would appear to explain the demographics of the affected patients. There is a predisposition for patients who already have OA in one or two joints, to develop OA in other joint groups. Several genetic factors have been identified.(51)

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The vast majority of OA cases are symmetrical. As such, an occupational basis for such cases is much more difficult to identify. There are a few occupations that have been consistently associated with one type of arthrosis (e.g., hip OA in farmers). However, there are relatively poor and/or inconsistent epidemiological studies in this area and the cause of symmetrical OA is controversial. A propensity for OA to develop in other joints once an individual has already developed symmetrical arthrosis in another body region likely signifies a genetic or other systemic predisposition (e.g., develop hand arthrosis after knee arthrosis or facet joint OA). This is sometimes referred to as "systemic osteoarthrosis." Another theory is that development of OA in one hip will result in development in the other due to abnormal gait mechanics. Treatment of other types of OA is not covered in this chapter as there are substantive management differences by body part, thus the reader is referred to other specific chapters.

Most hip OA cases appear to arise without obvious exposures. The condition tends to progress and most cases are not considered occupational. Cases that occur in only one joint are often post-traumatic, and it is that initial inciting event that determines whether the case is likely to work-related. For example, an individual fractures a femur at work and develops unilateral hip OA in that same hip 20 years later – the hip OA is thought to be occupational.

The sole occupation that has been consistently shown to be associated with hip OA is farming, although duration of farming activities have not been found to further increase that risk. The exposure is unclear and has been hypothesized to involve forceful exposures in youth resulting in slipped capital femoral epiphyses, which later develop OA through altered biomechanics. However, regardless of the lack of clarity regarding the mechanism of development, the association is strong.

Quality studies on the long-term prognosis of patients with OA are noticeably weak. One systematic review reported a finding of "no change" in functional status among hip OA patients over a 3-year period of follow-up, although conflicts in the available studies were noted.(52)

Osteoarthrosis: Initial Interventions/Role of Physical and Occupational Therapy and Other Non-pharmacologic or Non-invasive Interventions

Many patients with hip OA are able to control their pain adequately by avoiding activities that significantly provoke symptoms and by using over-the-counter medications. Due to the deep nature of the hip joint, topical agents, heat, and ice may be less helpful than for OA in other joints. As OA is generally characterized by morning stiffness or stiffness (and pain) after both long periods of inactivity or in association with unaccustomed increases in activity, patients may benefit from education. Regular participation in programs stressing aquatic or gentle aerobics (e.g., walking programs) or strengthening exercise may be beneficial especially if individualized to the patient's diagnosis, prior and desired activity levels, and overall preferences. Weight loss is thought to be indicated for patients who are overweight or obese, although a connection has yet to be clearly shown in the hip.(53-65)

Osteoarthrosis: Pharmacologic Management

Nonsteroidal anti-inflammatory drugs (NSAIDs) are most commonly used for patients with OA. Chronic NSAID therapy may warrant ancillary use of proton pump inhibitors, H-2 histamine blocking agents, or misoprostol to provide prophylaxis against gastrointestinal adverse effects. Selective Cox-2 inhibitors are also used due to lower risks of gastrointestinal effects. Tricyclic antidepressants, dual reuptake inhibiting antidepressants (i.e., SSNRIs) and acetaminophen may benefit certain patients. Highly select patients may also benefit from judicious use of low doses of opioids if they result in functional improvements. Older patients with significant comorbidities, including renal impairment and medications, should be carefully prescribed.

Osteoarthrosis: Role of Invasive Procedures

Invasive procedures are not indicated for managing most OA patients unless the condition cannot be satisfactorily controlled with other non-invasive treatments. In such cases, intraarticular injections with glucocorticosteroid and viscosupplementation are sometimes utilized. In advanced cases, joint replacement is often performed.

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OSTEONECROSIS [AVASCULAR NECROSIS (AVN)]

Osteonecrosis involves impairment of the blood supply to the head of the femur and may evolve to subsequent degeneration and ultimately collapse of the femoral head. It is particularly likely to occur in areas of tenuous blood supply that lacks collateral blood flow, thus most prominently affecting the femoral head. There are numerous reported risk factors, including male gender,(66) diabetes mellitus, glucocorticosteroid treatment or excess,(66) sickle cell anemia, sickle cell trait, alcoholism, organ transplantation,(67) and multiple myeloma.(66) The most prominent occupational risk factor for osteonecrosis is barotraumas ("the bends") which may occur both in diving, as well as working in compressed air environments (e.g., certain types of tunneling projects through unstable sediments requiring compressed air to maintain the workspace). Significant, discrete trauma is thought to be a risk factor. However, non-traumatic job physical factors are controversial. Some workers' compensation jurisdictions will consider a pre-existing, previously non-occupational case of advancing osteonecrosis after a discrete work injury, particularly including collapse, as having an occupational contribution. Treatment is primarily based on alleviating the exposure(s) thought responsible. A surgical "coring" procedure, vascularized and unvascularized bone grafting, and osteotomy are sometimes utilized. Severe cases may require arthroplasty.

HIP INSTABILITY

The hip is subject to both traumatic and atraumatic instability. Traumatic hip instability is typically the result of a posteriorly directed force. The spectrum of injury ranges from subluxation to dislocation with or without concomitant injuries. In addition to standard radiographic workup, the evaluation may include an MRI that may demonstrate the characteristic triad of findings of hemarthrosis, an iliofemoral ligament disruption, and a posterior acetabular lip fracture or posterior labral tear.(68) Anterior labral pathology is often present as well and may represent a traumatic avulsion of the labrum or indicate the presence of some underlying bony impingement. The presence of a significant hemarthrosis may warrant aspiration under fluoroscopy to reduce intracapsular pressure. CT scanning may be helpful to define the bony anatomy of associated fractures of the acetabulum or femoral head.

Atraumatic instability is a spectrum ranging from injuries in patients that are attributed to stereotypical use leading to microinstability to patients who manifest generalized ligamentous laxity. Pre-operative diagnosis of atraumatic instability of the hip is unclear and subjective. The labrum or iliofemoral ligament may be damaged from repeated force. These abnormal forces are theorized to cause increased tension in the joint capsule which can lead to painful labral injury, capsular redundancy, and subsequent microinstability. The hip must rely more on the dynamic hip stabilizers for stability once the static stabilizers of the hip such as the iliofemoral ligament or labrum are injured. The spectrum of atraumatic instability also includes patients with hip pain secondary to more generalized ligamentous laxity or, in the extreme form, in patients with connective tissue disorders such as Ehlers-Danlos syndrome or Marfan's syndrome. Physical findings include evaluation for ligamentous laxity and increased external rotation of the hip (in extension during the log roll or in flexion such as the FABER maneuver). Treatment usually consists of rehabilitation therapy and appropriate exercises. Individualized exercise programs may be warranted as the direction of instability may vary among individuals.

HIP DISLOCATION

Most hip dislocations occur due to violent or high-speed collision, a fall, post-arthroplasty, or a congenital joint malformation (some patients with inherited or congenital abnormalities such as dysplasia have a propensity for recurrence). The mechanism of injury determines whether the condition is work-related. A hip dislocation requires an x-ray and attempted relocation, often with anesthesia. In cases with recurrent dislocation of the joint after replacement, a revision procedure can be performed to attempt to reduce the frequency of dislocations. Pre-operative CT scanning may be helpful to determine the rotational alignment (anteversion) of the femoral and acetabular components.

HIP DYSPLASIA

Hip dysplasia, or developmental dysplasia of the hip (DDH), is a relatively common developmental problem which is heterogeneous in anatomic abnormalities and ranges in severity from mild to severe. It

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may be unilateral or bilateral and is multifactorial with certain risk factors reported (e.g., female gender, genetic factors, breech birth, firstborns, swaddling the legs of infants). The abnormalities involve a lack of appropriate fitting between the femoral head and acetabulum. In children, there is a propensity towards acetabular abnormalities that is usually accompanied by instability and dislocations and the Crowe classification system is sometimes used.

In adults, the condition is most often identified through an abnormal appearance of the acetabulum and/or proximal femur on x-ray. It leads to an increased risk of labral tears, chrondral damage, ligamentum teres hypertrophy, and osteoarthrosis with some surgeries performed to attempt to reduce the risk of osteoarthrosis.(69) Patients may also present in youth or adulthood with hip pain that may be increased with physical activity. The pain is often in the groin. There may be mechanical symptoms such as locking, painful clicking or restricted range of motion (ROM). Pain is reproduced with the impingement sign as well as by hyperextending the hip or placing the hip in the Femoral Abduction External Rotation (FABER) position. X-rays and ultrasound are used for diagnostic purposes. There may be an increased range of motion (ROM) of both hips, though the affected hip has less motion, often limited by pain. The hip joint may be prone to dislocation and instability and if so, rehabilitation therapy and exercises are most commonly provided. When severe, osteotomies and joint replacement is often performed.

HIP FRACTURE

Hip fractures include both frank and stress fractures. All fractures involve an application of force that is beyond the bone strength. Occupational fractures most commonly result from falls or motor vehicle accidents. These almost invariably require surgical fixation or sometimes arthroplasty. 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 assessment to address movement system impairments, such as muscle performance and motor patterns, may assist in reducing forces on the affected site.

HIP IMPINGEMENT

See Femoroacetabular Impingement.

LABRAL TEARS

The labrum is a triangular fibrocartilaginous structure attached at its base to the rim of articular cartilage surrounding the perimeter of the acetabulum. It is absent inferiorly where the transverse acetabular ligament completes the rim. The labrum provides some structural resistance to lateral and vertical motion of the femoral head within the acetabulum and has an important sealing function which limits fluid expression from the joint space in order to protect the cartilage layers of the hip. The labrum likely also provides some proprioceptive feedback.

While labral tears may occur as an isolated problem, they are usually associated with traumatic injuries, such as hip dislocation or subluxation, or with bony abnormalities, such as hip dysplasia and femoroacetabular impingement.(70) Labral tears less commonly may be the result of some other etiology including capsular laxity, iliop/psoas impingement,(71-74) or symptomatic internal coxa saltans.

Labral tears have been classified in different ways(75-79) – radial flap (most common at 57%), radial fibrillated labrum (22%), longitudinal peripheral tears (16%), and abnormally mobile tears (5.4%). They are now described more functionally as intra-substance tears and tears at the labral-chondral junction. The vascularity of the labrum comes from the capsule and bony acetabulum.(80) Many tears occur in articular nonvascular zone resulting in some labral repairs being unlikely to heal. Labral tears are frequently seen in conjunction with acetabular chondral lesions. Tears more commonly occur anterosuperioly due to the association between labral pathology and underlying bony abnormalities such as impingement and dysplasia. Both femoroacetabular impingement and dysplasia lead to injury to the anterosuperior labrum, albeit thought to be through different mechanisms. In the case of impingement, the anterosuperior labrum is compressed between the femoral head – neck region and the acetabular rim. In dysplasia, the anterosuperior labrum is overloaded due to loss of acetabular bony coverage and subsequent capsular and labral decompensation. In the majority of dysplasia cases, the labral tissue is hyperplastic in an attempt to create a soft-tissue substitute for the loss of acetabular coverage and is

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thus even more vulnerable to degenerative tearing. The location of the labral pathology in hip instability may be different than the most common anterosuperior location seen in the setting of impingement and dysplasia. Traumatic hip instability, usually the result of a posteriorly directed force, may result in a posterior labral tear, though an anterior labral injury, may also be present, indicating a traumatic avulsion of the labrum. Hip subluxation may occur from the same mechanism as a dislocation or be the result of a cutting or pivoting maneuver. Atraumatic instability is thought to include a spectrum ranging from stereotypical use leading to microinstability, to patients with generalized ligamentous laxity where repeated forces may result in labral injury.

The diagnosis of labral tears can be quite difficult because not only do the history, symptoms and physical exam vary among patients, but there is also a lack of familiarity with the diagnosis. Many patients present with mechanical symptoms such as buckling, clicking or catching, or painful restricted range of motion. Some can present with dull activity induced, positional pain that does not improve with rest. Common presenting symptoms include insidious onset of groin pain being moderate to severe. This pain may be aggravated with pivoting and walking or other activities. The patient may also notice the pain to be reproducible bringing the hip into extension from flexion. Pain with hyperflexion, internal rotation and adduction (impingement position) is present in the majority of patients. The pain and/or clunk may also be reproduced with the labral stress test (patient supine, hip is placed into full flexion, external rotation and abduction then moved to extension, internally rotated and adducted with reproduction of pain, clicking or clunking(81)) and/or with resisted straight leg raise, although the diagnostic value of this tests may be limited. Treatment is most commonly observation; however, therapy may be helpful and surgical repair is thought to be indicated for tears that are either highly symptomatic or fail to improve with observation. Some theorize labral tears may lead to progressive osteoarthrosis and suggest treatment reduces that risk, although this theory is currently unproven.(82-84)

LIGAMENTUM TERES RUPTURES

The function of the ligamentum teres in not fully understood. It is a triangular-shaped structure with a broad-based attachment to the posteroinferior portion of the cotyloid fossa of the acetabulum. It provides blood supply to the developing hip through a small artery to the fovea of the femoral head. There is no known mechanical function, though it has been suggested that this ligament plays a biomechanical role that contributes significantly to the stabilization of the hip.(85) Analysis of the material properties of this ligament has demonstrated similarities to other ligaments and confirms its ability to resist dislocation forces applied to the femoral head. It is tight in adduction, flexion, and external rotation. Disruption of the ligamentum can be associated with trauma and dislocation of the hip or it may occur without dislocation.(85) Disruption of the ligamentum may also occur with degenerative arthritis.(85) Patients suffering from ligamentum rupture as a result of trauma or dislocation will often have symptoms of instability and pain.

The prevalence of ligamentum teres ruptures seen at arthroscopy is more common than would be suspected, with an 8% incidence rate found in one study.(86) Acute disruptions of the ligamentum are thought to occur as a result of exaggerated movements of adduction and external rotation, although hip abduction is often the injury mechanism described with patient history. Diagnosis of these injuries can be difficult and a high index of suspicion with careful attention to the injury mechanism and the physical examination are critical to accurate evaluation. The high incidence of degenerative arthritis associated with complete ligamentum teres ruptures has been attributed to the original injury in many cases. However, recurrent instability and subluxation episodes may cause repeated injury to the femoral head and account for an increased incidence of osteonecrosis in these patients.

LOWER ABDOMINAL STRAINS

Lower abdominal strains are frequent occurrences in sports and occupational groups, particularly those involved in heavy lifting.(87) The pathophysiological abnormality is unclear. Pain onset is usually acute occurring in the context of a heavy lift or sports-related forceful exertion. Pain occurs most typically in the lower abdominal muscles often along the inguinal canal; however, there is no hernia. Whether abdominal strain is a risk for or a precursor to an indirect inguinal hernia is also unknown. There is thought that the

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disorder represents reflux of urine into the vas deferens during heavy lifting or strain (see epididymo-orchitis).

MERALGIA PARESTHETICA

Meralgia paresthetica is a peripheral entrapment neuropathy of the lateral femoral cutaneous nerve, a sensory nerve supplying the upper lateral aspects of the thigh.(88-90) While a nerve entrapment may occur at any point along the nerve, the condition is most commonly from a localized pressure in the area of the inguinal ligament, generally in obese, middle-aged adults in whom the obesity is presumed to produce the pressure on the nerve either directly,(89) or through tight clothing.(91, 92) In an occupational setting it may be due to pressure from tight, heavy tool belts or military armor.(91) Onset may be relatively acute, e.g., after one night's sleep or insidious. Other causes include trauma and scarring from prior trauma or post-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.

SUMMARY OF RECOMMENDATIONS AND EVIDENCE

All *Guidelines* chapters include analyses of numerous interventions, whether or not they are FDA-approved. For non-FDA-approved interventions, recommendations are based on the available evidence. This is not an endorsement of their use. Many of the medications recommended are utilized off-label.

The following is a general summary of the recommendations contained in this chapter:

Evaluation and Diagnostic Issues

- The hip joint or groin should be carefully evaluated with a history, physical examination and focused diagnostic testing. A complete physical examination is recommended, since pain can be referred, particularly from the back or knee to the hip joint or from the genitalia or hip to the groin.
- The initial hip or groin pain examination or consultation should focus on the detection of conditions that are remediable or "red flags" for potential alternate conditions (e.g., femoral head osteonecrosis or renal calculus).
- Initial evaluation of hip joint pain requires hip x-rays in some cases, but not in others, depending on the diagnosis and presentation. The threshold for additional x-rays particularly of the back and knees should be low and may be especially indicated depending on history and physical examination findings.
- Diagnostic ultrasound is helpful for evaluating many of these disorders, including gluteus medius tendinopathies, greater trochanteric bursitis, greater trochanteric pain syndrome/lateral hip pain, groin strains, femoroacetabular impingement, hip instability, dislocation, ligamentum teres ruptures, and labral tears.
- Magnetic resonance imaging (MRI) is particularly helpful for osteonecrosis, femoroacetabular impingement, gluteus medius tendinosis or tears, and trochanteric bursitis.
- Magnetic resonance arthrography is particularly helpful for labral tears, femoroacetabular impingement, gluteus medius tendinosis or tears, and trochanteric bursitis.
- CT scanning is helpful in the evaluation of the patient with a traumatic hip dislocation or arthroplasty-associated recurrent hip dislocation.
- Initial evaluation of groin pain frequently requires no diagnostic testing other than sometimes urinalysis.

Patient Education Issues

- Patients need reassurance that hip pain is common. If required, hip arthroplasty is a major surgical procedure, but with a good prognosis. However, most hip arthrosis patients do not require arthroplasty.
- Osteonecrosis has a variable prognosis which often requires surgery, depending on severity.

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- Groin pain is common and usually resolves completely with a good prognosis.
- Patients should be encouraged to maintain high a level of function; however, modifications may be helpful in reducing stresses to the hip.
- Rest and disuse of body parts are not recommended for the management of hip pain, groin pain and other conditions other than fractures, as they usually cause further disability and prolong treatment.

Occupational Issues

- Aside from hip fracture patients in whom prolonged time away from work is often required or stress fractures in whom significant restrictions to limit forceful use and weight bearing, patients should be encouraged to return to normal activity or work as soon as possible. Some situations might require modified duty. However, the more activities are reduced, the greater the time generally required for patient rehabilitation.
- If hip pain is present, reduced activity may be necessary if the physical requirements of the job exceed the patient's capabilities.
- If a groin strain is present, brief episodes of reduced heavy lifting or jumping may be appropriate.
- A functional capacity evaluation (FCE) can establish appropriate physical capacity for work although results should be interpreted with caution and the testing should be preferably conducted by someone (e.g., occupational or physical therapist) well experienced in dealing with patients who may self-limit due to pain. Address nonphysical factors, return to work programs and participatory ergonomics, as needed. Empower patients to accept responsibility for managing their recovery.

Adaptive Equipment/Assistive Devices and Other Allied Health Therapies

- Ambulatory assistive devices (e.g., canes and crutches) are helpful and generally considered mandatory for severely affected patients and are most often prescribed until the patient can ambulate without a limp. However, balance this use against problems of accelerated muscle weakness due to prolonged use of assistive devices results in these devices being potentially counterproductive for mildly affected patients.
- Ice, heat, ultrasound, and other similar modalities are rarely indicated for treatment of hip pain in the clinical setting. They may be reasonable for trochanteric bursitis. Heat modalities are recommended for treatment of groin strains.
- Consider heat and ice as a part of self care at home, particularly in the acute pain setting. They should provide temporary relief of symptoms, but can reinforce pain and illness behaviors in persons with chronic pain. There is belief that heat is not indicated in the acute phase of groin strains and some other injuries, although acute low back pain has been demonstrated to be successfully treated with heat. Quality evidence is lacking.
- There is no evidence to support prolonged and repetitive use of allied health therapies (e.g., massage, electrical therapies, manipulation, or acupuncture). Long-term and repetitive treatment, particularly if there is no documentation of functional improvement, is not indicated in managing patients with chronic pain, including hip pain from degenerative joint disease.

Exercise Issues

- Graded exercises to assist in achieving a return to normal function are indicated.
- Gentle exercises are useful to regain normal range of motion in acute pain and post-operative settings. Aggressive stretching may be contraindicated if symptoms are aggravated. It is important for patients to understand that while exercises after surgery can have some discomfort, they should not experience significant increase in pain or new onset of swelling.
- Aerobic and strengthening exercises appear most helpful for rehabilitation of most chronic hip pain conditions. Consultation with a physical therapist to determine the most appropriate exercises for the patient is in order.

Medications

- Initially manage most hip and groin pain conditions with NSAIDs or acetaminophen.

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- Opioids should be avoided in most cases. Opioids might be needed for managing select patients with confirmed moderate to severe hip degenerative joint disease. Short-term opioid use is rarely needed for severe groin strains.
- Glucocorticoid injections are indicated for trochanteric bursitis treatment.

Other Issues

- Hip replacement surgery is recommended for symptoms of severe hip degenerative joint disease that cannot be managed with other non-operative treatments (e.g. medications, injections).
- Groin strains may be accompanied by clinical epididymitis. If supporting history or physical examination findings are absent, this entity does not appear to require treatment with antibiotics.

Summary Tables: Recommendations and Evidence

Table 1 summarizes the recommendations from the Evidence-based Practice Hip Panel for diagnostic testing for hip and groin disorders. Table 2 is a summary of recommendations for managing these disorders. Table 3 is a summary of pre-, peri-, and post-operative rehabilitation recommendations related to these disorders. Recommendations are based on critically appraised higher quality research evidence, and on expert consensus observing First Principles when higher quality evidence was unavailable or inconsistent. **The reader is cautioned to utilize the more detailed indications, specific appropriate diagnoses, temporal sequencing, prior testing or treatment, and contraindications that are elaborated in more detail for each test or treatment in the body of this Guideline in using these recommendations in clinical practice or medical management.** These recommendations are not simple "yes/no" criteria, and the evidence supporting them is in nearly all circumstances developed from typical patients, not unusual situations or exceptions. (Studies were reviewed that included numerous disparate conditions beyond hip and groin pain; however, they are not included in this chapter in detail. The reader is referred to other chapters, especially the Chronic Pain chapter for a detailed review of many of those additional studies.)
Recommendations are made under the following categories:

- Strongly Recommended, "A" Level
- Moderately Recommended, "B" Level
- Recommended, "C" Level
- Insufficient-Recommended (Consensus-based), "I" Level
- Insufficient-No Recommendation (Consensus-based), "I" Level
- Insufficient-Not Recommended (Consensus-based), "I" Level
- Not Recommended, "C" Level
- Moderately Not Recommended, "B" Level
- Strongly Not Recommended, "A" Level

Table 1. Summary of Recommendations for Diagnostic and Other Testing for Hip and Groin Disorders

Test	Recommendation(s)
Antibodies	Antibody levels to evaluate and diagnose patients with hip pain if there is reasonable suspicion of a rheumatological disorder – **Recommended, Insufficient Evidence (I)** Antibody levels as a screen to confirm the existence of specific disorders (i.e., rheumatoid arthritis) – **Strongly Recommended, Evidence (A)**
Hip Arthroscopy	Arthroscopy to evaluate and diagnose patients with hip pain if there is a suspicion of labral tear, intraarticular body, femoroacetabular impingement, or there are other subacute or chronic mechanical symptoms **– Recommended, Insufficient Evidence (I)** Arthroscopy for diagnosing acute hip pain **– Not Recommended, Insufficient Evidence (I)** Arthroscopy to diagnose or treat acute, subacute, or chronic hip osteoarthrosis in the absence of a remediable mechanical defect such as symptomatic labral tear – **Not**

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	Recommended, Insufficient Evidence (I) Arthroscopy with chondroplasty for treatment of osteoarthrosis **– Not Recommended, Insufficient Evidence (I)**
Bone Scans	Bone scanning for select use in patients with acute, subacute or chronic pain to assist in the diagnosis of osteonecrosis, neoplasms, or other conditions with increased polyosthotic bone metabolism, particularly when more than one joint needs to be evaluated **– Recommended, Insufficient Evidence (I)** Bone scanning for routine use in hip joint evaluations **– Not Recommended, Insufficient Evidence (I)**
Computerized Tomography (CT)	Routine CT for evaluating acute, subacute, or chronic hip pain – **Not Recommended, Insufficient Evidence (I)** CT for evaluating patients with osteonecrosis or following traumatic dislocations or arthroplasty-associated recurrent dislocations – **Recommended, Insufficient Evidence (I)** CT for patients who need advanced imaging, but have contraindications for MRI **– Recommended, Insufficient Evidence (I)** Routine helical CT for evaluating acute, subacute, or chronic hip pain – **Not Recommended, Insufficient Evidence (I)** Helical CT for evaluating patients with osteonecrosis who have contraindications for MRI **– Recommended, Insufficient Evidence (I)** Helical CT for select patients with acute, subacute or chronic hip pain for whom advanced imaging of bony structures is thought to be potentially be helpful – **Recommended, Insufficient Evidence (I)** Helical CT for patients who need advanced imaging, but have contraindications for MRI **– Recommended, Insufficient Evidence (I)**
C-Reactive Protein, Erythrocyte Sedimentation Rate, and Other Non-specific Inflammatory Markers	Erythrocyte sedimentation rate or other inflammatory markers for screening for inflammatory disorders or prosthetic sepsis with reasonable suspicion of inflammatory disorder in patients with subacute or chronic hip pain – **Recommended, Insufficient Evidence (I)**
Local Anesthetic Injections and Epidurals	Local anesthetic injections to assist in the diagnosis of subacute or chronic hip pain **– Recommended, Insufficient Evidence (I)**
Electromyography (including Nerve Conduction Studies)	Electrodiagnostic studies to assist in the diagnosis of subacute or chronic peripheral nerve entrapments including lateral cutaneous nerve to the thigh (meralgia paresthetica) **– Recommended, Insufficient Evidence (I)** Nerve conduction study to confirm diagnosis or in patients in who surgery is contemplated – **Recommended, Insufficient Evidence (I)**
Magnetic Resonance Imaging (MRI)	MRI for select patients with subacute or chronic patients with consideration of accompanying soft tissue pathology or other diagnostic concerns – **Recommended, Insufficient Evidence (I)** MRI for diagnosing osteonecrosis – **Recommended, Insufficient Evidence (I)** MRI for routine evaluation of acute, subacute, or chronic hip joint pathology, including degenerative joint disease – **Not Recommended, Insufficient Evidence (I)** MRI to diagnose hamstring or hip flexor strains in more severe cases – **Recommended, Insufficient Evidence (I)** MRI to diagnose groin strains or adductor-related groin pain in more severe cases –

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	Recommended, Insufficient Evidence (I)
MR Arthrogram	MR arthrogram to diagnose femoracetabular impingement, labral tears, gluteus medius tendinsosis or tears, or trochanteric bursitis in patients with subacute or chronic hip pain **– Recommended, Insufficient Evidence (I)**
Roentgenograms (X-rays)	X-rays for evaluating acute, subacute or chronic hip pain or femoroacetabular impingement or dysplasia – **Recommended, Insufficient Evidence (I)** X-rays for diagnosing osteonecrosis – **Recommended, Insufficient Evidence (I)** X-rays to diagnose hamstring or hip flexor strains in more severe cases – **Recommended, Insufficient Evidence (I)** X-rays to diagnose groin strains or adductor-related groin pain in more severe cases – **Recommended, Insufficient Evidence (I)**
Single Proton Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET)	SPECT or PET for diagnosing acute, subacute or chronic hip pain – **Not Recommended, Insufficient Evidence (I)**
Ultrasound	Ultrasound for evaluating patients with gluteus medius tendinopathies, greater trochanteric bursitis, greater trochanteric pain syndrome/lateral hip pain, groin strains, femoroacetabular impingement, hip instability, dislocation, ligamentum teres ruptures, labral tears, or post-arthroplasty chronic pain where peri-articular masses are suspected – **Recommended, Insufficient Evidence (I)** Ultrasound to diagnose other hip disorders including osteonecrosis, osteoarthritis, dysplasia, or fractures **– No Recommendation, Insufficient Evidence (I)**
Urine Culture	Culturing urine to diagnose lower abdominal strain unless other symptoms are present – **No Recommendation, Insufficient Evidence (I)** Urine cultures for select patients to diagnose epididymitis or epididymito-orchitis – **Recommended, Insufficient Evidence (I)**

Strength-of-Evidence Ratings:

A **= Strong evidence-base**: Two or more high-quality studies.*

B = **Moderate evidence-base**: At least one high-quality study or multiple moderate-quality studies** relevant to the topic and the working population.

C = **Limited evidence-base**: At least one study of moderate-quality.

I **= Insufficient evidence**: Evidence is insufficient or irreconcilable.

*For therapy and prevention, randomized controlled trials (RCTs) with narrow confidence intervals and minimal heterogeneity. For diagnosis and screening, cross sectional studies using independent gold standards. For prognosis, etiology or harms, prospective cohort studies with minimal heterogeneity.

**For therapy and prevention, well-conducted cohort studies. For prognosis, etiology or harms, well-conducted retrospective cohort studies or untreated control arms of RCTs.

Table 2. Summary of Recommendations for Managing Hip and Groin Disorders

Hip and Groin Disorder	Treatment with Evidence Rating/Recommendation Level		
	Recommended	**No Recommendation**	**Not Recommended**
Acute, Subacute, or Chronic Hip and Groin Pain	Measures to prevent falls (I) Activities that do not substantially aggravate symptoms for most patients with acute, subacute, or chronic hip or groin pain (I) Bed rest for patients with clear	Ergonomic interventions to prevent or facilitate recovery (I) Yoga for chronic persistent hip pain (I) Norepinephrine reuptake	Bed rest for patients with acute, subacute, or chronic hip pain (I) Norepinephrine reuptake inhibiting anti-depressants for acute

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	contra-indication to weight-bearing status such as an unstable fracture (I) NSAIDs for chronic hip pain especially if due to osteoarthrosis (A) NSAIDs for acute or subacute hip pain (I) NSAIDs for acute flares (C) Proton pump inhibitors or misoprostol for patients at substantially increased risk for gastrointestinal bleeding (A) Sucralfate for patients at substantially increased risk for gastrointestinal bleeding (B) H2 blockers for patients at substantially increased risk for gastrointestinal bleeding (C) NSAIDs for patients with known cardiovascular disease or multiple risk factors for cardiovascular disease if the risks and benefits of NSAID therapy for pain are discussed (I) Acetaminophen (or the analog, paracetamol) for acute or subacute hip pain particularly in patients who have contra-indications for NSAIDs (I) Acetaminophen (or the analog, paracetamol) for chronic hip pain particularly in patients who have contraindications for NSAIDs (C) Acetaminophen or aspirin as a 1st-line therapy for patients with cardiovascular disease risk factors (A) Judicious use of opioids for acute severe hip pain (I) Opioids for select patients with subacute or chronic hip pain (I) Muscle relaxants for acute and subacute, moderate to severe hip pain from muscle spasm that is unrelieved by NSAIDs, avoidance of exacerbating exposures or other conservative measures (I) Capsicum for short-term treatment of acute or subacute hip pain as well as for acute exacerbations of	inhibiting anti-depressants for subacute or chronic hip pain (I) Topiramate for subacute or chronic hip pain (I) Gabapentin for subacute or chronic hip pain (I) 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, and zingiber officinicalis, avocado soybean unsaponifiables, oral enzymes, topical copper salicylate, S-Adenosylmethionine, and diacerein harpagoside for acute, subacute, or chronic hip pain (I) Acupuncture for acute or subacute hip pain (I) Diathermy for acute, subacute, or chronic hip pain (I) Infrared therapy for acute, subacute, or chronic hip pain (I) Ultrasound for acute, subacute, or chronic hip pain (I) Low-level laser therapy for acute, subacute, or chronic hip pain (I) Manipulation or mobilization for acute hip pain (I) Massage for acute, subacute, or chronic hip pain (I) Electrical therapies outside of research settings for acute, subacute, or chronic hip pain (I) Transcutaneous electrical nerve stimulation (TENS) for acute, subacute, or chronic hip pain (I) Botulinum injections (I) Biofeedback for chronic hip	hip pain (I) Selective serotonin reuptake inhibitors (SSRIs) for acute, subacute, or chronic hip pain (I) Skeletal muscle relaxants (I) Topiramate (I) Gabapentin for acute hip pain (I) Routine use of opioids for acute, subacute, or chronic non-malignant pain conditions (C) Topical NSAIDs (I) Wheatgrass cream (I) Lidocaine patches (I) Eutectic mixture of local anesthetics (EMLA) (I) Other creams/ointments (I) Tumor necrosis factor-alpha blockers for acute, subacute, or chronic hip pain (I) Complementary or alternative treatments or dietary supplements, etc. for acute, subacute, or chronic hip pain (I) Magnets and magnetic stimulation for acute, subacute, or chronic hip pain (I) Reflexology for acute, subacute, or chronic hip pain (I) Prolotherapy injections for acute, subacute, or chronic hip pain (I)

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	chronic hip pain as a counter-irritant (I) Canes and crutches for moderate to severe acute hip or groin pain or subacute and chronic hip or groin pain where the device is used to advance the activity level (I) Orthotics, shoe insoles, or shoe lifts for patients with significant leg length discrepancy with hip pain felt to be a consequence of that discrepancy (I) Cryotherapies for home use if efficacious for temporary relief of acute, subacute, or chronic hip pain (I) Self-application of low-tech heat therapy for acute, subacute, or chronic hip pain (I) Manipulation or mobilization for subacute or chronic hip pain (C) A psychological evaluation as part of the evaluation and management of patients with chronic hip pain (see indications) in order to assess whether psychological factors will need to be considered and treated as part of the overall treatment plan (I) Cognitive-behavioral therapy as an adjunct to an interdisciplinary program for subacute or chronic hip pain (I) Work conditioning, work hardening, and early intervention programs for chronic hip pain syndromes (I) Multidisciplinary or interdisciplinary program (IPRP) with a focus on behavioral or cognitive-behavioral approaches combined with conditioning exercise for patients who due to chronic hip pain, demonstrate partial/total work incapacity (I)	pain (I)	
Osteonecrosis	Measures to prevent falls (I) Reduction or elimination of activities that significantly provoke osteonecrotic symptoms, including avoidance of dysbaric exposures, or control of diabetes mellitus, elimination or reductions in glucocorticosteroid use, and/or	Ergonomic interventions to prevent or facilitate recovery (I) Institution of non-weight-bearing activities (I) Hyperbaric oxygen (I)	Glucocorticosteroids, including by injection, in early disease stages (I)

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	elimination of alcohol and tobacco products (I) Aggressive targeting of all coronary artery disease risk factors (I) Bisphosphonates particularly for mild to moderate cases of osteonecrosis (C) NSAIDs (I) Core compression surgery (I) Hip arthroplasty for osteonecrosis with collapse or unresponsive to non-operative treatment (A) Total hip arthroplasty as an effective operation to speed improvements in patient's symptoms and functional status in those with moderate to severe hip disease (A) Metal-on-metal hip resurfacing arthroplasty for select patients (C)		
Bilateral Osteoarthrosis or Hip Joint Disease	Measures to prevent falls (I) For bilateral disease, carefully selected patients may safely undergo simultaneous bilateral hip replacement (C) Total hip arthroplasty as an effective operation to speed improvements in patient's symptoms and functional status in those with moderate to severe hip disease (A) Metal-on-metal hip resurfacing arthroplasty for select patients (C)	Ergonomic interventions to prevent or facilitate recovery (I) Botulinum injections (I)	
Epididymo-Orchitis	Measures to prevent falls (I) NSAIDs (I) Age-appropriate antibiotics (I) Physical or occupational therapy (I)	Ergonomic interventions to prevent or facilitate recovery (I) Needle aspiration for epididymito-orchitis (I) Work limitations for patients with epididymitis or epididymo-orchitis, although limitations may be necessary depending on the severity of the condition and the physical job demands (I) Ice (I) Intermittent elevation (I)	Bed rest (I)
Gluteus Medius	Measures to prevent falls (I) Trochanteric glucocorticosteroid	Ergonomic interventions to prevent or facilitate recovery	

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Tendinosis and Tears	injections for gluteus medius tears with accompanying clinical bursitis (C) NSAIDs or acetaminophen for gluteus medius tears with accompanying clinical bursitis (I) Progressive, eccentric exercise for gluteus medius tendinosis and tears, particularly to strengthen the lateral hip musculature (I) Surgical repair for gluteus medius tears that are non-responsive to medical management (I)	(I)	
Greater Trochanteric Bursitis/ Greater Trochanteric Pain Syndrome	Measures to prevent falls (I) Limitations may be helpful in the acute phase (I) Trochanteric glucocorticosteroid injections for acute, subacute, or chronic trochanteric bursitis or greater trochanteric pain syndrome (C) NSAIDs or acetaminophen for acute, subacute, or chronic trochanteric bursitis or greater trochanteric pain syndrome (I)	Ergonomic interventions to prevent or facilitate recovery (I) Topical NSAIDs (I) Lidocaine patches (I) Eutectic mixture of local anesthetics (EMLA) (I) Other creams/ointments (I)	
Groin Strains and Adductor-Related Groin Pain	Measures to prevent falls (I) NSAIDs (I) Work limitations for patients with groin strains or adductor-related groin pain who perform high-physical jobs or cannot avoid job tasks thought to have resulted in the strain (I) Ice (I) Heat (I) Ace wraps (I) Physical or occupational therapy (I)	Ergonomic interventions to prevent or facilitate recovery (I) Work limitations for most groin strains or adductor-related groin pain (I)	Bed rest (I)
Hamstring and Hip Flexor Strains	Measures to prevent falls (I) NSAIDs (I) Work limitations for patients with hamstring or hip flexor strains who perform high-physical jobs or cannot avoid job tasks thought to have resulted in the strain (I) Ice (I) Heat (I) Ace wraps (I)	Ergonomic interventions to prevent or facilitate recovery (I) Work limitations for most hamstring or hip flexor strains (I)	Bed rest (I)

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	Physical or occupational therapy (I) Progressive agility, trunk stabilization and icing (PATS) (I)		
Hip Fracture	Measures to prevent falls (I) Bisphosphonates for select patients with osteopenia-related hip fractures (A) Calcitonin for patients with hip fracture, particularly those who are intolerant to or have other contra-indications for bisphosphonates (I) Transcutaneous electrical nerve stimulation (TENS) for emergency transport of patients with hip fracture (B) Acupressure for transporting patients with hip fracture to the hospital (B) Surgical treatment (C) Surgical intervention as soon as the patient is medically stable (I) Arthroplasty for older patients with displaced femoral neck and subcapital fractures (A)	Ergonomic interventions to prevent or facilitate recovery (I) Manipulation or mobilization (I)	
Femoro-acetabular Impingement, "Hip Impingement," and Labral Tears	Measures to prevent falls (I) NSAIDs (I) Local glucocorticosteroid injections (I) Physical or occupational therapy (I) Arthroscopic surgery or open repair for "hip impingement" or labral tear cases that fail conservative management (I)	Ergonomic interventions to prevent or facilitate recovery (I)	
Hip Osteoarthrosis	Measures to prevent falls (I) Aerobic exercise (B) Stretching exercises for select patients with significant reductions in range of motion that are not thought to be fixed deficits (I) Strengthening exercises (B) A trial of aquatic therapy for patients with hip osteoarthrosis who meet the referral criteria for supervised exercise therapy and have co-morbidities (e.g., extreme obesity, significant degenerative joint disease, etc.) that preclude	Ergonomic interventions to prevent or facilitate recovery (I) Norepinephrine reuptake inhibiting anti-depressants (I) Topiramate (I) Gabapentin (I) Glucosamine sulfate 1,500mg daily (single or divided dose), chondroitin sulfate, or methylsulfonylmethane for treatment hip osteoarthrosis (I)	Tumor necrosis factor-alpha blockers (I) Magnets and magnetic stimulation (I) Reflexology (I)

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	effective participation in a weight-bearing physical activity and who will either transition to a land-based program or a self-administered water-based program (I) NSAIDs for chronic hip pain especially if due to osteoarthrosis (A) Acupuncture for select use for chronic osteoarthrosis of the hip as an adjunct to more efficacious treatments (B) Cryotherapies for home use if efficacious for temporary relief of osteoarthrosis (I) Self-application of low-tech heat therapy (I) Intraarticular glucocorticosteroid injections (B) Intraarticular hip visco-supplementation injections (I) Hip arthroplasty for severe arthritides (A)	Glucosamine sulfate intra-muscular injections (I) Glucosamine sulfate intra-articular injections (I) Glucosamine sulfate, chondroitin sulfate, or methylsulfonylmethane for prevention of osteoarthrosis (I) Diacerein (I) Diathermy (I) Infrared therapy (I) Ultrasound (I) Low-level laser therapy (I) Manipulation or mobilization (I) Massage (I) Electrical therapies outside of research settings (I) Transcutaneous electrical nerve stimulation (TENS) (I) Botulinum injections (I)	
Lower Abdominal Strains	Measures to prevent falls (I) NSAIDs (I) Work limitations for patients with lower abdominal strains who perform high-physical jobs or cannot avoid job tasks thought to have resulted in the strain (I) Ice (I) Heat (I) Physical or occupational therapy (I)	Ergonomic interventions to prevent or facilitate recovery (I) Work limitations for most lower abdominal strains (I)	Bed rest (I)
Meralgia Paresthetica	Measures to prevent falls (I) Weight loss for patients who are overweight or obese, avoidance of aggravating exposures, and the wearing of loose clothing (I) Glucocorticosteroid injections for meralgia paresthetica if more conservative treatments are not efficacious (I) Surgical release for select patients (I)	Ergonomic interventions to prevent or facilitate recovery (I) NSAIDs (I) Topical lidocaine patches (I) Spinal cord stimulators for select patients (I)	

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**For therapy and prevention, well-conducted cohort studies. For prognosis, etiology or harms, well-conducted retrospective cohort studies or untreated control arms of RCTs.

Table 3. Summary of Recommendations for Pre-, Peri-, and Post-operative Issues Related to Hip and Groin Disorders

Recommended	No Recommendation	Not Recommended
Gabapentin for peri-operative management of hip pain to reduce need for opioids, particularly in patients with adverse effects from opioids (A) NSAIDs for post-operative hip pain (I) NSAIDs for prevention of heterotopic bone formation after arthroplasty (B) Acetaminophen (or the analog, paracetamol) for post-operative hip pain particularly in patients who have contraindications for NSAIDs (I) Judicious use of opioids for post-operative hip pain (I) Cryotherapy for hip arthroplasty and surgery patients (C) Acupuncture for hip arthroplasty procedures (B) One-day use of systemic antibiotics for patients undergoing surgical hip procedures (B) Pre-operative education program prior to hip arthroplasty (B) Prevention of venous thromboembolic disease for post-operative hip patients, particularly arthroplasty patients or other post-operative patients with prolonged reductions in activity (early ambulation is recommended) (A) Use of post-operative graded compression stockings for prevention of venous thromboembolic disease (B) Use of lower extremity pump devices for prevention of venous thromboembolic disease (B) Low-molecular weight heparin for prevention of venous thromboembolic disease (A)	Manipulation or mobilization for surgical patients (I) Pre-operative autologous blood donation (I) Routine peri-operative use of bisphosphonates (I) Routine post-operative use of calcitonin (I) Use of treatment in a geriatric unit or using interdisciplinary rehabilitation (I) Use of a late post-operative program for patients with mild reductions of questionable significance in the late post-operative period (I) Specific vocational or avocational pursuits post-operatively (I)	Tumor necrosis factor-alpha blockers for arthroplasty patients with peri-acetabular osteolysis (I)

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Factor Xa inhibitors for prevention of venous thromboembolic disease (A) Warfarin and heparin for prevention of venous thromboembolic disease (B) Aspirin for prevention of venous thromboembolic disease (B) A pre-operative exercise program particularly emphasizing cardiovascular fitness and strengthening especially for patients who exhibit evidence of weakness or unsteady gait. Flexibility components may be reasonable in those without fixed deficits. (B) Post-operative exercise program and rehabilitation program for hip arthroplasty surgery patients (B) For at least the first 6 weeks post-operatively, use walking aid as long needed (C) For at least the first 6 weeks post-operatively, add other recommendations only if needed (e.g., elevated toilet seats, prohibiting driving) (C) For at least the first 6 weeks post-operatively, ADL adaptive equipment as needed (e.g., long- handled reacher, long-handled shoe horn or sock aid) (I) Post-operative exercise program and rehabilitation program for hip fracture patients (B) Geriatric unit treatment for patients with multiple health care issues, particularly if there is moderate dementia (C) A late post-operative exercise program after either arthroplasty or hip fracture emphasizing cardiovascular fitness and strengthening or resistance for patients who exhibit significant evidence of weakness or unsteady gait. A home exercise program among motivated patients may be sufficient. (C)		

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**For therapy and prevention, well-conducted cohort studies. For prognosis, etiology or harms, well-conducted retrospective cohort studies or untreated control arms of RCTs.

BASIC PRINCIPLES AND DEFINITIONS

Acetabulum: A somewhat spherical structure which covers approximately 170º of the femoral head.

Acute, Subacute, or Chronic Pain: For purposes of identifying interventions at different stages of diseases, acute pain is defined as pain for up to 1 month; subacute, pain from 1 to 3 months; and chronic, pain of more than 3 months duration (see Chronic Pain chapter for additional information).

Active Therapy: The term “active therapy” is commonly used to describe treatment that requires the patient to assume an active role in rehabilitative treatment. Although there is no one specific treatment defined by this term, it most commonly includes therapeutic exercises, particularly aerobic activities and muscle reconditioning (weight lifting or resistance training).(93) Some studies have included active stretching and treatment with psychological, social, and/or educational components requiring active participation from the patient.(94)

Active Exercise Therapy: Active exercise therapy typically consists of cardiovascular training and muscle strengthening,(95, 96) although it may also include progressive or occasionally even active stretching, especially in patients with substantially reduced ranges of motion. Active exercise therapy is used as a primary treatment for chronic pain, is frequently initiated in the course of treating subacute pain, and is a primary treatment after various surgeries. The goal of active exercise therapy is to improve function.(95) The word “active” is used to differentiate individualized exercise programs designed to address and rehabilitate specific functional, anatomic or physiologic deficits from passive treatment modalities or from forms of “exercise” that require very little effort or investment on the part of the patient or provider.

Allied Health Therapies: These are treatment approaches that require extensive training and development of specific skills. Allied health therapies include manipulation, mobilization, massage, and acupuncture.

Bursae: Bursae are fluid-filled sacs within the body which provide lubrication in areas such as points where muscles move over bony projections.

Bursitis: Bursitis occurs when the bursae become inflamed and irritated. This results in pain when the overlying muscle is used. It may occur from a number of exposures, including when there is direct pressure, in those with adjacent tissue that is degenerative such as tendons, or with forceful and unaccustomed use.

Delayed Recovery: Delayed recovery is most commonly defined as an increase in the period of time prior to returning to work or to usual activities, when compared with the length of time expected, based on reasonable expectations, disorder severity, age, and treatments provided.

Enthesopathy: Disorder of the muscular or tendinous attachment to bone.

Femoral Neck: The femoral neck lies between the femoral head and femoral shaft, demarcated by the greater and lesser trochanters. As the blood supply to the femoral head runs through the femoral neck, a femoral neck stress fracture may disrupt the blood supply to the femoral head leading to osteonecrosis of the femoral head.

Femoral Neck Stress Fracture: Stress fractures of the femur occur mainly at the femoral neck and are classified as either tension fractures (at the superior aspect of the femoral neck) or compression fractures (at the inferior aspect of the femoral neck). Pain associated with femoral neck stress fractures may be poorly localized in the hip and may be referred to the thigh or back. Femoral neck stress fractures usually manifest insidiously; otherwise healthy persons report pain related to activity, which

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does not resolve with conservative therapy. These fractures may be mild causing only minimal bone changes and eventually heal, or they might progress to a complete fracture requiring surgical fixation. Stress fractures of the femoral neck are usually seen in young, active individuals who change activity level or who do strenuous activity to which they are unaccustomed.

Functional Capacity Evaluation (FCE): A comprehensive battery of performance-based tests used to attempt to assess an individual's ability for work and activities of daily living.(97) An FCE may be done to identify an evaluee's ability to perform specific job tasks associated with a job – a job-specific FCE, or his or her ability to perform physical activities associated with any job – a general FCE (see Chronic Pain and Low Back Disorders chapters for additional information).

Functional Improvement (especially objective evidence): Functional improvement entails tracking and recording evidence that the patient is making progress toward increasing his or her functional state (validated tools preferred).

Functional Restoration: A term initially used for a variant of interdisciplinary pain alleviation or at least amelioration characterized by objective physical function measures, intensive graded exercise and multi-modal pain/disability management with both psychological and case management features.(98-104) The term has become popular as a philosophy and an approach to medical care and rehabilitation. In that sense, the term refers to a blend of various techniques (physical and psychosocial) for evaluating and treating the chronic non-malignant pain patient, particularly in the workers' compensation setting (see Chronic Pain chapter for additional information).

Greater Trochanteric Bursitis: Trochanteric bursitis occurs when the trochanteric bursa is inflamed, although in most cases, there are not classic symptoms and signs of inflammation. Classic inflammation may occur with arthropathies or infectious agents. Patients usually complain of lateral hip pain because pain may radiate down the lateral aspect of the thigh. The hip joint itself is not involved. The condition is thought to occur either as a result of acute trauma such as contusions from falls, idiopathic, or from stereotypical use where the bursa becomes irritated due to friction by the iliotibial band (ITB). Leg-length discrepancy, hip abductor weakness, and lateral hip surgery are predisposing factors.

Groin: The groin includes the lower rectus abdominis musculature, the inguinal region, symphysis pubis, upper portions of the thigh adductor muscles, and the genitalia and scrotum. It consists of the area where the abdomen meets the legs. A groin strain is a disruption of a myotendinous junction. A complete muscular tear may occur.

Groin Injury: Most groin injuries are related to unaccustomed or high forces on the hip joint and surrounding bony and muscular support structures of the pelvis. The most common *acute* groin injuries are contusions and hematomas. The most common *chronic* groin conditions are strains of the muscle-tendon unit resulting from high force.

Harris Hip Score: The Harris Hip Score is one of the more commonly used scoring systems for hip disorders (see www.orthopaedicscore.com/scorepages/harris_hip_score.html and WOMAC and Hip Outcomes Score below). Scoring is based largely on the degree to which pain limits activities combined with ranges of motion.(105)

Hip Dislocation: Hip dislocations are relatively uncommon and usually result from a violent or high-speed collision or fall (up to 70% are due to motor vehicle accidents). Pain is usually severe, associated with an inability to bear weight and with shortening and rotation of one leg inward or outward. Hip dislocations are either anterior or posterior with posterior hip dislocations comprising the majority of traumatic dislocations. Most other dislocations occur due to a congenital malformation of the hip joint or occur after hip replacement.

Hip Dysplasia: Hip dysplasia, or developmental dysplasia of the hip (DDH), is a relatively common problem where there is less acetabular bony coverage over the femoral head.

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Hip Joint: The hip joint is a synovial ball-and-socket type joint based on the articulation of the head of the femur and the acetabulum of the pelvis. Five ligaments hold the femur in the acetabulum: the iliofemoral ligament, pubofemoral, ischiofemoral, transverse acetabular and femoral head ligaments. Dislocation of the hip joint is difficult due to the angulation of the proximal femur in relation to the acetabulum and the strength of these ligaments joined together.

Hip Outcome Score: This is a commonly used scoring system for hip disorders and prominently includes ratings of the degree of difficulty performing specific tasks. It also incorporates a sports rating system that is sometimes useful for more active patients (see http://outcomeregistry.binaryspectrum.com/HarrisHOS/HarrisHipScore Forms.aspx).

Hip Pain: Pain originating from the hip is usually felt in the buttock or groin area with radiation to the distal thigh and anterior medial aspect of the knee. Pain in the hip may also be due to referred pain from cardiovascular or metastatic processes, lumbar disc herniation with neurological impingement, retroperitoneal or pelvic tumor, or from aortoiliac insufficiency.

Osteonecrosis [Avascular Necrosis (AVN)] of the Femoral Head: Osteonecrosis occurs when the tenuous blood supply to the femoral head is interrupted. Osteonecrosis of the femoral head can be a result of traumatic or non-traumatic factors. The condition is painless early on, but as it advances, patients generally present with pain and limitation of motion. Pain most commonly localizes in the groin area, but also manifests in the ipsilateral buttock, knee, or greater trochanteric region. Pain is usually exacerbated by weight bearing and relieved with rest.

Pain Behavior: Pain behavior includes verbal and non-verbal actions (e.g., grimacing, groaning, limping, using pain relieving or support devices, requesting pain medications, etc.) which communicate the concept of pain.

Passive Modality: Passive modality refers to various types of provider-given treatments in which the patient is passive. These treatments include medication, injection, surgery, allied health therapies (e.g., massage, acupuncture, and manipulation), and various physical modalities such as hydrotherapy (e.g., whirlpools, hot tubs, spas, etc.), ultrasound, TENS, other electrical therapies, heat, and cryotherapies.

Primary Prevention: Primary prevention involves preventing the condition or risk factor from developing (e.g., physical activity programs to prevent obesity which results in osteoarthrosis).

Rehabilitation: The term “rehabilitation” is used in these *Guidelines* to mean physical medicine, therapeutic and rehabilitative evaluations, and procedures. Rehabilitation services are delivered under the direction of trained and licensed individuals such as physicians, occupational therapists, or physical therapists. Mental health professionals may also be incorporated in the treatment team, particularly for select chronic pain patients. Jurisdictions may differ on qualifications for licensure to perform rehabilitative evaluations and interventions.

Secondary Prevention: Secondary prevention involves reduction in the exposure or risk factor after the risk factor has already developed, but before the disease has occurred (e.g., use of fall protection equipment to prevent hip fractures).

Sprain: A sprain is the disruption of a joint’s ligaments.

Strain: Strain is the disruption of a myotendinous junction, usually from a high force, unaccustomed exertion(s). It may also occur during an accident. This term is occasionally used to describe non-specific muscle pain in the absence of knowledge of an anatomic pathophysiological correlate.

Synovitis: Synovitis refers to inflammation of a synovial membrane, although in most cases there are no classic symptoms or signs of inflammation. Classic inflammation occurs with crystalline arthropathies or infectious agents. Synovitis is usually painful, especially with motion. Fluctuating swelling may occur due to effusion within the synovial sac.

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Synovial Membrane: The synovial membrane incorporates the entire femoral head, the anterior neck, and the proximal half of the posterior neck of the femur.

Tenosynovitis: Tenosynovitis refers to inflammation of a tendon sheath, although in most cases there are no classic symptoms or signs of inflammation. Classic inflammation may occur with arthropathies or infectious agents.

Tertiary Prevention: Tertiary prevention has most typically been defined as amelioration of the condition after it has already developed. For example, after a patient has osteonecrosis, precluding him or her from diving or other decompression activities is a method of tertiary prevention.

Trochanteric Bursa: The trochanteric bursa lies between the femoral trochanteric process and the gluteus medius/iliotibial tract, just superficial to the greater trochanter of the femur.

Visual Analog Scale (VAS): The visual analog scale measures a patient's level of subjective pain from "no pain" to "worst pain."

Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index: The WOMAC index is the most common outcome measure other than standard and VAS pain ratings. It combines subjective ratings of pain with activities, stiffness, physical function, social function and emotional function measures.(106)

INITIAL ASSESSMENT

The physician performing an initial evaluation of a patient with hip or groin pain should seek a discrete explanatory diagnosis. A careful, thorough history is required. Review of systems that also involve the knee, spine, abdomen, and genitourinary tract is necessary. The examination of the 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. Medical history and physical examination findings can alert the physician to other pathology that presents with pain or other constitutional symptoms. Certain findings, "red flags," raise suspicion of serious underlying medical conditions (see Table 4). Potentially serious disorders include infections, tumors, or systemic rheumatological disorders.

Table 4. 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 a lifetime) Age >50 years Symptom consistent with disease in 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 bursitis 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); IV drug abuse; diabetes mellitus; or immunosuppression (due to corticosteroids, transplant, or HIV) History of recurring infections treated with antibiotics (e.g., repeated urinary tract infections)	Fever, tachycardia, tachypnea, hypotension Elevated white blood cell count (may be decreased in elderly or immunocompromised) Shift in the WBC differential towards immature cells ("left shift") Abnormal urinalysis Abnormal body part examination (e.g., pulmonary)

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	Foreign travel with exposure potential Insect bites	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 – urinary retention or bowel incontinence Hyper-reflexia or other evidence of myelopathy
Rheumatologic Disease	Diffuse arthralgias Prior arthropathies Skin changes, lesions, or ulcers Fatigue, malaise Subtle mental status changes	Polyarticular joint effusions (usually with warmth) X-ray 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 reviewing many common suggestive historical and examination findings.

MEDICAL HISTORY AND PHYSICAL EXAMINATION

MEDICAL HISTORY

The initial evaluation of patients with hip or groin pain should include a thorough medical history, as the vast majority of data to successfully evaluate and treat these patients is found in the history. A complete occupational history is necessary to assist the patient with successful accommodation and rehabilitation, as well as determine work-relatedness. Hip joint pathology reportedly has varying clinical presentations with pain experienced in various joints and body regions documented by fluoroscopically guided intraarticular bupivacaine injection (see Table 5 and Figure 1).(107) Other data from patients awaiting hip arthroplasty have suggested referral patterns to the groin, anterior thigh and knee.(108-114) Pain referral patterns are highly variable, thus physicians must have a clinical suspicion for hip joint pathology to properly evaluate and diagnose hip disorders.

Table 5. Frequency of Pain Referral to the Buttock, Thigh, Groin, Leg, Knee, and Foot

Anatomic Region	Percentage of Patients with Pain
Buttock	71
Thigh	57
Anterior	27
Lateral	27
Posterior	24
Medial	16
Groin	55
Leg	16
Lateral	8
Posterior	8
Anterior	4

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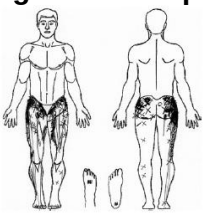
Medial	2
Foot	6
Knee	2

Lesher JM, Dreyfuss P, Hager N, Kaplan M, Furman M. Hip joint pain referral patterns: a descriptive study. *Pain Med*. 2008;9(1):22-5. Reprinted with permission from John Wiley and Sons.

Figure 1. Composite Preprocedural Pain Drawing from All Patients



Lesher JM, Dreyfuss P, Hager N, Kaplan M, Furman M. Hip joint pain referral patterns: a descriptive study. *Pain Med*. 2008;9(1):22-5. Reprinted with permission from John Wiley and Sons.

1. What may I do for you today? (This question helps to frame the discussion towards what the patient feels is the main purpose of the visit. This includes situations where it seems eventually tangential after a complete evaluation. This also helps ensure that the physician is able to eventually address the main purpose which is important to patient satisfaction.)

2. What are the symptoms? How does the worker act when describing them (may help ascertain the expression of and meaning of pain to the worker, while simple hand gestures and postures taken while describing the pain are often highly useful for diagnosis)?
   - What are your symptoms?
   - When did your symptoms begin?
   - Where are the symptoms located?
   - What activities make you worse or better?
   - Do you have pain or stiffness?
   - Do you have numbness or tingling?
   - Do you have pain or other symptoms elsewhere?
   - Have you lost control of your bowel or bladder?
   - Do you have fever, night sweats, or weight loss?
   - Are your symptoms constant or intermittent? What makes the problem worse or better?
   - What is the day pattern to your pain? Better getting out of bed in the morning, during the morning, mid-day, evening, or asleep? When is it worst? Do you have a problem sleeping? What position is most comfortable?
   - Since these symptoms began, have your symptoms changed? How?
   - How does having this pain affect your life?

3. How did the condition develop?
   Past:
   - Have you had similar episodes previously?
   - Have you had previous testing or treatment? What treatment? What were the results? With whom? How long did it take to get back to work? To light duty? (Was recovery similarly delayed?)
   - Did you receive a disability or impairment rating?
   - Was recovery complete? (Did you get a disability award?)

   Cause:
   - What do you think caused the problem?

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- How do you think it is related to work?
- Were you doing anything at that time when your symptoms began? (It is important to obtain all information necessary to document the circumstances and biomechanical factors of injury to assist the patient in obtaining compensation, where appropriate.)
- Did your symptoms begin gradually or suddenly? Did you notice the pain the day after the event?
- Did you slip, trip, fall, twist, jerk, or strike an object?
- For traumatic injuries: Was the area deformed? Did you lose any blood or have an open wound?

Job:

- What are your specific job duties?
- What are your work hours and breaks?
- Do you rotate jobs?
- How long do you spend performing each duty on a daily basis?
- Do you have assistance of other people or lifting devices?
- What do you do for work/modified duty?
- What is the hardest part of the job for you to do with your injury? Why?
- How much do you lift at work as a maximum? Usual lift?
- What was your previous job? What were those occupational factors?

Non-Occupational Activities:

- What other activities (hobbies, workouts, sports) do you engage in? At home or elsewhere? (For suspicion of hip osteoarthrosis: What prior activities did you engage in? What prior jobs?)
- Describe your current daily activities by explaining your activities from awakening to bedtime?
- Any heavy lifting? How? How often?
- Can you perform activities of daily living (e.g., dressing, bathing, grooming, etc.) or instrumental activities of daily living (e.g., shopping, food preparation, housekeeping, etc.)?
- Could these have contributed to the development of pain?

4. Assess treatments and how the responses may or may not have differed from expected outcomes.
   - What treatments have you had?
   - Did anything help decrease your symptoms? What and for how long?
   - Are you doing any exercises at home? Which ones? How often?
   - Are you taking any non-prescription medications and supplements?

5. Discuss symptom limitations.
   - How do these symptoms limit you?
   - If these symptoms limit you, how long have your activities been limited?
   - How long can you sit, stand, walk, and bend?
   - Can you lift? How much weight can you lift (use gallons of milk, groceries, etc., as examples)?
   - How much can you push or pull?

6. Are there other medical problems? For example:
   - Osteoarthrosis, rheumatoid arthritis or other arthritides
   - Fractures, lower extremity surgeries
   - Cardiovascular disease
   - Pulmonary disease
   - Gastrointestinal problems
   - Diabetes mellitus
   - Neurological disorders (including radiculopathies, headaches)
   - Psychophysiologic disorders (e.g., irritable bowel syndrome, chronic fatigue syndrome, sick building syndrome, fibromyalgia, and multiple chemical sensitivity)

7. Is there any psychological, psychiatric, mental health, substance use, alcohol, or tobacco disorder history?
   - Have you ever had a substance use problem? DUI? Detoxification?
   - Have you ever had an alcohol problem? (CAGE or MAST screening especially required for possible osteonecrosis)

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- Is there tobacco use? Prior use? (Assess number of packs per day/number of years)
- Is there use of other drugs? (Current and prior use)

8. What is the occupational psychosocial context?
   - Do you like your job?
   - What is your relationship with your co-workers and supervisor and how do they treat you?
9. Assess whether there are problems at home/social life. Does the patient feel in control of most situations? Is there support?
   - How do your family members get along with each other?
   - How do they help and support you, including assistance with chores?
   - Does your family treat you differently now that you are in pain? Have your roles at home changed because of your injury?
   - How do your friends treat you differently?
   - Do you get increased symptoms when you are dealing with problems with your family and friends? How often? When? Why?
10. Are there advocagenic (litigious) influences?
    - Do you have a workers' compensation claim for this injury?
    - Do you have a lawsuit or other legal action involving this pain problem?

PHYSICAL EXAMINATION

The objective of the physical examination of the hip is to help define the physical abnormality (ies) and narrow the diagnostic considerations to ultimately help focus the treatment plan. Physical examination data, including vital signs should be reviewed for potential inferences regarding infectious or neoplastic origins.

The physical examination should begin the moment the physician sees the patient. Observing how the patient sits, walks, and moves is of major importance, often more important than any other aspect of the exam. It also helps to have the patient demonstrate what positions seem to provoke or caused the symptoms as the demonstration is invariably of greater help than verbal descriptions.
Guided by the medical history, the physical examination includes:

- General observation of the patient, including changes in positions, stance and gait;
- Regional examination of the hip and groin;
- Examination of organ systems related to appropriate differential diagnoses;
- Neurologic screening;
- Testing for various specific hip and groin disorders;
- Monitoring for pain behavior during range of motion, changing postures as a clue to origin of the problem.

Most of the hip exam is not purely objective, as there is generally an element of cooperation for determination of strength or active range of motion and most maneuvers require a subjective statement of pain to be considered positive. However, atrophy, fasciculations and extremity length discrepancies are all wholly objective measures.

It is frequently helpful to obtain measurements of the patient's capabilities in the clinic to follow in subsequent clinic visits. These may include:

- Walking distance (observe in the hallway or outdoors and subsequently simultaneously interview the patient about their progress if a longer walking ability is demonstrated);
- Ability to climb stairs (walking to the nearest stairwell with the patient and observing capabilities);
- Repeated toe raises (number able to perform);
- Distance of heel walking;
- Squats (number);
- Sensory examination findings (e.g., monofilaments), or
- Movement inconsistent while in exam room with pain/injury problem.

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This also moves the examiner from the role of a more passive observer to a more active team leader, resulting in more informed decision making on exercise and other physical activity benchmarks. Active involvement of the provider is believed to be helpful to facilitate the patient's recovery.(115) The use of validated functional assessment tools to follow patient progress is recommended.

Physical Examination for Specific Diagnoses

Physical examination findings vary largely on the severity and acuity of the disorder. In general, conditions that arise acutely present with more pronounced physical examination findings. Patients with long-standing conditions have less prominent physical examination findings.

Osteonecrosis – Avascular Necrosis (AVN)
The physical examination findings of patients with osteonecrosis usually include reduced range of motion and pain with passive range of motion. There may be pain with weight bearing. Patients may be unable to bear weight if there has been collapse of the avascular bone.

Epididymo-orchitis
Physical examination findings of epididymoorchitis consist of unilateral epididymal with or without testicular tenderness. There is no dysuria, discharge, or abnormalities on urinalysis.

Femoroacetabular Impingement (FAI)
FAI patients have variable physical examination findings that include decreased internal rotation and adduction with the hip flexed to 90 degrees. Patients usually have a positive impingement test (pain with passive adduction and gradually internally rotating the flexed hip).

Gluteus Medius Tears
Patients with a relatively acute onset tear of the gluteus medius have an abnormal gait, as they are unable to horizontally stabilize their pelvis. Tenderness over the greater trochanter may be present and range of motion is usually reduced. Qualitative muscle strength weakness is present and tends to be worse with larger tears, although on a chronic basis, compensatory mechanisms of surrounding muscles help minimize abnormalities found on physical examination.

Greater Trochanteric Pain Syndrome
Same as trochanteric bursitis and possible findings of gluteus medius tears.

Groin Strain
Patients with groin strains avoid use or movement of the affected myotendinous junction, which is also focally tender on examination. If there is a complete rupture, there is a muscular defect and a hematoma usually forms acutely. Patients tend to have reduced qualitative muscle strength.

Hip Dislocations, Fractures, or Sprains
Patients with acute dislocations or fractures are unable to bear weight. Both conditions tend to have a shortened lower extremity that is usually externally rotated. However, patients with sprains are able to bear weight and use the joint, although pain is present.

Hip Dysplasia
In hip dysplasia, pain is often reproduced with the impingement sign. Pain is reproduced with hip hyperextension or placing the hip in the FABER position. Increased range of motion of both hips may be present, but the affected hip has less motion, often limited by pain.

Hip Instability
In cases of hip instability, range of motion may be increased and findings may be present for ligamentous laxity. Patients tend to have increased hip external rotation (in extension during the log roll or in flexion such as the FABER maneuver).

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Hip Osteoarthrosis
The physical examination for rheumatological issues should include an evaluation of all relevant joints as well as a comprehensive musculoskeletal examination. Common joints for abnormalities must be examined (DIP, PIP, MCP, wrist, shoulder, spine, hip, knees, great toe MTP) with low threshold for examining the remaining joints not listed. This includes observation, inspection, function, gait, palpitation, active and passive range of motion, and strength and stretch reflexes. There should be an evaluation to attempt to detect whether there are signs of degenerative joint disease that are present despite the absence of complaints (e.g., Heberden's nodes in a patient with knee arthritis, or crepitus on range of motion of the knee in a patient with hand complaints). These may provide evidence for a systemic arthropathy (whether osteoarthrosis or not). Presence of warmth and mild tenderness over the MCP joints is for example, a clue that what appears to be knee joint arthritis may be rheumatoid arthritis. These diagnostic clues have substantial long-term implications for successful secondary prevention. Threshold for a comprehensive rheumatological examination should generally be low, especially if arthritic issues are present in multiple joints. Range of motion is generally reduced, especially hip rotation, although it can be normal when mild.

Labral Tears
Labral tears present with variable findings. Pain may be reproducible on range of motion. The extent of the range of motion is often restricted. Pain may be reproduced with placing the hip into extension from flexion. Pain is present in the majority of cases with hyperflexion, internal rotation and adduction (impingement position). The pain and/or clunk may also be reproduced with the labral stress test and/or with resisted straight leg raise.

Ligamentum Teres Ruptures
The physical examination is usually normal in the absence of other findings. As this condition may accompany osteoarthrosis, those examination findings may be present.

Lower Abdominal Strains
The physical examination findings consist of focal tenderness in the affected muscle. Generally, there are no other findings on examination, although on occasion these may accompany epididymoorchitis.

Meralgia Paresthetica
Meralgia paresthetica patients have reduced sensation in the distribution of the lateral cutaneous nerve to the thigh.

Trochanteric Bursitis
Tenderness is invariably present over the greater trochanter. Pain is also usually present with hip range of motion. The total extent of the hip range of motion is usually normal.

WORK-RELATEDNESS

Acute occupational hip injuries are related to a specific acute traumatic event – the location of the event determines work-relatedness and is non-controversial. Most jurisdictions also request a physician opinion as to whether a disease or disorder should be considered work related for the purpose of workers' compensation. Physicians need to remember that their role is to supply opinion and that the "medical/scientific" answer and the "legal" answer as determined by regulations and case law precedents in a particular jurisdiction (workers' compensation system) are different (see Work-Relatedness chapter for determining work-relatedness). That said, there are few if any quality epidemiological studies addressing work-related hip disorders. Thus, aside from these specific circumstances (e.g., occupational fractures and other acute trauma, osteonecrosis from barotraumas, hip osteoarthrosis in farmers, trochanteric bursitis after a fall), most opinions are speculative.

OSTEONECROSIS – AVASCULAR NECROSIS (AVN)

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There are many non-occupational risk factors for osteonecrosis, including male gender,(66) diabetes mellitus,(116) glucocorticosteroid treatment or excess,(66, 117-119) alcohol,(120-126) gout,(118, 122) sickle cell anemia,(118, 124) sickle cell trait,(124) organ transplantation,(67, 127) multiple myeloma,(66) smoking,(121, 125, 126) or obesity.(121) The primary occupational risk factor is barotrauma ("the bends"), which may occur due to diving as well as working in compressed air environments (e.g., certain types of tunneling projects through unstable sediments requiring compressed air to maintain the workspace). Significant, discrete trauma is thought to be a risk factor (e.g., unilateral fracture and unilateral osteonecrosis).(128, 129) Occupational physical factors are controversial,(125) but it has been theorized that high force or repeated activities are risk factors. However, there are no quality studies to define work-relatedness.

FEMOROACETABULAR IMPINGEMENT

There are numerous associated non-occupational anatomic abnormalities (e.g., altered femoral neck morphology, such as due to slipped capital femoral epiphysis, anteverted femoral neck, femoral neck nonunion, developmental hip dysplasia, Legg-Calves-Perthes disease, osteonecrosis, a "pistol grip" femoral neck, and coxa vara, as well as acetabular morphologic variants, such as retroverted acetabulum, and deep acetabular socket [coxa profunda and protrusion]). However, no quality studies address occupational factors. There are cases that are theorized to have an underlying occupational contribution – i.e., patients have greater risk of FAI from stereotypical use in certain positions (e.g., baseball catcher's position, some construction workers).

GLUTEUS MEDIUS TEARS

Gluteus medius tears are degenerative tendon conditions and tears, similar to those in the rotator cuff, and are considered more analogous to diseases. However, discrete accidents may contribute to these tears. It is theorized that forceful use may contribute to the condition, thus it is possible this condition may be occupational in some circumstances. However, there currently are no quality epidemiological studies to identify occupational risk factors.

GROIN STRAIN

Groin strains involve myotendinous strains in the groin. Symptoms are usually acute onset and these injuries are considered more analogous to acute injuries than diseases, although repeated, unaccustomed use may precipitate the event. Thus, the nature of the forceful unaccustomed use determines whether the condition is work-related.

HIP DISLOCATIONS, FRACTURES AND SPRAINS

Hip dislocations, fractures, and sprains are consequences of significant trauma. The mechanism of trauma determines whether the condition is work-related. With dislocations, there is frequently an inherited or congenital abnormality with a propensity towards recurrences. In situations where there is inherited dysplasia, dislocation may occur in the context of a work event, but work-relatedness will be determined largely based on a specific definition of work-relatedness in the setting of pre-existing, non-occupational conditions.

HIP DYSPLASIA

Hip dysplasia is a non-occupational condition.

HIP INSTABILITY

Traumatic instability is not controversial as the location of trauma determines work-relatedness. Atraumatic instability is less clearly occupational as there are no quality studies that demonstrate increased risk for instability from occupational tasks. While a theory could be constructed for work-relatedness due to stereotypical use, factors are currently unclear.

HIP OSTEOARTHROSIS

There are numerous non-occupational factors as well as a few occupational factors for hip osteoarthrosis. The non-occupational factors include age,(130-135) obesity,(64, 136) bone mineral density,(137) rheumatoid arthritis, gout, other inflammatory arthropathies, reduced 25-hydroxyvitamin

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D,(135) heredity,(132) Heberden's nodes,(131-133, 138, 139) and osteoarthrosis involving other joints in the body ("systemic or generalized osteoarthrosis").(51, 131, 138-141) Unilateral hip osteoarthrosis as a consequence of a discrete occupational traumatic event (e.g., femur fracture) is considered occupational and is not substantially controversial. However, it is unclear whether symmetrical cases are work related in the absence of significant bilateral trauma.

Farmers have been consistently found to have an elevated risk for hip osteoarthrosis, but the reason for this increased risk is unclear. Greater time spent farming has not been found to result in a dose-response related increase risk of hip osteoarthrosis. This suggests support for the theory that forceful use in youth, with resultant slipped capital femoral epiphyses, may explain the condition.(50, 142-144)

There are no other occupations with consistent findings of work-relatedness, and no occupational epidemiological studies with measured workplace factors have been reported. There are theories and weak studies suggesting heavy lifting may be a risk factor. However, these studies used retrospective methods and thus are biased toward increased exposure estimation among those with hip osteoarthrosis. A study of runners found no greater prevalence of hip osteophytes and trended towards greater cartilage thickness on x-rays in runners compared with non-runners.(145) A population-based study from Denmark found a lack of increased risk for hip osteoarthrosis requiring arthroplasty with increased exposures by expert ratings incorporating standing/walking, sitting, whole body vibration and heavy lifting ranging from low (e.g., office workers) to medium (e.g., nurses) to high risk such as construction workers.(2)

LABRAL TEARS
Like other cartilaginous tears in the body, labral tears are likely degenerative and not work-related. For tears that occur with an acute symptomatic onset due to a discrete event, work-relatedness is largely non-controversial. When there is a symptomatic degenerative tear in the absence of trauma, work-relatedness is speculative.

LIGAMENTUM TERES RUPTURES
There are few studies of ligamentum teres rupture and there are no quality studies that address occupational factors. A ligamentum teres rupture in the setting of a discrete traumatic occupational event is not controversial. Other cases of possible work-relatedness are speculative.

TROCHANTERIC BURSITIS
Trochanteric bursitis appears to occur both in the presence and absence of trauma. There are no quality studies evaluating occupational factors. In settings where significant trauma has occurred to precipitate the bursitis, work-relatedness is not controversial. In the absence of trauma, a theory may be constructed whereby physical factors such as unaccustomed forceful use of the hip may cause the condition; however, this is speculative. Tests should be ordered if there is a reasonable probability that trochanteric bursitis is present and that the test results may change the management of the condition. Sometimes, the threshold for ordering a test is lower if the adverse effects resulting from missing the diagnosis are considerable.

SPECIAL STUDIES, DIAGNOSTIC AND TREATMENT CONSIDERATIONS

Diagnostic Criteria

The criteria presented in Table 6 follow the clinical thought process from the mechanism of illness or injury to unique symptoms and signs of a particular disorder and finally to test results (if tests are needed to guide treatment at this stage).

Table 6. Diagnostic Criteria for Non-red-flag Conditions

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Probable Diagnosis or Injury	Symptoms	Signs	Tests and Results
Hip Osteoarthrosis	Non-radiating hip pain. Morning stiffness or stiffness on standing after prolonged sitting. Sleep disturbance sometimes present; mood disturbance usually not present. Often other affected joints.	Range of motion (ROM) generally reduced especially hip rotation. May be normal when mild.	X-rays 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 x-rays usually ordered. Other testing usually not necessary.
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. Other testing usually not necessary in acute treatment setting.
Labral Tears	Non-radiating 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 majority. Pain and/or clunk may also be reproduced with the labral stress test and/or with resisted straight leg raise.	X-rays often ordered. MRI is sometimes ordered, and MR arthrography often helpful.
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.	X-rays required. MRI and CT may be ordered for further evaluation of the femoral head. Bone scans sometimes ordered particularly for evaluation of other joints.
Trochanteric Bursitis	Non-radiating lateral hip pain. Pain worse with activity.	Tender over greater trochanter. Pain with hip ROM. Extent of ROM usually normal.	X-rays sometimes ordered. Other testing usually not required.
Femoroacetabular Impingement	Non-radiating 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).	X-rays usually ordered. MRI and MR arthrography helpful.
Gluteus Medius Tears	Non-radiating 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.	X-rays usually ordered. MR helpful.
Greater Trochanteric Pain Syndrome	Non-radiating hip pain. Pain increased when lying on the affected side or stair	Tender to palpation over the greater trochater. Antalgic gait sometimes present and increased	X-rays usually ordered. MRI sometimes helpful.

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	climbing.	pain with stair climbing.	
Groin Strain	Focal pain in the muscle-tendon junction affected. May have epididymal pain if inguinal area involvement.	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 less motion, often limited by pain.	X-rays often sufficient
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).	X-rays usually ordered. MRI may be helpful.
Ligamentum Teres Ruptures	May be asymptomatic or have experienced pain if ligament tear with discrete traumatic event. Event usually involved exaggerated adduction and external rotation or abduction.	Exam usually normal in the absence of other findings. May accompany osteoarthrosis, thus those exam findings may be present.	X-rays 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(146); 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.(147)

Note: The above highlights are footnotes

DIAGNOSTIC TESTING AND OTHER TESTING

ANTIBODIES

There are numerous antibodies that are markers for specific rheumatic diseases (e.g., rheumatoid factor, anti-nuclear antibodies, anti-Sm, anti-Ro, anti-La for rheumatoid arthritis, systemic lupus erythematosus, Sjogren's, mixed connective tissue disorder, etc.). Patients with rheumatic disorders are at increased risk for degenerative joint disease of the hip.

1. *Recommendation*: *Antibodies for Diagnosing Hip Pain with Suspicion of Chronic or Recurrent Rheumatological Disorder*
   Antibody levels are recommended to evaluate and diagnose patients with hip pain if there is reasonable suspicion of a rheumatological disorder.

   Indications – Patients with hip pain with suspicion of rheumatological disorder.

   Strength of Evidence **– Recommended, Insufficient Evidence (I)**

2. *Recommendation*: *Antibodies to Confirm Specific Disorders*
   Antibody levels are strongly recommended as a screen to confirm the existence of specific disorders such as rheumatoid arthritis.

   Indications – Patients with hip pain and a presumptive diagnosis of a rheumatological disorder.

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Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale for Recommendations
Elevated antibody levels are highly useful for confirming clinical impressions of rheumatic diseases. **However, ordering of a large, diverse array of antibody levels without targeting a few specific disorders diagnostically is not recommended routinely in patients with hip pain as wide-ranging, non-focused test batteries are likely to result in inaccurate diagnoses due to false positives and low pre-test probabilities.** Providers should also be aware that false-negative results occur. Measurement of antibody levels is minimally invasive, unlikely to have substantial adverse effects, and is low to moderately costly depending on the specific test ordered. They are recommended for focused testing of a limited number of diagnostic considerations.

HIP ARTHROSCOPY
Arthroscopy of the hip has been increasingly utilized for diagnosis and treatment of hip disorders as this procedure is less invasive and has lower complication rates than open procedures.(148-151) It is performed through small incisions using a camera to view the inside of a joint. However, indications for either diagnostic or therapeutic procedures are not well defined with quality studies. There is some belief that this procedure is more appropriate for younger and more physically active patients.(151)

1. *Recommendation*: *Hip Arthroscopy for Diagnosing Hip Pain with Suspicion of Labral Tear, Intraarticular Body, Femoroacetabular Impingement, or Other Subacute or Chronic Mechanical Symptoms*
   Arthroscopy is recommended to evaluate and diagnose patients with hip pain if there is a suspicion of labral tear, intraarticular body, femoroacetabular impingement, or there are other subacute or chronic mechanical symptoms.

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

   Strength of Evidence **– Recommended, Insufficient Evidence (I)**

2. *Recommendation*: *Hip Arthroscopy for Diagnosing Acute Hip Pain*
   Arthroscopy is not recommended for diagnosing acute hip pain.

   Strength of Evidence **– Not Recommended, Insufficient Evidence (I)**

3. *Recommendation*: *Hip Arthroscopy for Treatment of Osteoarthrosis without Mechanical Symptoms*
   Arthroscopy is not recommended to diagnose or treat acute, subacute, or chronic hip osteoarthrosis in the absence of a remediable mechanical defect such as symptomatic labral tear.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

4. *Recommendation*: *Hip Arthroscopy with Chondroplasty for Osteoarthrosis*
   Arthroscopy with chondroplasty is not recommended for treatment of osteoarthrosis.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Arthroscopy of the hip is increasingly utilized to treat several hip disorders, especially ones with mechanical symptoms. Complication rates from hip arthroscopic procedures range from 1.3 to 1.6%(148-150) with more serious injuries tending to be related to nerve retraction, neuropraxias, infection, or complex regional pain syndrome.(148-150, 152-155) Symptomatic labral tears and removal of foreign bodies have been reported as successfully treated in uncontrolled case series.(79, 151, 156-162) Labral tears reportedly should involve the most limited resection possible as removing excessive quantities of labrum tends to increase risk of instability.(163, 164) Labral repair has been reported as successful in case series.(80, 165) Femoroacetabular impingement is also a potential indication.(151, 166) A microfracture procedure has been utilized to treat both knee(167) and hip chondral lesions.(40, 168) By

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analogy with the knee joint, where quality evidence has demonstrated a lack of efficacy of chondroplasty,(169) chondroplasty of the hip joint is not recommended.(170, 171) Arthroplasty is invasive, has some adverse effects, and is costly. However, it is indicated for patients with persistent mechanical symptoms.

Post-operative rehabilitation for arthroscopic procedures is thought to differ from other surgical hip procedures,(151) and prolonged partial weight-bearing protocols lasting from 10 days (e.g., labral resection, labral repair, capsular modification) to 4 weeks (e.g., osteoplasty, microfracture) have been developed. (151, 166) Some physicians believe that range-of-motion exercises should begin within 4 hours of an arthroscopic impingement procedure.(166) However, quality evidence suggesting that the rehabilitation solely related to this procedure is different is lacking. In fact, quality evidence for other procedures suggests more rapid rehabilitation protocols result in superior outcomes (see Post-operative Rehabilitation). There is evidence that younger healthier patients who undergo arthroscopy do not require different rehabilitation protocols(151) than older healthier patients. Thus, the primary issues are pre-operative functional status and projected post-rehabilitation status. In general, following usual hip rehabilitation protocols is indicated, although the rate of progress is often be accelerated compared with more extensive surgical procedures and is particularly accelerated for younger healthier patients who may not require retraining in gait or weight bearing.

Evidence for the Use of Hip Arthroscopy
There are no quality studies evaluating the use of arthroscopy for hip pain.

BONE SCANS
Bone scans involve intravenous administration of a radioactive tracer medication that is preferentially concentrated in areas of metabolic activity in bone. Radioactivity is then detected by a large sensor and converted into skeletal images. There are many causes for abnormal radioactive uptake including metastases, infection, inflammatory arthropathies, fracture, or other significant bone trauma. Thus, positive bone scans are not highly specific. Bone scans have been used to diagnose early osteonecrosis of the femoral head prior to findings on x-ray.

1. *Recommendation: Bone Scanning for Select Use in Patients with Acute, Subacute, or Chronic Pain*
   Bone scanning is recommended for select use in patients with acute, subacute, or chronic pain to assist in the diagnosis of osteonecrosis, neoplasms, or other conditions with increased polyosthotic bone metabolism, particularly when more than one joint needs to be evaluated.

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

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Routine Use of Bone Scanning for Routine Hip Joint Evaluations*
   Bone scanning is not recommended for routine use in hip joint evaluations.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
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). 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 as it does not alter treatment or management. Bone scanning is minimally invasive, has minimal potential for adverse effects (essentially equivalent to a blood test), but is high cost. It is also generally inferior to MRI.

Evidence for the Use of Bone Scans
A comparative study of 143 bone scans of hip pain patients included 23 normal control patients.(172) Most of the patients (53%) presented with painful hips at the time of bone scanning. Including definitely and probably positives resulted in estimated sensitivity of 43% and specificity of 90%. The authors

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concluded that bone scintigraphy is “not indicated to diagnose possible contralateral AVN if the hip is asymptomatic.”

COMPUTERIZED TOMOGRAPHY (CT)
Computerized tomography (CT) remains an important imaging procedure, particularly for bony anatomy, whereas MRI is superior for soft tissue abnormalities. CT may be useful for hip joint abnormalities where advanced bone imaging is required. CT may be helpful for evaluating AVN and following traumatic dislocations or arthroplasty-associated recurrent dislocations. CT also may be useful to evaluate the spine in patients with contraindications for MRI (most typically an implanted metallic-ferrous device).

1. *Recommendation: Routine CT for Evaluating Acute, Subacute, or Chronic Hip Pain*
   Routine CT is not recommended for evaluating acute, subacute, or chronic hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

2. *Recommendation: CT for Evaluating Patients with Osteonecrosis (AVN), Dislocations, or Contraindications for MRI*
   CT is recommended for evaluating patients with 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 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.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Computerized tomography is considered superior to MRI for imaging of most hip abnormalities where advanced imaging of calcified structures is required. A contrast CT study is minimally invasive, has few if any adverse effects, but is costly. CT is therefore recommended for select use.

Evidence for the Use of CT
There are no quality studies addressing the use of CT for evaluating hip pain.

C-REACTIVE PROTEIN, ERYTHROCYTE SEDIMENTATION RATE, AND OTHER NON-SPECIFIC INFLAMMATORY MARKERS
There are many markers of inflammation that may be measured serologically. These include C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, and an elevated total protein-albumin gap.

Recommendation: Erythrocyte Sedimentation Rate or Other Inflammatory Markers for Screening for Inflammatory Disorders in Subacute or Chronic Hip Pain Patients
Erythrocyte sedimentation rate or other inflammatory markers are recommended for screening for inflammatory disorders or prosthetic sepsis with reasonable suspicion of inflammatory disorder in patients with subacute or chronic hip pain.

Indications – Patients with hip pain with suspicion of rheumatological disorder.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
Erythrocyte sedimentation rate is the most commonly used systemic marker for non-specific inflammation and is elevated in numerous inflammatory conditions including rheumatological disorders as well as infectious diseases. C-reactive protein is a marker of systemic inflammation that has been associated with an increased risk of coronary artery disease. However, it is also a non-specific marker for other inflammation. Other non-specific markers of inflammation include ferritin, and an elevated protein-albumin gap, which have no known clinical roles. CRP and ESR measurements are minimally invasive,

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have low risk of adverse effects, and are low cost. They are recommended as a reasonable screen for systemic inflammatory conditions especially if the hip pain patient also has other pains without clear definition of a diagnosis or those with fibromyalgia or myofascial pain syndrome, although the specificity is not high. **However, ordering of a large, diverse array of anti-inflammatory markers without targeting a few specific disorders diagnostically is not recommended.**

Evidence for the Use of C-reactive Protein, Erythrocyte Sedimentation Rate, or Other Non-specific Inflammatory Markers
There are no quality studies evaluating the use of C-reactive protein, erythrocyte sedimentation rate, or other non-specific inflammatory markers for hip pain.

CYTOKINES
See Chronic Pain chapter.

HELICAL CT SCANS
Helical CT scans are sometimes used for diagnosing osteonecrosis. There is quality evidence that they are superior to MRI or x-ray for identifying subchondral fractures in the femoral head.(173) Bone scans were traditionally used for diagnosis and may be positive even though an x-ray may be normal;(174) however, they have largely been replaced by MRI scans.

1. *Recommendation: Routine Helical CT for Evaluating Acute, Subacute, or Chronic Hip Pain*
   Routine helical CT is not recommended for evaluating acute, subacute, or chronic hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

2. *Recommendation: Helical CT for Evaluating Osteonecrosis*
   Helical CT is recommended for evaluating patients with osteonecrosis who have contraindications for MRI.

   Indications – Patients with hip pain from osteonecrosis who have contraindications for MRI (e.g., implanted hardware), increased polyosthotic bone metabolism.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: Helical CT for Select Patients with Acute, Subacute, or Chronic Hip Pain*
   Helical CT is recommended for select patients with acute, subacute, or chronic hip pain for whom advanced imaging of bony structures 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 hardware) are also candidates.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
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.(173) In addition, there are patients who have contraindications for MRI (e.g., implanted ferrous metal), and in those patients who require evaluation of AVN, helical CT is recommended. Helical CT has few if any adverse effects, but is costly. It is recommended for use in select patients.

Evidence for the Use of Helical CT Scans
There are no quality studies evaluating the use of helical CT scans for diagnosing hip pain.

LOCAL ANESTHETIC INJECTIONS AND EPIDURALS FOR HIP PAIN DIAGNOSIS
Local anesthetic injections are sometimes used for diagnostic confirmation of hip and groin conditions (for therapeutic injections, see Injections). These injections are also sometimes used to differentiate pain

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from a distant site, such as the knee or spine. Diagnostic injections include intraarticular injections (hip or knee), ilioinguinal, genitofermoral, saphenous, and lumbar epidurals. Local nerve block or sacroiliac joint injection should be used to assist in diagnosis. Immediate and delayed results of injection(s) should be recorded.

Recommendation: Local Anesthetic Injections to Diagnose Subacute or Chronic Hip Pain
Local anesthetic injections are recommended to assist in the diagnosis of subacute or chronic hip pain.

Indications – Patients with subacute or chronic hip pain from unclear source.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
Local anesthetic injections for diagnostic purposes appear helpful for confirming the diagnostic impression, although there are no quality studies evaluating these injections for purposes of evaluating hip pain. 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. These injections are minimally invasive, have minimal potential for adverse effects, and are moderately costly.

Evidence for the Use of Local Anesthetic Diagnostic Injections
There are no quality studies evaluating the use of local anesthetic diagnostic injections for hip pain.

ELECTROMYOGRAPHY (including Nerve Conduction Studies)
Electrodiagnostic studies have also been used to confirm diagnostic impressions of other peripheral nerve entrapments, including the lateral cutaneous nerve to the thigh (meralgia paresthetica). (See Low Back Disorders chapter for discussion of electrodiagnostic studies to evaluate back-related disorders that may present as hip pain.)

Recommendation: Electromyography for Diagnosing Subacute or Chronic Peripheral Nerve Entrapments
Electrodiagnostic studies are recommended to assist in the diagnosis of subacute or chronic peripheral nerve entrapments including lateral cutaneous nerve to the thigh (meralgia paresthetica).

Indications – Patients with subacute or chronic paresthesias with or without pain particularly if unclear diagnosis.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
Electrodiagnostic studies may assist in confirming peripheral nerve entrapments such as the lateral cutaneous nerve to the thigh. These studies are minimally invasive, have minimal potential for adverse effects (essentially equivalent to a blood test), and are moderately costly.

Evidence for the Use of Electromyography
There are no quality studies evaluating the use of electrodiagnostic studies for diagnosing peripheral nerve entrapments relevant to the hip.

FUNCTIONAL CAPACITY EVALUATIONS
See Chronic Pain chapter.

MAGNETIC RESONANCE IMAGING (MRI)
Magnetic resonance imaging (MRI) is not generally used as an initial or secondary test for most hip joint problems since it tends to be less helpful for imaging bones. It is considered the imaging test of choice for soft tissues. MRI is the gold standard for evaluating AVN after x-rays (67, 172, 175) and for evaluating osteonecrosis patients and is used to quantify the volume of affected tissue including marrow edema which is inversely correlated with prognosis.(176-180)

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1. *Recommendation: MRI for Hip Joint Pathology including Diagnosing Femoroacetabular Impingement, Gluteus Medius Tendinosis or Tears, Trochanteric Bursitis, and in Select Patients with Post-arthroplasty Chronic Pain or Periarticular Masses*
   MRI is recommended for select patients with 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 gluteus medius tendons or masses (generally not indicated for acute hip pain).

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: MRI for Diagnosing Osteonecrosis (AVN)*
   MRI is recommended for diagnosing osteonecrosis.

   Indications – Subacute or chronic hip pain thought to be related to osteonecrosis (AVN), particularly when the diagnosis is unclear or if additional diagnostic evaluation and staging is needed.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: MRI for Routine Evaluation of Acute, Subacute, Chronic Hip Joint Pathology*
   MRI is not recommended for routine evaluation of acute, subacute, or chronic hip joint pathology, including degenerative joint disease.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
MRI has not been evaluated in quality studies for hip joint pathology.(41, 181) However, it is likely particularly helpful for soft tissue abnormalities. There are no quality studies evaluating the use of MRI for AVN, hip joint pathology, or osteonecrosis. There is low-quality evidence that MRI may be less sensitive for detection of subchondral fractures than helical CT or plain x-rays in patients with osteonecrosis.(173) MRI has been suggested for evaluations of patients with symptoms over 3 months.(181-184) **As there are concerns that MRI is inferior to MR arthrography, particularly for evaluating the labrum,**(185) **MRI is recommended for evaluating the joint, but not the labrum.** There are reports of negative MRIs, yet finding gluteus medius tendon tears at surgery, thus MRIs appear to potentially have similar limitations imaging tendons in hip joint as in the shoulder.(186) MRI is not invasive, has no adverse effects aside from issues of claustrophobia or complications of medication, but is costly. MRI is not recommended for routine hip imaging, but is recommended for select hip joint pathology particularly involving concerns regarding soft tissue pathology.

Evidence for the Use of MRI
There are no quality studies evaluating the use of MRI for diagnosing hip pain.

MR ARTHROGRAM
Recommendation: MR Arthrogram for Diagnosing Femoroacetabular Impingement, Labral Tears, Gluteus Medius Tendinosis or Tears, or Trochanteric Bursitis in Patietns with Subacute or Chronic Hip Pain
MR arthrogram is recommended to diagnose femoroacetabular impingement, labral tears, gluteus medius tendinosis or tears, or trochanteric bursitis 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, gluteus medius tendinosis or tears, trochanteric tears, or other hip joint concerns.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
The use of MR arthrograms has not been evaluated in quality studies. However, they appear helpful in evaluating and confirming femoroacetabular impingement, gluteus medius tendinosis or tears, or trochanteric bursitis as soft tissue abnormalities.(185) Enhanced MR arthrogram allows better labral evaluation and is recommended for diagnosing femoroacetabular impingement, gluteus medius

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tendinosis or tears, or trochanteric bursitis compared to other imaging procedures.(41, 42, 47, 69, 76, 181, 183-185, 187-196) MR arthrography is minimally invasive, has no adverse effects aside from issues of claustrophobia or complications of medication, but is costly. However, it is likely the best imaging procedure available for these patients and is recommended for select use.

Evidence for the Use of MR Arthrogram
There are no quality studies evaluating the use of MR arthrogram for diagnosing femoroacetabular impingement, gluteus medius tendinosis or tears, or trochanteric bursitis.

X-RAYS
X-rays are the most basic of the anatomical tests, show bony structure and, after many decades of use, are the initial test for evaluating most cases of hip pain.(197-200) Two or three views are generally performed. It should be noted that the threshold for x-ray of the lumbosacral spine and/or knee joint should be low, particularly if the findings on x-ray are either normal or do not readily explain the degree of abnormality on x-ray. For osteonecrosis, plain x-ray results differ by stage of disease. Early x-rays are usually normal or have less distinct trabecular patterns since the living part of the bone does not image with x-rays.(174) As the disease progresses, x-rays begin to show osteoporotic areas, progressing to sclerotic areas and finally flattening and bony collapse.(174) X-rays have also been reported as helpful for diagnosing hip dysplasia(201) and femoroacetabular impingement.(202-207)

1. *Recommendation: X-rays for Acute, Subacute, or Chronic Hip Pain, or Femoroacetabular Impingement or Dysplasia*
   X-rays are recommended for evaluating acute, subacute, or chronic hip pain, or femoroacetabular impingement or dysplasia.

   Indications – In the absence of red flags, moderate to severe hip pain lasting at least a few weeks, and/or limited range of motion.

   Frequency/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 months to years subsequently to re-evaluate the patient's condition, particularly if symptoms change.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: X-rays for Diagnosing Osteonecrosis*
   X-rays are recommended for diagnosing osteonecrosis.

   Indications – All patients thought to have osteonecrosis (AVN).

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
X-rays are helpful to evaluate most patients with hip pain, both to diagnose and to assist with the differential diagnostic possibilities. There are no quality studies evaluating their efficacy. There is a low-quality study suggesting x-rays have higher sensitivity than MRI for detection of subchondral fractures in patients with osteonecrosis.(173) X-rays are non-invasive, are low to moderate cost, and have little risk of adverse effects; therefore, they are recommended.

Evidence for the Use of X-rays
There are no quality studies evaluating the use of x-rays for hip pain or diagnosing osteonecrosis. There is 1 comparative clinical study in Appendix 2.

SINGLE PROTON EMISSION COMPUTED TOMOGRAPHY (SPECT) AND POSITRON EMISSION TOMOGRAPHY (PET)
Single proton emission computed tomography (SPECT) is a 3-dimensional imaging technique in which radionucleotide tracers that release gamma radiation are used to create multiplanar re-formations. Positron emission tomography (PET) is another technique that investigates functional and, to a lesser degree, anatomical details within the brain, but uses positron-emitting radionucleotides.

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Recommendation: SPECT or PET for Diagnosing Acute, Subacute, or Chronic Hip Pain
SPECT or PET is not recommended for diagnosing acute, subacute, or chronic hip pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
SPECT and PET scanning of the brain may be of use in assessing the status of cerebrovascular perfusion, tumors, or neurodegenerative conditions, but aside from providing information of interest for research, they have not been shown to be useful in influencing the management of patients with chronic pain states, including chronic hip pain. There is no quality evidence to support the use of these scans to evaluate patients with hip pain. PET scanning is expensive and SPECT scanning is moderately so; both are minimally invasive. SPECT scanning may be useful in detecting inflammatory disease in the spine or other areas that might not be amenable to evaluation by other studies.

Evidence for SPECT and PET
There are no quality studies evaluating the use SPECT or PET for the management of hip pain.

ULTRASOUND
Diagnostic ultrasound has been used to evaluate the hip joint, especially the soft tissues, effusions,(208) dysplasia,(209, 210) and labral tears,(211) as well as occult fractures.(212)

1. *Recommendation: Ultrasound for Evaluating Gluteus Medius Tendinopathies, Greater Trochanteric Bursitis, Greater Trochanteric Pain Syndrome/Lateral Hip Pain, Groin Strains, Femoroacetabular Impingement, Hip Instability, Dislocation, Ligamentum Teres Ruptures, Labral Tears, or Post-arthroplasty Chronic Pain Where Peri-articular Masses Are Suspected*
   Ultrasound is recommended for evaluating patients with gluteus medius tendinopathies, greater trochanteric bursitis, greater trochanteric pain syndrome/lateral hip pain, groin strains, femoroacetabular impingement, hip instability, dislocation, ligamentum teres ruptures, labral tears, or post-arthroplasty chronic pain where peri-articular masses are suspected.

   Indications – Patients with hip pain thought to be from these disorders.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Ultrasound for Other Hip Disorders including Osteonecrosis, Osteoarthrosis, Dysplasia, or Fractures*
   There is no recommendation for or against the use of ultrasound to diagnose other hip disorders including osteonecrosis, osteoarthritis, dysplasia, or fractures.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations
Ultrasound has been found to be helpful in evaluating tendinopathies, including tendon ruptures. There is no clear indication for the use of ultrasound to evaluate osteoarthrosis. Ultrasound is not invasive, has no adverse effects, and is moderately costly. It is recommended for disorders with soft tissue pathology.

Evidence for the Use of Diagnostic Ultrasound
There are no quality studies evaluating the use of diagnostic ultrasound for hip pain.

INITIAL CARE

Assuring that there is not a remediable condition or red flag is the treating physician's first concern, prior to considering the patient's comfort measures. Nonprescription analgesics may provide sufficient pain relief for most patients with acute and subacute hip pain. If treatment response is inadequate (i.e., if symptoms and activity limitations continue) or the physician judges the condition limitations to be more significant, prescribed pharmaceuticals or physical methods may be added. Co-morbid conditions,

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invasiveness, adverse effects, cost, and physician and patient preferences guide the choice of treatment. Initial care and comfort items may include non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, heat, exercises, and/or advice on activities. Education about hip pain should begin at the first visit.

This guideline recommends interventions with quality evidence of proven efficacy. Known complication rates and safety profiles, if available, should always be utilized in decision making and were considered in developing this guideline. In addition to those treatments reviewed herein, there are many other theoretically potential treatments possible for management of hip and groin conditions. However, in the absence of moderate- to high-quality studies supporting their efficacy, (213) these other interventions are not recommended and are indicated as **Not Recommended, Insufficient Evidence (I)**.

ACTIVITIES AND ACTIVITY MODIFICATION

There are substantial differences in the way that activities and activity modifications are typically managed for acute versus chronic pain. Acute pain may benefit from activity limitations, while chronic pain is almost never improved with activity limitations. Acute hip or groin pain is often improved by avoiding those occupational and non-occupational activities that result in a *substantial* increase in pain. Even in the acute pain setting, appropriate activity modifications are difficult to identify. For example, because prolonged inactivity usually results in increased pain upon movement, it is easy to erroneously conclude that the activity aggravated the pain. However, even in that setting, some activity is usually desirable. In general, activities causing a *significant* increase in hip or groin symptoms should be reviewed with the patient and modifications advised when appropriate. These modifications may include lifting adjustments, frequency of postural changes, workstation design, or other activities may require at least temporary modification.

Chronic hip or groin pain is managed substantially differently from acute pain. Almost invariably, rehabilitation of chronic hip or groin pain involves gradually performing the occupational and non-occupational activities that result in increased pain to achieve increased function. The same types of limitations are often needed, but the progressive performance of increasing frequencies, intensity, and/or durations of these activities is generally necessary to rehabilitate these problems. Every attempt to maintain the patient at maximal levels of activity, including work activities, should be made, as it is in the patient's best short- and long-term interest. Written activity limitations guidance communicates the status of the patient, and also gives the patient information on what he or she should or should not do at home.

Work Activities

Work activity modifications are often necessary during the treatment course for patients with hip or groin pain. Advice on how to avoid aggravating activities that at least temporarily increase pain includes a review of work duties to decide whether or not modifications can be accomplished without employer notification and to determine whether modified duty is appropriate and available. Making every attempt to maintain patients at the maximal levels of activity, including work activities, is strongly recommended as it is in their best interest, particularly among patients with chronic hip or groin pain.

The first step in determining whether work activity modifications are required usually involves a discussion with the patient regarding whether he or she has control over his or her job tasks. In such cases where the worker can make modifications, e.g., receive assistance to lift a box or alternate sitting and standing as needed, there may be no requirement to write any restrictions even if the pain is limiting. In some situations, it may be advisable to confirm this report with the patient's supervisor to signal to the supervisor that the person is under treatment. In some cases, specified limitations may be a better treatment strategy. Assessment of work activities and potential for modifications may also be facilitated by a worksite visit and analysis by a health care provider with appropriate training (e.g., typically a physician, occupational therapist, physical therapist, or some ergonomists).

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Work limitations should be tailored by taking into account the following factors: 1) job physical requirements; 2) the safety of the tasks, in consideration of the diagnosed condition, age, and relevant biomechanical limitations; 3) severity of the problem; 4) work organizational issues (overtime, work allocation, wage incentives); and 5) the patient's understanding of his or her condition. Sometimes it is necessary to write limitations or to prescribe activity levels that are above what the patient feels he or she can do, particularly when the patient feels that sedentary activity is advisable. In such cases, the physician should be careful to not overly restrict the patient; education about the pain problem and the need to remain active should be provided.

Common limitations involve modifying the weight of objects lifted, frequency of lifts, and posture – all while taking into account the patient's capabilities. For severe cases of acute hip or groin pain, frequent initial limitations for occupational and non-occupational activities include:

- No lifting of more than 10 pounds;
- No prolonged or repeated bending (flexion);
- No prolonged or repeated crouching and squatting;
- Avoidance of prolonged, low frequency whole body vibration; and
- Alternate sitting and standing frequently.

These work (and home) activity guidelines are generally reassessed every week in the acute phase with gradual increases in activity recommended so that patients with severe non-specific hip or groin pain evolve off modified duty in no more than 6 to 12 weeks. The amount of weight handled can be progressively increased. An alternative is to return the patient at first to 1 to 2 hours a day on his or her prior full duty job, with the remainder of the day spent at modified duty. The number of hours of full duty work can be increased every 1 to 2 weeks.

However, individualization is often necessary and if the prior job physical tasks involved frequent lifting of more than 100 pounds, then restricted work guidance may reasonably be substantially greater, e.g., 25 pounds lifting and carrying at first. Progressively increased activity is important and prolonged sedentary activity is often unhelpful, thus restrictions that state "sedentary work" is *not* appropriate for most hip or groin patients. Physicians should recognize that patient expectations regarding return-to-work status are often set prior to the first appointment,(214) thus education may be necessary to set realistic expectations and goals. It is best to communicate to the patient early in the treatment that limitations will be progressively reduced as he or she progresses. This should also be communicated at each successive visit so that the patient is advised well in advance of the treatment plan.

It is best to communicate early in the treatment that limitations will be progressively reduced as the patient progresses. Experienced physicians communicate the intended changes in restrictions for the coming week (similar to forecasting increases in exercise program components) at the current visit to reduce the element of surprise and help actively facilitate the patient's most important elements of an active, functional restoration program. Tailoring restrictions is required in nearly all patients with chronic hip pain as there is great variability in symptoms and dysfunction. The employer should also be consulted when developing strategies to expedite and support integrating the patient back into the workplace (see Participatory Ergonomics, Low Back Disorders chapter). The physician can make it clear to patients and employers that:

- Patients usually have increased pain performing almost any function (even light duty) early in rehabilitation;
- Increases in symptoms should be heard with a sympathetic ear and factors which are associated with significant increases in pain should be addressed;
- Increases in pain do not equate to injury for patients with chronic pain;
- Any restrictions are intended to allow for time to build activity tolerance through exercise and work reconditioning; and
- Where appropriate, it may help to mention to the patient that this rehabilitative plan will also help him or her regain normal non-occupational activities.

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Table 7 provides recommendations on activity modification and duration of absence from work. These guidelines are intended for patients without comorbidity or complicating factors, including serious prior injuries. They are targets to provide a guide from the perspective of physiologic recovery. The physician should make it clear to the patient and employer that:

- moderately heavy lifting, carrying, or working in awkward positions may aggravate symptoms; and
- any restriction is intended to allow for spontaneous recovery or time to build activity tolerance through exercise.

Table 7. Guidelines for Modification of Work Activities and Disability Duration*

Disorder	Activity Modifications and Accommodation	Recommended Target for Disability Duration**		
		Job Classification *Dictionary of Occupational Titles*	**Modified Duty Available**	**Modified Duty Not Available**
Hip Osteoarthrosis	Avoid substantially aggravating activities	Sedentary Light Moderate Heavy Very Heavy	0 days 0 days 0 days 0 to 28 days 0 to indefinite	0 days 0 days Up to 30 days Up to 90 days Up to indefinite
Hip/Groin Pain (includes sprain, relocated/ dislocated hip and groin strains)	Avoid substantially aggravating irritating activities (e.g., heavy lifting, prolonged or repeated bending or stooping, prolonged maintenance of any one posture including sitting, rotating on a fixed foot, prolonged or repeated crouching and squatting) until full activity possible or 90 days have elapsed.	Sedentary Light Moderate Heavy Very Heavy	0 to 1 days 0 to 3 days 0 to 14 days 3 to 28 days 3 to 42 days	Up to 14 days Up to 14 days Up to 56 days Up to 84 days Up to 84 days
Osteonecrosis	Avoid substantially aggravating irritating activities (e.g., lifting, stooping, prolonged standing, walking, prolonged or repeated crouching and squatting) or until surgical procedure has occurred and work ability is assessed based on surgical result.	Sedentary Light Moderate Heavy Very Heavy	0 to 14 days* 0 to 21 days* 14 to 42 days* 91 to 119 days* 119 to 147 days*	Up to 42 days* Up to 56 days* Up to 84 days* Up to 182 days* Up to 182 days*
Greater Trochanteric Bursitis	Avoid pressure on affected hip. Avoid activities that substantially aggravate symptoms	Sedentary Light Moderate Heavy Very Heavy	1 to 7 days 1 to 14 days 1 to 21 days 1 to 56 days 1 to 91 days	14 days 21 days 42 days Indefinite Indefinite
Hip Fracture	After pinning, graded increase in activity over 3 months		30 to 60 days	120 days

*Assumes good results with non-operative treatment and arthroplasty or coring is not required.

Disability durations primarily reflect consensus of the Evidence-based Practice Hip Panel. Disability duration data also reviewed with permission from Reed Group, Ltd. (Reed P. *The Medical Disability Advisor. Workplace Guidelines for Disability Duration, 5th Ed*. 2005. Westminister, Colorado: Reed Group, Ltd.)(215) Additional consensus recommendations and actual data on disability durations are available in *The Medical Disability Advisor. Workplace Guidelines for Disability Duration, 5th Ed.*

Note: The highlight above is a footnote

ERGONOMIC INTERVENTIONS

The physician may recommend work and activity modifications or ergonomic redesign of the workplace in order to facilitate recovery and prevent recurrence of the problem.(216) Physicians may refer patients for an ergonomic evaluation to be conducted on-site by a qualified professional such as an ergonomist, occupational or physical therapist, or other health safety specialist. The employer's role is to accommodate activity limitations and prevent further problems through ergonomic changes which may help return an employee to full activity. In some cases, it may be desirable to conduct an ergonomic analysis of the activities that are thought to be contributing to the symptoms, although there are no

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quality ergonomic survey instruments for the lower extremity. However, it is important for the patient, physician, and employer to know that there are no quality studies regarding ergonomic interventions to prevent hip and groin conditions, nor are there quality studies regarding return to work and secondary prevention. Thus, suggested changes to the work environment are necessarily empiric. As falls result in considerable hip morbidity (including fractures) and fall protection equipment has resulted in far fewer fatalities in industry over the past few decades, fall protection is a priority for preventing acute injuries.

1. *Recommendation: Fall Protection*
   Measures to prevent falls are recommended.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Ergonomic Interventions for Hip or Groin Disorders*
   There is no recommendation for or against the use of ergonomic interventions to prevent or facilitate recovery from hip or groin disorders.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations
Ergonomic interventions for upper extremity disorders have been attempted in numerous occupational settings.(217) However, there are no quality studies evaluating these interventions for the lower extremity (in the upper extremity, some interventions thought beneficial were found to be unhelpful). Thus, without quality evidence, there is no recommendation for or against the use of ergonomic interventions to prevent or facilitate recovery from hip or groin disorders. However, as falls continue to cause morbidity and deaths, fall protection equipment is recommended.

EXERCISE

Exercise for Osteoarthrosis
Exercises have been utilized for treatment of osteoarthrosis – these include aerobic, strengthening, and flexibility exercises.(218-247) There are reports of low physical activity levels in arthritic patients,(248) and some evidence for efficacy of strengthening exercises among these patients.(231) Others have concluded that there is little evidence in support of efficacy of strengthening and aerobic exercise in hip OA patients and no evidence to support home versus group therapy.(222) Multiple studies have attempted to examine effectiveness for patients with rheumatoid arthritis.(249, 250) There are many studies involving knee pain patients (220, 228, 251-260) (see Knee Disorders chapter); however, whether those results are generalizable to patients with hip pain is unclear and many studies mixed knee and hip osteoarthrosis patients. While some research indicates that there is a lack of evidence supporting efficacy, others have opined that “Exercise may be the most effective, malleable, and inexpensive modality available to achieve optimal outcomes for people with osteoarthritis.”(261)

Available research consists mostly of low- to moderate-quality trials (see exercise evidence table). Some research has included both inflammatory conditions as well as osteoarthrosis, thus the entire body of exercise-related articles has been included. Most studies have combined different exercises into programs that at least partially obscure effects of a specific exercise prescription (e.g., flexibility versus aerobic versus strengthening). However, some patterns do appear present in the available literature. While these recommendations are specific to hip or knee osteoarthrosis, the reader may be interested that these recommendations also appear to apply to the rheumatoid arthritis patient, as materially different results were not found with that population (see exercise evidence table).

1. *Recommendation: Aerobic Exercise for Hip Osteoarthrosis*
   Aerobic exercise is moderately recommended for treatment of hip osteoarthrosis.

   Indications – Hip osteoarthrosis. Patients with significant cardiac disease or potential for cardiovascular disease should be evaluated prior to instituting vigorous exercises following ACSM *Guidelines for Exercise Testing and Prescription,* 7th ed.,(262) in regards to health screening and risk stratification. A self-directed program is recommended for all patients. Supervised programs may be

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particularly indicated for patients who require supervision to initiate a program or otherwise need assistance with motivation or concomitant fear avoidant belief training for a few appointments to help initiate the program.

Frequency/Duration – Dose is unclear. Walking at least 4 times a week at 60% of predicted maximum heart rate (220 - age = maximum heart rate) is recommended.(263, 264) Nearly all patients should be encouraged to maintain aerobic exercises on a long-term basis for fitness purposes, including lower extremity muscle strength, as well as to maintain optimal health.

Indications for Discontinuation – Intolerance (rarely occurs), development of other disorders.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

2. *Recommendation: Stretching Exercises for Hip Osteoarthrosis*
   Stretching exercises are recommended for select patients with significant reductions in range of motion that are not thought to be fixed deficits.

   Indications – Patients with significant reductions in range of motion that are thought to be non-fixed deficits (e.g., limitations based on stiffness or disuse rather than osteophytes).

   Frequency/Duration – Generally taught as home exercises – 1 to 3 appointments.

   Indications for Discontinuation – Worsening of symptoms, identification that deficits are fixed, or achievement of exercise program goals.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: Strengthening Exercises for Hip Osteoarthrosis*
   Strengthening exercises are moderately recommended for treatment of hip osteoarthrosis.

   Indications – May be added with aerobic exercises as an exercise program. In limited circumstances where range-of-motion deficits are considerable but thought to not be fixed, strengthening is sometimes added after beginning flexibility exercises.

   Frequency/Duration – Home program frequency at least 2 to 3 times a week for hip osteoarthrosis. Supervised treatment frequency and duration is dependent on symptom severity and acuity and presence of comorbid conditions.

   Indications for Discontinuation – Development of a strain, failure to improve.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendations

There are multiple RCTs addressing exercise for hip and/or knee osteoarthrosis patients. As there is not a strong rationale for believing there are major differences in efficacy for hip versus knee OA, this summary assumes the outcomes are similar in both sets of patients. Most of these studies combined different exercises. Some exercise programmatic components were unstructured and others did not clearly describe the interventions. These limitations restrict drawing strong evidence-based conclusions regarding any single intervention. Yet, there are quality studies comparing exercise to non-exercise controls that allow drawing evidence-based conclusions on the relative value of aerobic, stretching, and strengthening exercises.

Authors of a meta-analysis concluded the literature demonstrates efficacy of exercises for hip osteoarthrosis patients, especially for those containing strengthening exercises.(231) However, a high-quality trial of knee OA suggests while both aerobic and resistance training are helpful, aerobic exercises are modestly superior to resistance training and far superior to an educational control,(256) which suggests weight bearing may be beneficial and raises questions about which exercise may be superior for hip osteoarthrosis patients.

All quality studies including a major component of documented compliance with increased aerobic exercise found benefits of aerobic exercise.(263, 265, 266) Strengthening exercise results appear similar. There is not clear superiority of aerobic or strengthening exercises or vice versa. The available

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quality evidence suggests aerobic and strengthening exercises are superior to flexibility or range of motion exercises.(263) Some but not all data suggest increased exercise intensity results in superior outcomes. But not all studies that have assessed inflammatory markers and joint scores among those with OA or RA have found reductions in erythrocyte sedimentation rates and lower joint scores among those exercising. Pool-based programs have been evaluated and evidence of superiority of water-based programs is lacking (see aquatic therapy below).

Problems with compliance and persistence with exercise programs after discharge are considerable. Evidence is mixed regarding whether supervised exercise programs are necessary or whether home-based programs are sufficient. Physicians need to encourage ongoing patient compliance with these programs. Exercise programs are not invasive, have low adverse effects, and are low to moderate cost depending on numbers of supervised appointments. Programs emphasizing aerobic and strengthening exercises are moderately recommended and stretching is recommended for patients with considerable reductions in range of motion that do not appear fixed.

Evidence for the Use of Exercise for Osteoarthrosis
There are 2 high-quality and 20 moderate-quality RCTs or crossover trials incorporated in this analysis. There is 1 low-quality RCT in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Exercise Advice for Osteoarthrosis						
Veenhof 2006 RCT	4.0	N = 200 Hip or knee OA	Behavioral graded activity program vs. usual care for 12 weeks and a maximum 18 sessions, then up to 5 booster sessions.	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 WOMAC physical function subscales not different between groups. Patient global assessments % improved (13 weeks/65 weeks): BGA 41/56 vs. UC 36/49 (NS).	"Because both interventions resulted in beneficial long-term effects, the superiority of (behavioral graded activity program) over (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."	Cluster randomization by physical therapist. Baseline data somewhat worse disease in usual care group. Many protocol deviations. Data suggest behavioral graded exercise program ineffective compared with usual care.
Exercise for Osteoarthrosis						
Ettinger 1997 RCT	8.0	N = 439 Knee OA	Aerobic exercise program (3-month facility-based, 15 month home walking, 1 hour with 40 minutes walking a session, 3 sessions a week) 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,	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 strength 89.0 vs. 90.2 vs. 87.0 Nm at 30º. Overall self-reported disability scores: 1.72 vs.	"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.

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			step up, heel raise, chest fly, upright row, military press, biceps curl, pelvic tilt) vs. health education program (monthly 1.5 hour education session for 3 months, included exercise topics).	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.		
Hoeksma 2004 RCT	8.0	N = 109 Hip OA	Manual therapy (stretching, manipulation and mobilization of hip joint) vs. exercise program (tailored to patients needs). Both 2 times a week for 9 treatments.	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.
Van Baar 1998 RCT	7.5	N = 201 Hip or knee OA	Individual exercise therapy with PT (strength, ROM, ADLs) 1 to 3 times a week vs. no exercise for 12 weeks treatment and 24 weeks follow-up. Both groups treated with education and medication.	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 RCT	6.5	N = 180 Lumbar spine, knee and hip OA	Spa therapy vs. "usual therapy" for 3 weeks. Spa included "journey, rest, blaneotherapy, spring water and medical	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	"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

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			attention."	weeks): spa (50±20/-15±29/-9±28) vs. controls (47±22/1±22/3±24), p <0.0001.		months; results not significantly different by months 4-6 by tablet count.
Ravaud 2004 RCT	6.0	N = 867 rheuma-tologists N = 2,957 (2216 knee OA; 741 hip OA)	Standardized tools (adjusted medications) vs. booklet with exercises and videotape (ROM and strength) for HEP 4 times a week/6 months vs. standardized tools and exercise vs. usual medical care by rheumatologists. All patients given rofecoxib 12.5mg QD first month and 25mg QD after if needed.	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 "has done his best to preserve their muscular function and their physical activities" (p <0.001).	"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.
Tak 2005 RCT	5.5	N = 109 Hip OA	Hop with the Hip exercise program (strengthening, treadmill, weight control, assistive devices) weekly 1-hour appointments for 8 weeks vs. no intervention.	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.
Hopman-Rock 2000 RCT	5.0	N = 120 Hip or knee OA	Two hour weekly exercise sessions (1.25 hour education, 45-minute exercises with HEP at least 3 times a week for 6 weeks vs. non-interventional controls.	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.
Mangione 1999 RCT	5.0	N = 39 Knee OA	High (70% heart rate max from graded exercise test) vs. low (40% HR max) intensity	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±9	"Cycling may be considered as an alternative exercise modality for patients with knee OA. Low-intensity cycling was as	Data suggest no meaningful differences between low vs. high bicycle exercise program.

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			stationary cycling for 1 hour session, 3 times a week for 10 weeks.	8.72 vs. LO 491.12± 103.74/526.94± 113.74 (NS).	effective as high-intensity cycling in improving function and gait, decreasing pain, and increasing aerobic capacity."	
Halbert 2001 RCT	4.5	N = 69 Hip or knee OA	Individualized physical activity advice (at 0, 3, 6 months; emphasis on aerobic 3 sessions a week for ≥20minutes) vs. nutritional pamphlet.	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.
Minor 1989 RCT	4.0	N = 120 OA (hip, knee, or tarsal) or RA	Aerobic walking vs. aerobic pool 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.	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.
Exercise for Rheumatoid Arthritis						
Lyngberg 1994 RCT	6.0	N = 24 RA with low dose steroids for 2 years	Progressive interval training – aerobic with ergometer – bicycling and strengthening exercises, stretching trained muscles twice a week, 45 minutes for 3 months vs. no program.	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 Crossover	6.0	N = 20 RA, moderatel	Training program of aerobic capacity training and	No significant change in ESR, C3. Number of swollen joints decreased after training (77 to 56, p	"RA-patients with some activity are trainable without aggravating the disease, even in the	Main outcomes of serological markers of inflammation

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Trial		y active disease	dynamic strength exercises 45 minutes twice a week for 8 weeks vs. no program	<0.02). No comparable reduction in swollen joints during control period (42 to 49). Hemoglobin level increased approximately 8% (p<0.01) with training.	chronically swollen joints. The rheumatoid arthritis activity decreased with fewer swollen joints and higher hemoglobin level after training."	negative. However, disease activity reduced with exercise as measured with blinded assessor.
Baslund 1993 RCT	4.5	N = 18 RA	Progressive bicycle training (ergometric bicycle 4-5 times a week with 3 short exercise periods of 5 minutes to target HR) vs. controls for 8 weeks.	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, 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.	"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 measures). Training group's VO2max improved despite use of short bursts of exercise.
van den Ende 1996 RCT	4.5	N = 100 RA	High intensity group exercises (12 exercises, 20 minute cycling to 70-85% HR Max, 1 hour sessions, 3 times a week), vs. low intensity group exercise program (ROM, isometric strengthening, 1 hour sessions, twice a week) vs. low intensity individual exercise program (same exercises, durations unclear) vs. home exercise program (ROM and isometric exercises at least 2 times a week for 15 minutes); all 12 weeks.	Mean aerobic capacity ($V0_2$max) 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.
Daltroy 1995 RCT	4.5	N = 71 RA or systemic lupus erythe-matosus	12-week home cardio-pulmonary conditioning program with stationary bicycles provided.	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	"[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

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			Prescription 60-80% HR max, 3 times a week for 30 minute sessions vs. controls to maintain current activity level for 12 weeks.	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.		disorders. RA controls exercised somewhat longer at baseline, providing some potential bias against exercise.
Hansen 1993 RCT	4.5	N = 75 RA	Five groups: 1 non-exercise controls (E). 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 training only; B) weekly PT (15 minute standard program, 15 minute biking, 15 minute relaxation; C) weekly in-hospital training as per B; D) same as C but hot pool instead of bikes; all 2 years.	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 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."	"[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 with HEP. Lack of data from end of training impair ability to conclude short to intermediate term efficacy (or lack) of the program.
Smith 1998 RCT	4.5	N = 24 RA	Aquaerobics 1 hour, 3 times a week vs. 8-10 ROM exercises, isometric strengthening (possibly home exercise program) 10 each, 2-3 times a day/10 weeks.	Active joints (baseline/11 weeks): aquaerobics (8.3±6.0/7.5±6.1) vs. ROM (10.6±5.6/7.1±4.6). Both groups improved duration on treadmill. ROM group alone showed improvement in walking category and total HAQ.	"[P]articipation in either program may results in improved exercise tolerance without exacerbating joint activity."	Small sample size. Arthritis duration longer in controls. Controls not well described, appears a home exercise program which would provide different treatment contact times between 2 groups biased in favor of aquaerobics. Active joints trended to ROM group by blinded assessor. Other data also favor ROM group.
Ekdahl 1990 RCT	4.5	N = 67 RA	Dynamic program, strengthening and aerobic capacity 12 visits (2 a week/6 weeks)	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. (-	"[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.

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			vs. dynamic program, ROM and strengthening exercises 4 visits (2 at 1 week, 1 at 3 weeks, 1 at 6 weeks) vs. static program 12 visits vs. 4 visits. HEP daily	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.		
Ekblom 1975 RCT	4.5	N = 34 RA, hospitalized but "non-acute stage	"Ordinary" physical rehab program – QAM, 5 a day 1 week (control) vs. ordinary program plus training group (bicycle ergometer and quadriceps table strengthening) 20-40 minutes BID for 5 weeks	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 fitness in the RA patient."	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.
Harkcom 1985 RCT	4.0	N = 20 women RA, functional class II	Bicycle ergometer 3 times a week for 12 weeks, 3 different exercise time progressions.	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 RCT	4.0	N = 70 RA	Strength training (50-70% repetition max) vs. ROM exercise 45 minute sessions, twice a week for 24 months. Strength group encouraged to do recreational physical activity (walk, cycle, swim, ski) 2-3 times a week 30-45 minutes vs. ROM "free to continue their recreational physical activities" except strengthening	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 = 0.002-0.025. Joint damage not significant. Walking speed	"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.

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				increased 16±17% in strength training, p <0.001, vs. 9±12% controls, p = 0.025.		

AQUATIC THERAPY (HYDROTHERAPY)

Aquatic therapy involves the performance of aerobic and/or flexibility and/or strengthening exercises in a pool to minimize the effects of gravity, particularly where reduced weight-bearing status is believed to be desirable.(263, 267-269)

1. *Recommendation: Aquatic Therapy for Hip Osteoarthrosis*

   A trial of aquatic therapy is recommended for patients with hip osteoarthrosis who meet the referral criteria for supervised exercise therapy and have co-morbidities (e.g., extreme obesity, significant degenerative joint disease, etc.) that preclude effective participation in a weight-bearing physical activity and who will either transition to a land-based program or a self-administered water-based program.

   Frequency/Duration – Begin with 3 to 4 visits a week, with demonstrated evidence of functional improvement within the first 2 weeks to justify additional visits. The program should include up to 4 weeks of aquatic therapy with progression towards a land-based, self-directed physical activity or self-directed aquatic therapy program by 6 weeks. For some patients with hip osteoarthrosis, aquatic exercise may be the preferred method. In these few cases, the program should become self managed and if any membership to a pool is covered, coverage should be continued if it can be documented that the patient is using the facility at least 3 times per week and following the prescribed exercise program.

   Indications for Discontinuation – Non-tolerance, failure to progress, or reaching a 4 to 6 week timeframe.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations

Aerobic exercise is beneficial for treatment of hip osteoarthrosis compared to no program; (267) however, evidence of superiority to land-based programs is lacking.(263, 268, 269) Instead, the quality literature appears to document comparable efficacy between land- and water-based exercise programs.(263, 268, 269) Aquatic programs are performed in lukewarm rather than higher temperature. As noted previously, other forms of exercise have been shown to be effective in the treatment of hip OA, but for a few select patients who are unable to tolerate those land-based therapies, aquatic therapy is moderate cost, not invasive, and has little potential for adverse effects.

Evidence for the Use of Aquatic Therapy

There is 1 high-quality and 3 moderate-quality RCTs incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Hinman 2007 RCT	8.0	N = 71 Hip or knee OA	Aquatic physical therapy (45-60 minute sessions, twice weekly) vs. no aquatic physical therapy for 6 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	6.5	N = 105	Water exercise (walking, strengthening)	WOMAC function (baseline/ follow-up): hydro (34.0/ 33.0) vs. gym (28.0/27.0) vs.	"[B]oth the gym and hydrotherapy interventions	Some baseline differences with less distance

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RCT		Hip and/or knee OA	vs. gym (cycling, strengthening) vs. no-exercise. Exercise sessions 3 a week for 6 weeks. Control group had nightly phone calls to record changes in condition, drug use, or injuries.	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).	produce positive functional outcomes for patients with OA."	walked in hydrotherapy (257m) vs. gym (336m) vs. control (388m). WOMAC function also different. Graphic data support increases in distance walked and walking speed.
Sylvester 1990 RCT	4.5	N = 14 Hip OA	Hydrotherapy (2-1/2 hour sessions a week for 6 weeks) vs. diathermy and supervised exercises (same exercises as in pool).	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.
Minor 1989 RCT	4.0	N = 120 OA (hip, knee or tarsal) or RA	Aerobic walking vs. aerobic pool 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.	Aerobic capacity (baseline/12 weeks): walk (18.9±4.8/22.4±4.8 mL/kg/min) 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 and pool groups. Improvements greater in OA vs. RA for exercise endurance, but better for total active RA joints. Both appear to benefit. Suggests aerobic exercise reduces active RA joints.

YOGA

Yoga has been used to treat patients with low back pain (270-272) (see Low Back Disorders chapter).

Recommendation: Yoga for Chronic Persistent Hip Pain

There is no recommendation for or against the use of yoga for treatment of chronic persistent hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation

There are no quality studies of yoga for treatment of patients with chronic persistent hip pain. Yoga may be appropriate for highly motivated patients; however, compliance is an issue.

GENERAL PRINCIPLES OF TREATMENT/FOLLOW-UP VISITS

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Patients need individualized treatment and follow-up that incorporates the severity of the condition, co-morbidities, occupational demands, psychosocial factors, patient motivation, and need for encouragement. The speed and ability to return to work is one of the critical factors that requires either more or fewer follow-up appointments with more appointments generally required for those whose limitations have not been accommodated. The worker should be transitioned to work or from modified work to full work, at the earliest date possible, and should be supported during that transition, and told of the likelihood of increased symptoms in conjunction with being reassured that pain does not equate to injury.

ACTIVITY MODIFICATION

Recommendation: Activity Modification for Acute, Subacute, or Chronic Hip or Groin Pain
Activities that do not substantially aggravate symptoms are recommended for most patients with acute, subacute, or chronic hip or groin pain.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
There are no quality studies evaluating modification of activity for hip or groin pain. Common post-arthroplasty limitations have included no lifting over a weight limit, no running, and no jumping. Lifting limits may commonly be 50 pounds, but are frequently based on prior weight lifting capabilities and anticipated future abilities. However, there are no quality studies proving that these limitations are required and many patients resume and exceed pre-operative physical activity levels. While modification of activity is not invasive, it may result in increased disability through disuse, or increased cardiovascular mortality through lack of exercise. It also may result in high cost through lost productivity. Thus implementation of activity modifications should be carefully balanced against increased longer term morbidity and other costs. In cases where the activity does not aggravate the symptoms or disease, activity modifications are not recommended, rather activity is recommended.

Evidence for the Use of Activity Modification
There are no quality studies evaluating the use of activity modification for hip and groin pain.

BED REST

1. *Recommendation: Bed Rest for Patients with Acute, Subacute, or Chronic Hip Pain*
   Bed rest is not recommended for patients with acute, subacute, or chronic hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

2. *Recommendation: Bed Rest for Unstable Fractures*
   Bed rest is recommended for patients with clear contraindication to weight-bearing status such as an unstable fracture.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Bed rest is unlikely to be beneficial and generally should be avoided for all patients other than those with clear contraindication to weight-bearing status due to an unstable fracture.

Evidence for the Use of Bed Rest
There are no quality studies evaluating the use of bed rest for hip and groin pain.

MEDICATIONS

ANTI-DEPRESSANTS

Anti-depressants have been used to treat chronic pain including low back pain (see Chronic Pain and Low Back Disorders chapters). There are two main classes of anti-depressant medication used to manage pain. The first class, tricyclic anti-depressants (TCAs), primarily work through inhibiting the re-uptake of norepinephrine and include the antidepressants amitriptyline, doxepin, imipramine,

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desipramine, nortriptyline, protriptyline, maprotiline, and clomipramine. The second class, the selective serotonin reuptake inhibitors (SSRIs), includes fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, escitalopram, and duloxetine.

1. *Recommendation: Norepinephrine Reuptake Inhibiting Anti-depressants for Hip Osteoarthrosis or Subacute or Chronic Hip Pain*
   There is no recommendation for or against the use of norepinephrine reuptake inhibiting anti-depressants for treatment of hip osteoarthrosis or subacute or chronic hip pain (see Chronic Pain chapter for more details).

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: Norepinephrine Reuptake Inhibiting Anti-depressants for Acute Hip Pain*
   Norepinephrine reuptake inhibiting anti-depressants are not recommended for treatment of acute hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

3. *Recommendation: Selective Serotonin Reuptake Inhibitors for Acute, Subacute, or Chronic Hip Pain*
   Selective serotonin reuptake inhibitors (SSRIs) are not recommended for treatment of acute, subacute, or chronic hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Norepinephrine reuptake inhibiting anti-depressants (e.g., amitriptyline, doxepin, imipramine, desipramine, nortriptyline, protriptyline, maprotiline, and clomipramine) and mixed norepinephrine and serotonin inhibitors (e.g., venlafaxine, bupropion, and duloxetine) have evidence of efficacy for treatment of chronic low back pain and other chronic pain conditions (see Low Back Disorders chapter). There is strong evidence of lack of efficacy for treatment of chronic low back pain with SSRIs, thus they appear unlikely to successfully treat hip pain. However, there is no quality evidence evaluating these medications for treatment of hip osteoarthrosis or other hip pain. There also are no clear analogous disorders for which evidence-based guidance may be reliably derived.

Evidence for the Use of Norepinephrine Reuptake Inhibiting Anti-depressants and Mixed Norepinephrine and Serotonin Inhibitors
There are no quality studies evaluating the use of norepinephrine reuptake inhibiting anti-depressants and mixed norepinephrine and serotonin inhibitors for treatment of hip osteoarthrosis or other hip pain.

ANTI-CONVULSANT AGENTS (including Gabapentin and Pregabalin)
Since the 1960s, anti-convulsant agents have been used off-label to treat certain chronic pain syndromes,(273) particularly neuropathic pain.(274) Anti-convulsants are thought to have analgesic properties. Several have been used to manage chronic pain conditions including carbamazepine, valproic acid, gabapentin, phenytoin, clonazepam, lamotrigine, tiagabine, pregabalin, topiramate, levetiracetam, oxcarbazepine, and zonisamide (see Chronic Pain chapter for more details).

1. *Recommendation: Topiramate for Hip Osteoarthrosis or Subacute or Chronic Hip Pain*
   There is no recommendation for or against the use of topiramate to treat hip osteoarthrosis or other subacute or chronic hip pain.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: Topiramate for Acute Hip Pain*
   Topiramate is not recommended to treat acute hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

3. *Recommendation: Gabapentin for Hip Osteoarthrosis or Subacute or Chronic Hip Pain*

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There is no recommendation for or against the use of gabapentin to treat hip osteoarthrosis or subacute or chronic hip pain (see Chronic Pain chapter for more details).

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

4. *Recommendation: Gabapentin for Acute Hip Pain*
   Gabapentin is not recommended to treat acute hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

5. *Recommendation: Gabapentin for Peri-operative Management of Hip Pain*
   Gabapentin is strongly recommended for peri-operative management of hip pain to reduce need for opioids, particularly in patients with adverse effects from opioids.

   Indications **–** Peri-operative pain management.

   Frequency/Dose – Limit to immediate peri-operative period, usually a few days.

   Indications for Discontinuation – Resolution, intolerance.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale for Recommendations
There are no quality studies to support the use of anti-convulsant agents for hip pain patients. Quality evidence suggests topiramate is weakly effective for treatment of low back pain patients and gabapentin is unhelpful. However, there is quality evidence that gabapentin reduces need for opioids when administered as part of perioperative pain management.(275-278)
Evidence for the Use of Anti-convulsant Agents
There are no quality studies evaluating the use of topiramate or gabapentin for hip osteoarthrosis or other hip pain. There are 4 high-quality RCTs incorporated in the analysis for peri-operative pain(275-278) (see Chronic Pain chapter for a description of these studies).

BISPHOSPHONATES
Bisphosphonates are a class of pharmaceutical agents that reduce osteoclastic activity in the bones resulting in net gain of bone mass. These medications appear efficacious in treatment of complex regional pain syndrome patients (see Chronic Pain chapter). However, they are more commonly utilized for treatment of osteoporosis, as well as primary and secondary prevention of fractures. Adverse effects include gastritis, reflux esophagitis (can be severe and erosive causing stricture and achalasia), and osteonecrosis of the jaw (uncommon).(279)

Recommendation: Bisphosphonates for Hip Fracture Patients
Bisphosphonates are strongly 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. Patients should have cause of the osteopenia established and osteomalacia ruled out. Adequate Vitamin D and calcium must be present to initiate restoration therapy.

Frequency/Duration – Taken in oral or parenteral formulations as per manufacturer recommendations.

Indications for Discontinuation – Resolution of bone mass decrements, adverse effects, intolerance.

Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale for Recommendation
There are numerous quality studies of bisphosphonates for primary and secondary prevention of fractures with a uniform conclusion that they prevent hip fractures.(280-304) By definition, patients with hip fractures had insufficient bone mass resulting in failure. Some occupational patients might not require these medications if they suffered a high-energy impact. However, the vast majority of patients with hip fracture are candidates for treatment if for no reason other than tertiary prevention. There is quality

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evidence that hip fracture patients develop more bone mass, thus bisphosphonates are strongly recommended.

CALCITONIN

Calcitonin increases calcium uptake from the gastrointestinal tract while also decreasing bone resorption. The salmon calcitonin formulation that is nasally inhaled has been most used more recently due to ease of administration and longer half-life than human calcitonin. Adverse effects are relatively rare and include nausea, vomiting, decreased appetite, abdominal pain, injection site reactions, nasal symptoms, rhinitis, sinusitis, anaphylaxis, bronchospasm, hypersensitivity reactions, osteogenic sarcoma, and hypocalcemic tetany.

Recommendation: Calcitonin for Hip Fracture Patients

Calcitonin is recommended as a treatment option for patients with hip fracture, particularly those who are either intolerant to or have other contraindications for bisphosphonates.

Indications – Hip fracture patients who are intolerant to or have contraindications for bisphosphonate use.

Frequency/Duration – Parenteral administration may be preferred as potential less benefit with intranasal administration; duration of use indefinite depending on status of bone mass.

Indications for Discontinuation – Recovery of normal bone mass, intolerance, adverse effects.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations

There is one high-quality study suggesting modest benefits from calcitonin in hip fracture patients.(305) Thus, there is weak evidence of efficacy in contrast with literature on bisphosphonates, which have much better evidence for efficacy. Calcitonin is minimally invasive, has relatively few adverse effects, and is moderately costly. Calcitonin is recommended for patients who have adverse effects or contraindications for a bisphosphonate.

Evidence for the Use of Calcitonin

There is 1 high-quality RCT incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Huusko Calcif Tissue Int 2002 RCT	8.5	N = 260 Acute hip fracture	Intranasal salmon calcitonin 200 IU daily vs. placebo nasal spray for 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.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) AND ACETAMINOPHEN (Including Cytoprotection)

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for treatment of osteoarthrosis and are considered efficacious, although most studies did not last longer than 6 weeks (see NSAIDs/acetaminophen evidence table).(306-308) Most quality studies included both knee and hip OA patients; however, meaningful differences in outcomes between these two patient populations were not apparent in the studies that included stratified analyses.

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NSAIDs inhibit prostaglandin synthesis thus impairing inflammation. However, the mechanism of action for treatment of hip pain is somewhat unclear. There are several classes of NSAIDS: 1) salicylates – aspirin, diflunisal, salicyl salicylate (salsalate); 2) arylalkanoic acids – diclofenac, etodolac, ketorolac, nabumetone, sulindac, tolmetin; 3) 2-arylpropionic acids – ibuprofen, fenoprofen, ketoprofen, naproxen; 4) n-arylanthranilic acids – mefenamic acid; 5) oxicams – piroxicam, meloxicam; 6) COX-2 inhibitors – celecoxib, rofecoxib, etoricoxib; and 7) sulphonanilides – nimesulide. Acetaminophen is considered an analgesic, not an anti-inflammatory agent, and blocks the activation of COX by another enzyme, peroxidase. Tissues with high levels of peroxidase (i.e., platelets and immune cells) are "resistant" to acetaminophen, but tissues with low levels of peroxidase (i.e., nerve and endothelial cells that participate in pain and fever) are "sensitive" to acetaminophen.(309) There have been recent suggestions that NSAIDs may reduce cartilage synthesis;(310) however, there also are many studies documenting reductions in inflammatory mediators,(311-314) thus raising the possibility that NSAIDs actually delay cartilage destruction.

There are four commonly used cytoprotective classes of drugs – misoprostol, sucralfate, histamine Type 2 receptor blockers (famotidine, ranitidine, cimetidine, etc.), and proton pump inhibitors – esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole. There is not generally believed to be substantial differences in efficacy for prevention of gastrointestinal bleeding,(315) although evidence suggests the histamine-2 blockers are less effective for protecting the gastric mucosa and evidence also suggests sucralfate is weaker than proton pump inhibitors (see NSAIDs/acetaminophen evidence table). There are combination products of NSAIDs/misoprostol that have documented reductions in risk of endoscopic lesions (see NSAIDs/acetaminophen evidence table).

There are two isoenzymes of cyclooxygenase, COX-1 and Cox-2. NSAIDs are (non) selective to different degrees. COX-2 selective agents were designed to reduce inflammation while not increasing risks for gastrointestinal bleeding. It appears that certain COX-2 selective agents may increase the risk of cardiovascular events.

1. *Recommendation: NSAIDs for Treatment of Acute Flares or Acute, Subacute, Chronic, or Post-operative Hip Pain*
   NSAIDs are strongly recommended for treatment of chronic hip pain especially if due to osteoarthrosis. NSAIDs are recommended for acute flares and acute, subacute, or post-operative hip pain.

   Indications – Acute, subacute, chronic, or post-operative hip pain.

   Frequency/Dose/Duration – Per manufacturer's recommendations. Over-the-counter (OTC) agents may suffice and be tried first. COX-2 selective NSAIDs should be used with caution, or avoided altogether in the acute post-operative period in situations where bone healing is required, such as in fracture repair or in hip replacements where cementless acetabular and/or femoral components are utilized.(316) Essentially all NSAIDs have proven efficacious for this indication (see NSAIDs/acetaminophen evidence table). As-needed-use may be reasonable; however, nearly all trials used scheduled doses. There is evidence that nocturnal dosing is superior for hip OA if the patient primarily has morning or nocturnal pain,(317) although the study was of indomethacin and may only apply to shorter half-life agents (reproducibility of these findings and generalizability to other NSAIDs such as celecoxib with a longer half-life has not been shown).(318)

   Indications for Discontinuation – Resolution of hip pain, lack of efficacy, or development of adverse effects that necessitate discontinuation. Taking anti-coagulation regimens as concomitant use with non-selective COX inhibitors may increase the risk of hemorrhaging.

   Strength of Evidence – **Strongly Recommended, Evidence (A) – Chronic hip pain especially from OA**
   Recommended, Evidence (C) – Acute flares
   Recommended, Insufficient Evidence (I) – Acute, subacute, or post-operative hip pain

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2. *Recommendation: NSAIDs for Patients at Risk for GI Adverse Effects*
Concomitant prescriptions of cytoprotective medications are recommended for patients at substantially increased risk for gastrointestinal bleeding.

Indications – Patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications, particularly if longer term treatment is contemplated. At-risk patients include those with a history of prior gastrointestinal bleeding, the elderly, diabetics, and cigarette smokers. Physicians are cautioned that H2 blockers might not protect from gastric ulcers.(319-321)

Frequency/Dose/Duration – Dose and frequency for proton pump inhibitors, sucralfate, and H2 blockers are as recommended by manufacturer. Duration is the extent of the NSAID therapy; use is at times permanent for those with recurrent bleeds or other complications.

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

Strength of Evidence – **Strongly Recommended, Evidence (A) – Proton pump inhibitors,**
misoprostol
Moderately Recommended, Evidence (B) – Sucralfate
Recommended, Evidence (C) – H2 blockers

3. *Recommendation: NSAIDs for Patients at Risk for Cardiovascular Adverse Effects*
NSAIDs are recommended for patients with known cardiovascular disease or multiple risk factors for cardiovascular disease if the risks and benefits of NSAID therapy for pain are discussed.

Dose/Frequency – 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.(322)

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

4. *Recommendation: NSAIDs for Prevention of Heterotopic Bone Formation after Arthroplasty*
NSAIDs are moderately recommended for the prevention of heterotopic bone formation after arthroplasty.

Indications – Post-operative arthroplasty patients, particularly those with prior heterotopic bone formation. Due to their inhibitory effects on platelet function, non-selective COX inhibitors should be used with caution or avoided altogether in the post-operative period if patients are also receiving pharmacoprophylaxis (e.g., warfarin, low molecular weight heparins) to prevent venous thromboembolic disease. Concomitant use of non-selective COX inhibitors and anti-coagulation regimens may increase the risk of hemorrhage. There is also concern that COX inhibitors, particularly COX-2 inhibitors, may inhibit bone healing. Therefore, these agents should be used with caution, or avoided altogether, in the acute post-operative period in situations where bone healing is required, such as in fracture repair or in hip replacements where cementless acetabular and/or femoral components are utilized.(316)

Dose/Frequency – Dose and frequency per manufacturer's recommendations. Quality trials have utilized regimens of ibuprofen 400mg TID, diclofenac 75mg QD or BID, and indomethacin 25mg or 50mg TID (see NSAIDs/acetaminophen evidence table). As there are no quality head-to-head comparative trials, duration of treatment is unclear. Available studies utilized different treatment durations ranging from 4 days to 6 weeks. One trial compared 4 day with 8 day treatment and found the longer treatment duration superior.(323) Another trial evaluating 1 week versus 3 weeks treatment found no statistically significant different in outcome with duration; however, the trial appears underpowered and there was a trend towards benefit from the longer treatment

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duration.(324) Post-operative patients have reportedly been particularly susceptible to gastrointestinal bleeding and consideration of prophylaxis has been recommended.(325)

Indications for Discontinuation – Completion of course of treatment, adverse effects, or intolerance (NSAIDs may cause an increased risk of gastrointestinal bleeding).

Strength of Evidence – **Moderately Recommended, Evidence (B)**

5. *Recommendation: Acetaminophen for Treatment of Acute, Subacute, Post-operative, or Chronic Hip Pain*

Acetaminophen (or the analog, paracetamol) is recommended for treatment of acute, subacute, chronic or post-operative hip pain particularly in patients who have contraindications for NSAIDs.

Indications – All hip pain, including acute, subacute, chronic and post-operative.

Dose/Frequency – Per manufacturer's recommendations; may be utilized on an as-needed basis. It has been suggested that 1gm doses are more effective than 650mg doses particularly in post-operative patients;(326, 327) however, this level is now above the maximum dose recommended by an FDA advisory committee of 650mg and evidence of hepatic toxicity has been reported at 4gms a day particularly among those consuming excessive alcohol. There also is no quality evidence for superiority of 1gm dosing for treatment of osteoarthrosis.(326)

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

Strength of Evidence – **Recommended, Insufficient Evidence (I) – Acute, subacute, or post-operative hip pain**

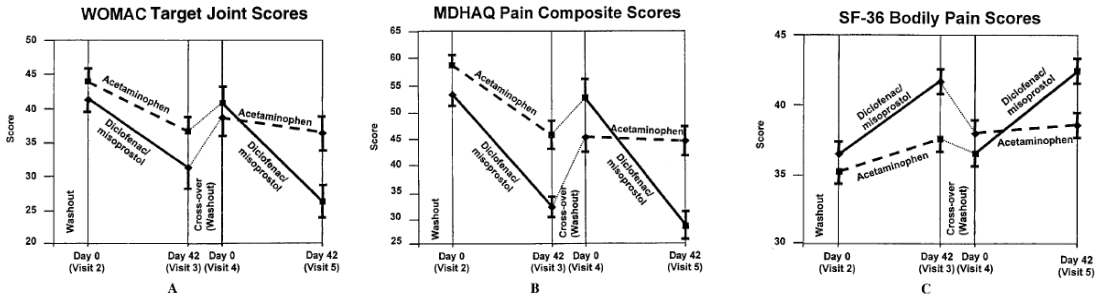
Strength of Evidence – **Recommended, Evidence (C) – Chronic hip pain**(328, 329)

6. *Recommendation: Acetaminophen for Treatment of Hip Pain in Patients with Cardiovascular Disease Risk Factors*

Acetaminophen or aspirin are strongly recommended as the first-line therapy for patients with cardiovascular disease risk factors.

Strength of Evidence – **Strongly Recommended, Evidence (A)**

Figure 2. Changes in Scores on A, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), B, the Visual Analog Pain Scale of the Multidimensional Health Assessment Questionnaire (MDHAQ), and C, the Short Form 36 Health Survey Pain Scale



Lower scores on the WOMAC and MDHAQ pain scales indicate clinical improvement. Note greater declines in WOMAC and MDHAQ pain scores when patients took diclofenac 1 misoprostol than when they took acetaminophen.

Pincus T, Koch GG, Sokka T, Lefkowith J, Wolfe F, Jordan JM, Luta G, Callahan LF, Wang X, Schwartz T, Abramson SB, Caldwell JR, Harrell RA, Kremer JM, Lautzenheiser RL, Markenson JA, Schnitzer TJ, Weaver A, Cummins P, Wilson A, Morant S, Fort J. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. *Arth Rheum*. 2001;44(7):1587-98. Reprinted with permission from John Wiley and Sons.

Rationale for Recommendations

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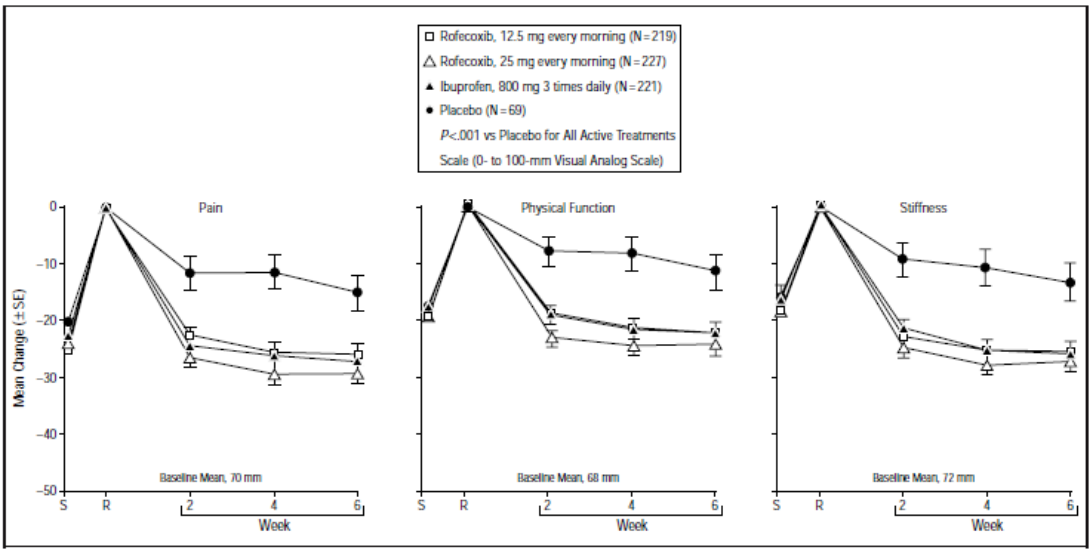
There is abundant quality evidence that NSAIDs improve pain and produce higher functional status among chronic hip pain patients, particularly those with osteoarthrosis or rheumatoid arthritis.(329-343) There are a few studies of osteoarthrosis flares that also consistently document benefits.(340, 344, 345) There are no quality studies of acute, subacute or post-operative hip pain, however, by analogy to other MSDs including LBP (see Low Back Disorders chapter); successful treatment of hip pain may be reasonably anticipated. Results are positive whether considering COX-1 (non-selective) or COX-2 (selective) NSAIDs (see Figures 3 and 4), although the magnitude of benefit is not generally large for any given medication. While there are many quality trials comparing various NSAIDs, there is no consistent quality evidence of superiority of one over another or of one class over another nor is there consistent quality evidence for superiority of enteric-coated or sustained release preparations. Most studies have not found cyclooxygenase-2 selective medications to be superior to other NSAIDs for pain control;(306, 307, 346) however, there is quality evidence they reduce risk of gastrointestinal adverse effects (see Figure 6).(306, 307, 346) There is one quality study suggesting that evening dosing of indomethacin resulted in better pain control, but the study has not been replicated.(317) There is no similar result with the longer half-life agent celecoxib.(318) There is quality evidence that NSAIDs are less impairing than opioids, yet with comparable efficacy (see Chronic Pain and Low Back Disorders chapters). 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.

Due to their inhibitory effects on platelet function, non-selective COX inhibitors should be used with caution, or avoided altogether, in the post-operative period if patients are also receiving pharmacoprophylaxis (e.g., warfarin, low molecular weight heparins) to prevent venous thromboembolic disease. Concomitant use of non-selective COX inhibitors and anti-coagulation regimens may increase the risk of hemorrhage. There is also concern that COX inhibitors, particularly COX-2 inhibitors, may inhibit bone healing. Therefore, these agents should be used with caution or avoided altogether in those acute post-operative period where bone healing is required, such as in fracture repair or hip replacements where cementless acetabular and/or femoral components are utilized.(316) There is evidence that NSAIDs are as effective for pain relief as opioids including tramadol,(347, 348) and dextropropoxyphene,(349) although slightly less efficacious than codeine.(350, 351)

Figure 3. Mean Change Plots of the Primary Efficacy End Points in the 6-week Ibuprofen Study



S indicates screening visit; R, randomization visit/baseline assessment

Saag K, van der Heijde D, Fisher C, Samara A, DeTora L, Bolognese J, Sperling R, Daniels B for the Osteoarthritis Studies Group. Rofecoxib, a new cyclooxygenase 2 inhibitor, shows sustained efficacy, comparable with other nonsteroidal anti-inflammatory drugs. A 6-week and a 1-year trial in patients with osteoarthritis. *Arch Fam Med*. 2000;9:1124-34. Reprinted with permission from the American Medical Association.

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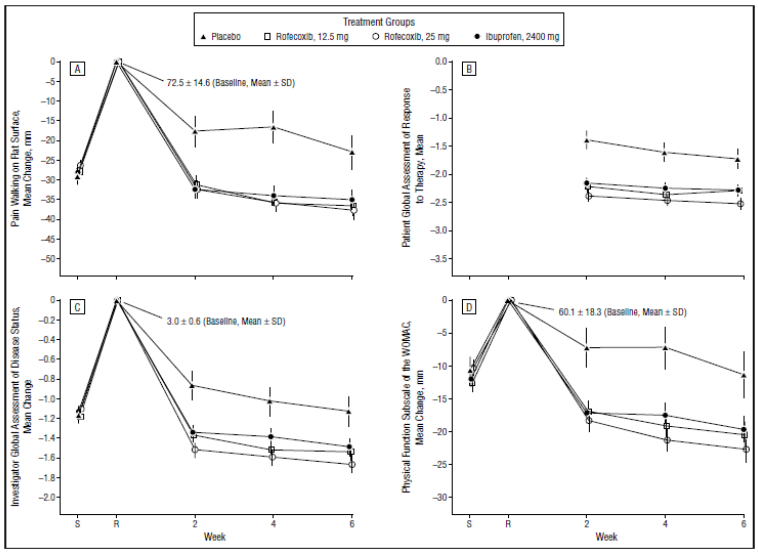
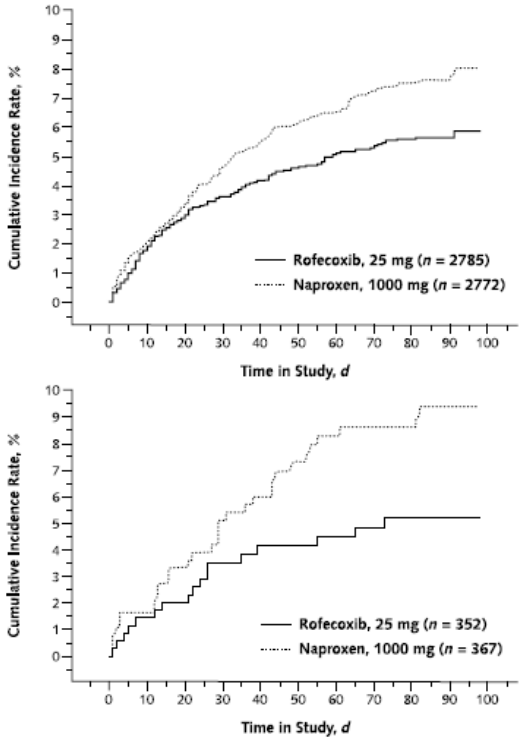
Figure 4. Treatment Effects over Time for the 3 Primary Clinical Efficacy End Points



S indicates screening visit; R, randomization visit; and WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index. Error bars indicate 84% confidence intervals. All active treatments were superior to placebo (P<.001).

Day R, Morrison B, Luza A, Castaneda O, Strusberg A, Nahir M, Helgetveit KB, Kress B, Daniels B, Bolognese J, Krupa D, Seidenberg B, Ehrich E for the Rofecoxib/Ibuprofen Comparator Study Group. A randomized trial of the efficacy and tolerability of the COX-2 inhibitor rofecoxib vs ibuprofen in patients with osteoarthritis. *Arch Intern Med*. 2000;160:1781-7. Reprinted with permission from the American Medical Association.

Figure 5. Cumulative Incidence of Discontinuation due to Gastrointestinal Adverse Events



Top. The incidence among the overall study sample.
Bottom. The incidence among patients who used low-dose aspirin.
For both parts, Kaplan–Meier curves display the time course of cumulative incidence of discontinuations due to gastrointestinal adverse events by treatment group.

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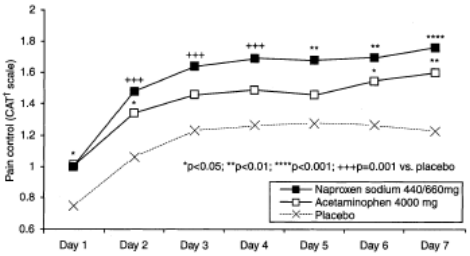
Lisse JR, Periman M, Johansson G, Shoemaker JR, Schechtman J, Skalky CS, Dixon ME, Polis AB, Mollen AJ, Geba GP for the ADVANTAGE Study Group. Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis. A randomized, controlled trial. *Ann Intern Med*. 2003;139:539-46. Reprinted with permission from the American College of Physicians.

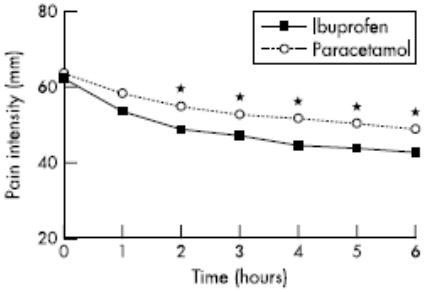
Figure 6. Daily Evaluation of Pain Control



†CAT; five point categorical scale (0-4)

Golden HE, Moskowitz RW, Minic M. Analgesic efficacy and safety of nonprescription doses of naproxen sodium compared with acetaminophen in the treatment of osteoarthritis of the knee. *Am J Therapeutics.* 2004;11:85-94. Reproduced with permission from Wolters Kluwer Health.

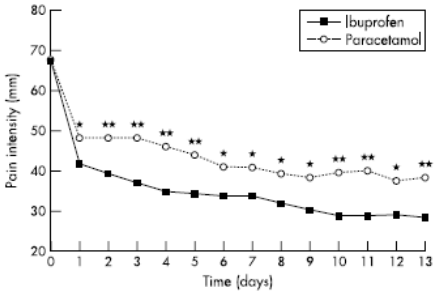
Figure 7. Evolution of the Pain Intensity during 6 hours after the First Dose



*p<0.05, Student's *t* test

Reproduced from *Ann Rheum Dis*, Boureau F, Schneid H, Zeghari N, Wall R, Bourgeois P, The IPSO study: ibuprofen, paracetamol study in osteoarthritis. A randomized comparative clinical study comparing the efficacy and safety of ibuprofen and paracetamol analgesic treatment of osteoarthritis of the knee or hip, Vol. 63, pp. 1028-34, 2004 with permission from BMJ Publishing Group Ltd.

Figure 8. Evolution of the Pain Intensity over 14 days of Treatment Assessed by a VAS



*p<0.05; **p<0.005, Student's *t* test

Reproduced from *Ann Rheum Dis*, Boureau F, Schneid H, Zeghari N, Wall R, Bourgeois P, The IPSO study: ibuprofen, paracetamol study in osteoarthritis. A randomized comparative clinical study comparing the efficacy and safety of ibuprofen and paracetamol analgesic treatment of osteoarthritis of the knee or hip, Vol. 63, pp. 1028-34, 2004 with permission from BMJ Publishing Group Ltd.

A systematic review and meta-analysis of observational studies of NSAIDs found that the risk for serious cardiovascular events was elevated in combined analyses for some NSAIDs, but not for others.(352) Many of the studies supporting these estimates were based on large pharmaceutical databases that were adequately powered to detect effects, but had limited ability to control for potential confounding. There is one reported study of NSAIDs and myocardial infarctions that controlled for two major confounders – aspirin and body mass index.(353) Summary estimates from that study for non-selective NSAIDs suggested that they are protective against cardiovascular events. Study weaknesses included a

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50% participation rate and reliance on recall. However, the American Heart Association has cautioned against the use of NSAIDs, especially COX-2.(322) Thus, current evidence is unclear if there is increased risk, no risk, or reduced risk of cardiovascular events from the use of any NSAIDs other than rofecoxib which appears to have a modestly elevated relative risk.(352) It is recommended that the risks of NSAIDs use, including cardiovascular risk factors, be discussed with patients.

Risks of gastrointestinal events are also recommended for assessment, particularly including prior history of gastrointestinal bleeding and source, length of treatment, age, smoking, diabetes mellitus and other medical factors. Those with greater risk should be considered for treatment with acetaminophen, NSAID plus misoprostol, proton pump inhibitors (see below), or a COX-2 selective agent (see NSAIDs/acetaminophen evidence table).(306, 307, 342, 346, 354, 355)

Gastrointestinal adverse events are generally considered the most significant of the risks of NSAIDs. A large volume of high- and moderate-quality evidence consistently shows proton pump inhibitors are effective for prevention and or treatment of gastric and duodenal ulcers and erosions.(356-365) There is only one quality head-to-head trial, and it found no difference in efficacy between pantoprazole and omeprazole.(358) Misoprostol has also been consistently shown to be effective compared with placebo.(366-375) Relatively fewer studies have shown sucralfate to be effective compared with placebo;(376) H2 blockers appear more effective for treatment of duodenal than gastric mucosa.(319-321) There are relatively few quality trials comparing efficacy of the different classes of agents. Pantoprazole but not lansoprazole has been found modestly superior to misoprostol.(315, 377) No difference was found between famotidine and lansoprazole.(378) Misoprostol has been reported superior to ranitidine,(379, 380) cimetidine,(381) and sucralfate.(371, 382) In short, while the evidence is not definitive, available quality evidence suggests proton pump inhibitors and misoprostol appear superior to H-2 blockers and sucralfate. While COX-2 selective agents have generally been recommended as either third- or fourth-line medications for routine use in osteoarthrosis patients, when there is a risk of gastrointestinal complications, they are often preferred. For patients at high risk of gastrointestinal bleeding, there is evidence that a combination of proton pump inhibitor plus COX-2 selective agent is efficacious.(383)

There is consistent quality evidence that NSAIDs prevent heterotopic bone formation in post-arthroplasty patients (See NSAIDs/acetaminophen evidence table),(323-325, 384, 385) although there is no quality evidence that prophylactic treatment with NSAIDs results in improved functional outcomes.(325) Still, these medications are successful at preventing heterotopic bone formation and these NSAIDs are moderately recommended for this purpose. Consideration should be given for concomitant use of gastro-protective medication for those patients treated with NSAIDs.

NSAIDs are not invasive, have low side effect profiles in a healthy working age patient population, and when generic medications are used are low cost. The potential for NSAIDs to increase the risk of cardiovascular events needs to be carefully considered in patients and will likely require additional quality studies to fully address.

Acetaminophen (or the analog, paracetamol) may be a reasonable alternative for treatment of acute, subacute, post-operative or chronic hip pain, (328, 329) although quality evidence is available that documents acetaminophen is consistently less efficacious in comparison with NSAIDs(336, 386-391) and at least two quality trials with placebo comparisons have been negative including one with a large sample size of 779 patients(336, 392) (see Figure 3). A recent FDA advisory committee recommended reduction of the maximum dose to 650mg, which is less than the 1gm dose used in most quality trials, thus the degree of successful treatment of osteoarthrosis with lower doses of acetaminophen is currently somewhat unclear.

All trials that compared acetaminophen with NSAIDs found either that the NSAID significantly reduced pain more than acetaminophen or the differences, while not statistically significant, favored the NSAID.(336, 386-391, 393) One trial found superior onset of symptom relief at 2 hours into treatment with ibuprofen compared to paracetamol with relief continuing for the full 2-week duration of the trial (see

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Figures 7 and 8). These findings are consistent with quality evidence for treatment of low back pain (see Low Back Disorders chapter). Thus, there is quality evidence that NSAIDs are more efficacious than acetaminophen for pain relief of musculoskeletal conditions including osteoarthrosis. Sub-analyses have suggested NSAIDs are particularly more efficacious for those with more severe osteoarthrosis (see NSAIDs/acetaminophen evidence table). However, evidence also indicates higher rates of gastrointestinal adverse effects among NSAID users and generally lower overall adverse effects profiles for acetaminophen, providing rational for utilization of acetaminophen to treat some patients and some recommend acetaminophen as the initial treatment.

Evidence for the Use of NSAIDs and Acetaminophen
There are 26 high (one with two reports)(106, 325, 330, 331, 337, 338, 354, 356, 358-361, 368, 386, 387, 390, 394-404) and 125 moderate-quality (one with two reports)(315, 317-321, 323, 324, 328, 329, 332-336, 339-345, 347-351, 355, 357, 362-367, 369-382, 384, 385, 388, 389, 391, 392, 405-474) RCTs and randomized crossover trials incorporated in this analysis. There are 25 low-quality RCTs(475-499) and crossover trials in Appendix 2.

Note: Highlighted footnotes need to be strung together and numbered in order when superscripted. The older version of Endnote only let me add 50 citations in one group.

Note: Trials are aggregated within these categories to provide some structure. However, while many of these could be multiply listed in the different categories, they are listed only once to conserve space.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
NSAIDs vs. Placebo						
Kruger 2007 RCT	9.5	N = 167 Knee or hip OA	Oxaceprol 400mg TID vs. placebo for 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.
Pope 2004 N of 1 trials	8.5	N = 51 Hip, knee or hand OA	Multiple crossover trials of diclofenac 50mg plus misoprostol 200µg vs. placebo for 2 week durations for 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.
Mejjad 2000 Randomized Crossover Experimental Trial	7.5	N = 16 Unilateral hip OA	Etodolac 300mg vs. placebo one dose. Assessed effects on gait.	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 decreased between t0 and t180 for etodolac and placebo groups (p <0.0009 and p <0.03, respectively).	"[W]alking speed increased under etodolac, but not 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.	Small sample size. Suggests drug had positive effect on gait in 3-hour experiment.

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Berry 1992 RCT	5.5	N = 184 Hip or knee OA	Lornoxicam 6mg QD vs. 4mg BID vs. 6mg BID vs. placebo for 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, however trend towards higher adverse events at higher doses (placebo 9% vs. 7, 12, 17% lornoxicam doses).	"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.
Caroit 1976 Crossover Trial	5.5	N = 9 Hip OA	Ketoprofen 50mg TID vs. placebo; 2 week treatment each treatment.	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 2 RCTs	5.5	N = 180 Hip OA N = 237 Knee OA	Meclo-fenamate sodium 100mg TID vs. placebo for 4 weeks. Meclo-fenamate dose could be reduced.	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.
Gillgrass 1984 Crossover Trial	4.5	N = 18 Hip or knee OA	Nabumetone 1gm BID vs. placebo for 2 weeks each.	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.
Famaey 1976 Possible Crossover Trial	4.0	N = 20 Hip OA	Ketoprofen 50mg TID vs. placebo for 2 weeks.	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.
Acetaminophen or Paracetamol vs. Placebo						
Amadio 1983 Crossover Trial	7.0	N = 25 Knee OA	Acetaminophen 1gm QID vs. placebo for 6 weeks	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).	"Acetaminophen in a dose of 4000 mg/day is an effective alternative to salicylates in the treatment of osteoarthritic pain of	Suggests efficacy of acetaminophen.

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				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.	the knees, with few adverse effects."	
Miceli-Richard 2004 RCT	6.5	N = 779 Knee OA	Paracetamol 1gm QID vs. placebo for 6 weeks	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."	Large sample size. Suggests paracetamol is not clearly effective for knee OA.
NSAIDs vs. Acetaminophen or Paracetamol						
Golden 2004 2 RCTs	8.5	N = 465 Knee OA	Naproxen sodium 220mg TID (BID if over 65 years) vs. acetaminophen 1gm QID vs. placebo QID	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.
Temple 2006 RCT	8.0	N = 581 Mild to moderate hip or knee OA	Acetaminophen 1g Q4-6 hours vs. naproxen 375mg BID for up to 12 months. Single dummy.	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 Curr Rheumatol Rep 2001 Pincus Arth Rheum 2001 Randomized Crossover Trial	7.5	N = 227 Hip or knee OA	Diclofenac 150mg plus misoprostol 400µg vs. 4,000 mg acetaminophen for 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).	"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.	No placebo arm. Data demonstrate diclofenac superior for pain relief and measures of function to acetaminophen, particularly for moderate to severe disease.

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				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%.	Acetaminophen was associated with fewer adverse effects."	
Boureau 2004 RCT	7.5	N = 222 Knee or hip OA	Ibuprofen 400mg TID vs. paracetamol 1,000mg TID for 14 days. Double dummy.	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.
Case 2003 RCT	6.5	N = 82 Medial knee OA	Diclofenac 75mg BID vs acetaminophen 1000mg QID vs. placebo for 12 weeks. Double dummy	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.
Blandino 2001 Crossover	4.5	N = 227 Hip or knee OA	Diclofenac plus misoprostol vs.	WOMAC improved 12.2 points for diclofenac vs. 6.6 for acetaminophen. Second 6-week period	"The NSAID diclofenac was found to be more effective than acetaminophen in	Few study details. Results suggest diclofenac more effective than

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Trial			acetaminophen	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.	patients with moderate to severe arthritis."	acetaminophen for pain and functional improvement.
NSAIDs vs. Opioids						
Beaulieu 2008 RCT	7.5	N = 129 Hip and/or knee OA	Tramadol CR 200mg vs. diclofenac SR 75mg. Doses titrated (up to 400mg a day vs. up to 150mg).	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.
Pavelka 1998 Crossover trial	7.0	N = 60 Hip or knee OA without clinical joint inflamma-tion	Tramadol 50-100mg up to TID vs. diclofenac 25-50mg up to TID for 4 weeks. Doses titrated.	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.
Parr 1989 RCT	6.5	N = 846 Mostly hip or knee OA	Diclofenac sodium slow release 100mg QD vs. dextro-propoxyphene 180mg plus paracetamol 1.95gm QD	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	"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.

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				(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).		
Quiding 1992 Crossover Trial	6.0	N = 26 Hip OA	Ibuprofen 200mg plus codeine 30mg vs. ibuprofen 200mg plus placebo. Used single and repeated dosings; 6 doses in 24-hour period each regimen.	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.
Kjaersgaard-Andersen 1990 RCT	6.0	N = 158 Hip OA	Codeine plus paracetamol (60mg/1g TID) vs. paracetamol (1g TID)	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%.
NSAIDs vs. Other NSAIDs and Trials with Multiple Treatment Arms						
Zacher 2003 RCT	11.0	N = 516 Knee or hip OA	Etoricoxib 60mg QD vs. diclofenac 50mg TID for 6 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 =	"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.

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				0.007). GI adverse effects in E 12.9% vs. D 14.2%.		
Puopolo 2007 RCT	10.0	N = 548 Hip or knee OA	Etoricoxib 30mg QD vs. Ibuprofen 800mg TID vs. placebo for 12 weeks. Double dummy.	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 RCT (2 trials)	9.5	N = 736 Knee or hip OA	Two trials: 1) Rofecoxib 12.5 QD vs. 25mg QD vs. ibuprofen 800 TID vs. placebo 6 weeks; 2) rofecoxib 12.5mg QD vs. 25mg QD vs. diclofenac 50mg TID for 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 RCT	9.5	N = 85 Hip or knee OA	Flurbiprofen-SR 200mg vs. diclofenac sodium-SR 100mg QHS for 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	"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.

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				passive motion, joint swelling) NS. More drug-related adverse reactions in diclofenac sodium-SR (n = 15) than flurbiprofen-SR (n = 9), NS.		
Hawel 2003 RCT	9.0	N = 148 Hip OA	Dexibuprofen 400mg BID vs. celecoxib 100mg BID for 15 days. Double dummy.	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.
Fleischmann 2008 RCT	9.0	N = 3,036 Hip, knee or spine OA	Lumiracoxib 100mg QD vs. lumiracoxib 100mg BID vs. celecoxib 200mg QD. Double dummy.	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.
Geba 2002 RCT	9.0	N = 382 Knee OA	Rofecoxib 12.5mg a day vs. rofecoxib 25mg a day vs. celecoxib 200mg a day vs. acetaminophen 1gm QID for 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.
Day 2000 RCT	8.5	N = 809 Knee or hip OA	Rofecoxib 12.5mg QD vs. 25mg QD vs. ibuprofen 800mg TID for 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.

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Bellamy 1986; 1988 RCT	8.0	N = 57 Hip and/or knee OA	Isoxicam 200mg QD vs. piroxicam 20mg QD for 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.
Fioravanti 2002 RCT	8.0	N = 287 Moderat e or severe hip and/or knee OA	Nimesulide-beta-cyclodextrin 400mg BID vs. naproxen 500mg BID for 2 weeks scheduled treatment and 5.5 months on-demand dosing	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 RCT	8.0	N = 290 Knee or hip OA	Diclofenac SR 75mg BID vs. diclofenac 50mg TID for 7 days. Double dummy.	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.
Bradley 1991 RCT	7.5	N = 184 Knee OA	Ibuprofen 600mg QID vs. ibuprofen 300mg QID vs. acetaminophe n 1gm QID for 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 RCT	7.5	N = 501 Knee or hip OA	Etoricoxib 60mg QD vs. naproxen 500mg BID vs. placebo for 12 weeks. Double dummy.	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,	"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

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				-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 present.
Reginster 2007 RCT	7.5	N = 997 Hip or knee OA	Etoricoxib 60mg QD vs. naproxen 500mg BID vs. placebo 12 weeks. Then placebo randomized to active treatment for 40 weeks, 86-week follow-up.	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 RCT	7.5	N = 135 Hip or knee OA	Lornoxicam 4mg TID vs 8mg BID vs diclofenac 50mg TID for 12 weeks with 40 week continuation phase. Double dummy.	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.
Lisse 2003 RCT	7.0	N = 5,557 Knee, hip hand or spine OA	Rofecoxib 25mg a day vs. Naproxen 500mg twice daily for 3 months. Double dummy.	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.

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Lindén 1996 RCT	7.0	N = 255 Hip OA	Meloxicam 15mg vs. 30mg vs piroxicam 20mg QD for 6 weeks	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 N of 1 trials	7.0	N = 13 Hip or knee OA	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	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.
Smugar 2006 2 RCTs	7.0	N = 2,603 Knee or hip OA	1) rofecoxib 12.5mg vs. rofecoxib 25mg vs. celecoxib 200mg vs. placebo QD for 6 weeks; 2) same medications except no rofecoxib 12.5mg arm	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 RCT	7.0	N = 120 Knee and/or hip OA	Etodolac SR 600mg QD vs. tenoxicam 20mg QD for 8 weeks. Double dummy.	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	"[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	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.

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				(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).	treated with etodolac SR."	
Pincus 2004 Randomized crossover trial	6.5	N = 1,080 Knee or hip OA	Placebo vs. acetaminophen 1000mg QID vs. celecoxib 200mg QAM. 6 weeks each. Double dummy. Patients received 2 of 3 treatments.	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 Crossover trial	6.5	N = 27 Knee or hip OA	Floctafenine 300mg QID vs. enteric-coated aspirin (ACSA) 625mg QID vs. placebo for 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 RCT	6.5	N = 944 Knee or hip OA	Rofecoxib 12.5 QD vs. naproxen 500mg BID for 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 RCT	6.5	N = 336 Hip or knee OA	Meloxicam 7.5mg QD vs. diclofenac sodium SR 100mg QD for 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.
Bellamy 1995 RCT	6.0	N = 382 Hip, knee or	Nabumetone 1,000mg vs. diclofenac SR 200mg QPM	More on nabumetone titrated to higher dose (69% vs. 53%, p = 0.002). Physician	"Nabumetone is efficacious and well tolerated in patients with OA of the hip,	Variable doses used. High dropout rate (43%) at 6 months precludes

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		shoulder OA	for 3 months. Dose could be titrated once after 2 weeks of initial dose. Double dummy.	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).	knee or shoulder. In this group of patients it is similar in efficacy and superior in tolerability to diclofenac SR."	strong conclusions.
Herrman 2000 RCT	6.0	N = 263 Knee and/or hip OA	Oxaceprol 400mg TID vs. diclofenac 50mg TID for 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 RCT	6.0	N = 26 Knee or hip OA	Oxaprozin 1,200mg QD vs. naproxen 250mg TID for 8 weeks. Double dummy.	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 RCT	6.0	N = 583 Knee or hip OA	Lumiracoxib 50mg vs 100mg vs. 200mg BID vs. 400mg QD vs. diclofenac 75mg BID vs. placebo for 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 RCT	6.0	N = 335 Moderate to severe knee or hip OA	Nabumetone 1,000-2,000mg QD vs. diclofenac 50mg BID-TID for 12 weeks; doses titrated	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	"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.

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				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%]).		
Cannon 2000 RCT	6.0	N = 784 Hip or knee OA	Rofecoxib 12.5 QD vs 25mg QD vs. diclofenac 50mg TID for 1 year	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 RCT	6.0	N = 252 Severe hip OA	Piroxicam 20mg QAM vs. naproxen 500mg QAM and 250mg. QPM. Trial length unclear (possibly 1 month), but observed for 5 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.

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Baumgartner 1996 RCT	6.0	N = 61 Knee or hip OA	Two SR tablets of ibuprofen 1,600mg vs, diclofenac 100mg SR QPM for 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 Crossover trial	6.0	N = 36 Knee or hip OA	Rhus Tox vs. placebo vs. fenoprofen 600mg TID	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 RCT	6.0	N =143 Hip and/ or knee OA	Flurbiprofen 50mg BID vs. sulindac 150mg BID for 42 days.	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 RCT	6.0	N = 230 Hip and/or knee OA	Isoxicam 200mg QD vs. Naproxen 500mg BID for 4 weeks. Double dummy.	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).

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Gordin 1984 Crossover trial	6.0	N = 44 Hip or knee OA	Slow-release formulation of indomethacin (50mg) vs. diflunisal (250mg); 2 tablets daily for 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.
Bauer 1999 RCT	5.5	N = 150 Knee or hip OA	Oxaceprol 200mg TID vs. diclofenac 25mg TID for 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 Crossover trial	5.5	N = 25 Hip or knee OA	Nabumetone 1gm QHS vs. naproxen 250mg BID for 7 days each	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 RCT	5.5	N = 48 Knee or hip OA	Tenoxicam 20mg QD vs. piroxicam 20mg QD vs. placebo for 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 RCT	5.5	N = 467 Hip OA	Valdecoxib 5mg QD vs. 10mg QD vs. naproxen 500mg BID vs. placebo for 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	"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.

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				adverse effects lower compared with naproxen (11.0% vs. 4.5% vs. 4.2% vs. 1.7%).		
Marcolongo 1997 RCT	5.5	N = 113 Hip OA	Ketoprofen controlled-release 200mg QD vs. indomethacin 50mg BID for 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 RCT	5.5	N = 1,061 Hip OA	Celecoxib 100mg vs. 200mg vs. 400mg QD vs. naproxen 500mg BID vs. placebo for 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 RCT	5.5	N = 70 Knee or hip OA	Tolmetin sodium 400mg BID vs. Naproxen 250mg BID for 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	"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.

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				motion (p <0.05).		
Yocum 2000 RCT	5.5	N = 774 Hip or knee OA flare	Meloxicam 3.75 vs. 7.5 vs. 15mg a day vs. diclofenac 50mg BID vs. placebo for 12 weeks. Double dummy.	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.
Corts Giner 1991 RCT	5.0	N = 85 Knee or hip OA	Droxicam 20mg QHS vs. diclofenac 50mg TID for 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.
Bingham 2007	5.0	N = 1,207 (Study 1:	Etoricoxib 30mg QD vs. celecoxib	WOMAC pain scores (baseline/12 weeks): etoricoxib 67.4±16.2/	"Etoricoxib 30mg qd was at least as effective as celecoxib	No significant differences in efficacy or side

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2 identical RCTs		N = 599; Study 2: N = 608) patients who were prior NSAID or aceta-minophe n users	200mg QD vs placebo for 12 weeks.	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.	200mg qd and had similar safety in the treatment of knee and hip OA; both were superior to placebo."	effects prolife of etoricoxib compared to celecoxib. 20% dropout at 12 weeks in both groups.
Kiff 1994 RCT	5.0	N = 1,023 RA or OA	Diclofenac 50mg misoprostol 200µg vs. diclofenac 50mg vs. ibuprofen 600mg. All BID or TID at physician discretion for 4 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 Crossover Trial	5.0	N = 50 Knee and/or hip OA	Naproxen 250mg BID vs indometacin [sic] 25mg QID for 4 weeks for each drug. Double dummy.	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 RCT	5.0	N = 178 Hip OA	Dexibuprofen (400mg TID) vs. dexibuprofen (200mg TID) vs. ibuprofen (800mg TID) for 15 days	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.

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Davies 1980 Crossover trial	5.0	N = 21 Hip OA	Tolmetin sodium 400mg TID vs. indomethacin 25mg TID for 2 weeks. Double dummy.	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 RCT	5.0	N = 60 Knee or hip OA	Tiaprofenic acid 200mg TID vs indomethacin 33.3mg TID for 3 months	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 RCT	5.0	N = 370 Hip or knee OA	Nimesulide 100mg BID vs. naproxen 250mg QAM and 500mg QPM	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.
Car 1978 RCT	5.0	N = 79 Hip OA	Diclofenac 50mg BID vs. naproxen 250mg BID for 2 weeks. Double dummy.	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	5.0	N = 35 Hip and/	Diflunisal 250mg BID vs. ibuprofen	No symptoms or improvement at Week 8 in 16/17 (94.1%)	"No significant differences between diflunisal and ibuprofen	Allocation and baseline variables unclear. No

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RCT		or knee OA	400mg TID for 8 weeks. Double dummy.	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.	in the treatment of osteoarthritis of the hip and/or knee."	differences in efficacy or safety profile. OTC ibuprofen dosage used.
Frank 1977 Crossover Trial	5.0	N = 30 Hip OA	Flurbiprofen 50mg TID vs. indomethacin 25mg TID daily for 2 weeks intervals	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 Crossover Trial	5.0	N = 53 Hip or knee OA	Fenbufen 200mg TID vs. aspirin 1.2g TID for 8 weeks	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.
Kogstad 1981 Crossover Trial	4.5	N = 164 Hip or knee OA	Piroxicam 20mg QAM vs. naproxen vs. placebo 250mg BID for 4 weeks each	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 1977-1978 2 randomized crossover trials	4.5	N = 24 N = 40 Hip and knee OA	Tolmetin 400mg TID vs. 200mg TID for 2 weeks. Tolmetin 400mg TID vs. ketoprofen 50mg TID daily for 2 weeks. Double dummy.	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.	"[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	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.

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				Blood urea nitrogen levels increased on tolmetin and ketoprofen (p <0.05).	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."	
Lund 1987 RCT Same trial as Jensen 1986	4.5	N = 108 Hip or knee OA	Tenoxicam 20mg QD vs. piroxicam 20mg QD for up to 24 months in this report	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 Crossover trial	4.5	N = 56 Knee and/ or hip OA	Etodolac 300mg BID vs. naproxen 500mg BID for 4 weeks each	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 (2).	"[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 Crossover trials	4.5	Study 1: N = 46 RA Study 2: N = 42 hip OA	Orudis 25mg QID vs. Indomethacin 25mg QID	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 RCT	4.5	N = 309 Mostly hip or knee OA	Isoxicam 200mg QD vs. indomethacin 25mg TID for 2 weeks. Double dummy.	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	"[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.

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				(83.1%) (NS). Significant improvements both groups after 7 days drug therapy (p <0.001).		
Knüsel 1982 RCT	4.5	N = 50 Moderate to severe hip OA	Carprofen 100mg TID vs. diclofenac-sodium 50mg TID for 21 days	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 RCT	4.5	N = 38 Acute MSDs in athletes	Piroxicam 40mg QD for 2 days then 20mg QD vs. naproxen 500mg BID for 2 days then 375mg BID for 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 RCT	4.5	N = 33 Hip OA	Niflumic acid 200mg vs. niflumic acid 250mg vs. indomethacin 25mg vs. phenylbutazone 100mg	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 Crossover Trial	4.5	N = 226 Hip, knee or spine OA	Naproxen 500mg BID vs. ibuprofen 400mg TID for 6 weeks total	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 =	"Naproxen and ibuprofen were both effective treatments for this group of osteoarthritics seen in general practice. Naproxen was more effective than ibuprofen and was	Use of submaximal dose ibuprofen compared with full dose naproxen precludes an ability to assess which is more efficacious.

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				0.009), night pain (p = 0.056); 10 patients on naproxen, 5 on ibuprofen withdrew from trial because of side-effects.	preferred by more patients, but was associated with a larger number of side-effects."	
Gordin 1985 Crossover Trial	4.0	N = 21 Hip or knee OA	Slow-release indomethacin (50mg) vs. naproxen (250mg), 2 tablets daily for 3 weeks	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 Crossover Trial	4.0	N = 75 Hip or knee OA	Naproxen 1000mg QD vs. Piroxicam 20mg QD for 4 weeks each	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.
Verbruggen 1982 Crossover Trial	4.0	N = 21 Hip, knee or spine OA	Nabumetone 1gm QHS vs. naproxen 250mg BID for 2 weeks each	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.
Gastrointestinal Complications						
Agrawal 1999 RCT	9.5	N = 1,398 Hip or knee OA	Upper GI safety of arthrotec 75 (diclofenac sodium 75mg misoprostol 200µg) BID vs. nabumetone 1,500mg QD vs. placebo for 6 weeks	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.
Bocanegra 1998 RCT	7.5	N = 572 Knee or hip OA	Diclofenac (D50/M200) 50mg plus misoprostol 200µg TID vs. diclofenac 75mg plus misoprostol	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	"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	Lack of details on blinding, randomization. 6 week study with pre and post endoscopy demonstrated GI protective effect of misoprostol.

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			200µg BID (D75/M200) vs. diclofenac 75mg bid (D) vs. placebo for 6 weeks.	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.	with significantly lower incidence of gastric and/or duodenal ulcers."	
Lisse 2003 RCT	7.0	N = 5,557 Knee, hip hand or spine OA	Rofecoxib 25mg day vs. naproxen 500mg twice daily for 3 months. Double dummy.	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.
Melo Gomes 1993 RCT	6.5	N = 643 Hip and/ or knee OA	Diclofenac sodium 50mg plus misoprostol 200µg BID vs. piroxicam 10mg BID vs. naproxen 375mg BID for 4 weeks	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 RCT	6.5	N = 970 Hip or knee OA	AZD3582 750mg BID vs. naproxen 500mg BID vs. placebo for 6 weeks	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.

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Hayllar 1996 Crossover Trial	5.0	N = 19 Hip or knee OA	Flosulide 20mg BID vs. naproxen 500mg BID each for 2 weeks	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 RCT	5.0	N = 394 Hip or knee OA	Nabumetone 1,500mg QHS vs. diclofenac retard 100mg QHS for 12 weeks	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.
Høyeraal 1993 RCT	4.0	N = 208 Hip and knee OA	Tiaprofenic acid 300mg BID vs. naproxen 500mg QAM and 250mg QPM vs. placebo BID for 3 weeks. Double dummy.	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.
Education Regarding NSAIDs						
Edworthy 1999 RCT	7.0	N = 252 Hip or knee OA	Diclofenac with misoprostol treatment with in depth computer program about disease, treatment, patient involvement vs. medication	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,	"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.

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			with generic information about OA	pain, or disability; greater improvement in stiffness in experimental group (p = 0.04).		
Heterotopic Bone Prevention						
Fransen 2006 RCT	9.0	N = 902 THA	Ibuprofen 400mg TID vs. placebo for 14 days after total hip arthroplasty	No differences in hip pain after 6 to 12 months (mean difference -0.1, p = 0.59) or physical function (-0.1, p = 0.48). Secondary outcomes (global assessments and physical activity) also negative. Risk of severe ectopic bone formation Booker grade 3 or 4 with ibuprofen (0.69, 95% CI 0.57-0.83). Bleeding risk, ibuprofen RR = 2.09, p = 0.46.	"These data do not support the use of routine prophylaxis with NSAIDs in patients undergoing total hip replacement surgery."	Author suggests guidelines should be based on clinically important outcomes and not on radiographic findings. Data show ibuprofen significantly reduces risks of ectopic bone formation, but with double risk of major bleeding.
Sell 2004 RCT	7.5	N = 245 THA	Cholestyramine-bound diclofenac 75mg QD vs. BID for 14 days post op	In diclofenac 150mg, 19% slight heterotopic ossification (Booker 1, none more severe) vs. 75mg which had 17% grade 1 and 4% grade 2 Booker. No clinical difference after 6 months.	"Although the two doses displayed similar efficacy the author recommends the lower dose because of the lower instance of adverse gastrointestinal event (23% vs. 38%, p=0.02)."	Co-administration of proton pump inhibitors likely resulted in lower side effect profile. No placebo control.
Kjaersgaard-Andersen 1989 RCT	5.0	N = 176 All lubinus THA	Indomethacin 25mg TID vs. placebo for 6 weeks post-operative	One year after THA, development of Grace II or III heterotopic bone formation differed: indomethacin 0/90 (0%) vs. placebo 44/86 (51.2%). Six weeks after arthroplasty, mean ESR: indomethacin 15mm an hour vs. placebo 21mm an hour.	"The present study has shown the development of severe ecotopic ossification after THA to result in a significant elevation in the six-weeks ESR. Moreover, at 12 weeks after arthroplasty, reasons other than deep infection may cause ESR to rise above 35 mm/hour."	Data suggest indomethacin reduces heterotopic bone formation. Trend towards higher ESR in those forming heterotopic bone.
Persson 1998 RCT	4.5	N = 144 All Charnley THA	Ibuprofen 400mg TID for 3 weeks vs. ibuprofen for 1 week and placebo for 2 weeks vs. placebo for 3 weeks	Both ibuprofen-treated groups showed less HO than placebo-treated group (p = 0.001 for 21 days of treatment, and p = 0.008 for 8 treatment days). After 12 months, 21-day treatment group had no patient with grade III or IV HO vs. 2 grade III in 8-day group vs. 5 grade III and 2 grade IV in placebo (p = 0.002), 21-day treatment group and p = 0.005 for 8-day group). No difference between 2 active treatments (p = 0.8).	"[P]ostoperative prophylaxis with NSAIDs is highly effective in preventing clinically relevant degrees of HO after THA. The treatment should start early postoperatively and continue for at least 8 days. It appears to be cost-effective and the treatment of choice in patients at risk for HO."	Lack of study details. Data suggest at least one week of treatment after hip arthroplasty is effective to prevent heterotopic bone formation. Data suggest larger trial may indicate 3 weeks is superior for prevention of more advanced bone formation, however this study underpowered for that outcome.

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Dorn 1998 RCT	5.0	N = 249 Cement-less THA	Indomethacin 50mg TID for 4 days vs. 8 days	At 1 year, Booker grades II, III and IV heterotopic bone: 4 days 13/104 (12.5%) vs. 8 days 3/105 (2.9%) (p <0.05).	"[T]he incidence of heterotopic bone formation after total hip arthroplasty was not statistically different after 4-day and 8-day treatment. The incidence of substantial heterotopic bone formation was statistically significantly less (p=0.03) after the 8-day treatment."	No placebo group. Randomized by government ID number. Data suggest longer treatment superior.
Osteoarthrosis Measurement Tools						
Averbuch 2004 RCT	5.5	N = 206 Hip OA flare-up	Naproxen sodium 500mg BID vs. placebo for 12 weeks. Pain measured in Visual analog vs categorical scales.	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.
Miscellaneous						
Wagentiz 2007 RCT	10.0	N = 210 Hip and/ or knee OA	Diclofenac 100mg in a SR-cap vs. SR-tab QAM for 14 days	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.
Rashad 1989 RCT	5.0	N = 105 Hip OA awaiting arthro-plasty	Indomethacin 50mg QD vs. 75mg QD vs. azapropazone 600mg QD vs. 900mg QD for variable lengths of treatment followed to arthroplasty	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).
Timing of Medication						

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Vinje 1993 Crossover trial	7.0	N = 163 Hip or knee OA	Ketoprofen 200mg QAM vs. QPM for 4 weeks each	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.
Levi 1985 Crossover trial	7.0	N = 66 Hip or knee OA	Indomethacin SR 75mg. Medication taken at 8am vs. noon vs. 8pm vs. placebo for 1 week intervals	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).
Stengaard-Pedersen 2004 RCT	5.5	N = 697 Knee or hip OA	Celecoxib 200mg QAM vs. celecoxib 200mg QPM vs. celecoxib 100mg BID for 12 weeks	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.
Enteric-coating						
Bakshi 1993 RCT	7.0	N = 129 Knee and/ or hip OA	Diclofenac dispersible vs. enteric-coated 50mg TID for 12 weeks	No differences in treatment efficacy (graphic data, approximately 60% reductions in VAS joint pain with activity). No differences in adverse 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%).	"Overall assessments of efficacy by the patients and the investigator indicated a positive response rate for both 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."	Data suggest comparability with no benefits of enteric coating of diclofenac.
Bakshi 1996 RCT	5.5	N = 216 Hip or knee OA	Diclofenac resinate capsules 75mg BID vs. enteric-coated diclofenac sodium tablets 50mg TID. Double	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	"[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	No placebo comparisons. No baseline provided on comparability. Generally comparable medication preparations, however trends in

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			dummy.	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).	formulation is effective for controlling the symptoms of osteoarthritis."	favor of diclofenac residinate.
Sustained Release vs. Immediate Release						
Toft 1985 Crossover Trial	5.0	N = 84 Hip and/ or knee OA	Ketoprofen sustained-release formulation 200mg QD vs. normal formulation 100mg BID 3 weeks each	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.
Bacon 1990 Randomized Crossover Trial	4.5	N = 77 Hip and/ or knee OA	Indomethacin controlled-release tablet 75mg QD vs indomethacin immediate release capsule 25mg TID for 4 weeks	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.
GI Issues: Proton Pump Inhibitors						
Chan 2002 RCT	9.5	N = 210 RA, OA, and other forms of arthritis with ulcer bleeding	Omeprazole 20mg plus amoxicillin 1g plus clarithromycin 500mg vs. omeprazole 20mg and placebo antibiotics each BID for 1 week	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 suggests antibiotics plus omeprazole effective.
Labenz 2002 RCT	9.0	N = 832 H pylori positive	Omeprazole 20mg BID vs. amoxicillin 1g BID vs. clarithromycin 500mg BID for 1 week	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);	"In H pylori infected patients, all three active therapies reduced the occurrence of NSAID associated peptic ulcer and dyspeptic	All diclofenac 50mg twice a day for 5 weeks. Other arms treatment for 1 week. Three treatment arms all reduced risk

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			(OAC), plus 4 weeks of placebo QD (OAC-P); OAC for 1 week plus 4 weeks omeprazole 20mg QD (OAC-O); omeprazole 20mg QD for 1 plus 4 weeks (O-O); or placebo for 5 weeks (P-P)	OAC-O: 80 (11.1-96), 4.7 (0.8-8.6); O-O: 100, 5.8 (2.1-9.5).	symptoms requiring therapy."	comparably. Results may not be generalized beyond H pylori infected patients.
Scheiman 2006 RCT	9.0	VENUS study: N = 844; PLUTO study: N = 585 At-risk patients (≥60 years and/or ulcer history)	Esomeprazole 20mg vs. esomeprazole 40mg vs. placebo QD for 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 RCT	9.0	N = 595 Rheumatic patients on continual NSAIDs with at least 1 more re-cognized risk factor that contributes to GI injury	Pantoprazole 20mg vs. pantoprazole 40mg vs. omeprazole 20mg QD for 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.
Yeomans 2008 RCT	9.0	N = 991 Patients ≥60 years without baseline gastro-duodenal ulcer receiving aspirin 75-325mg daily	Esomeprazole 20mg QD vs. placebo for 26 weeks.	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.
Dorta 2000 RCT	8.5	N = 12 Healthy volunteer	Two-week course of omeprazole (40mg) plus	No differences in healing scores after administration of placebo/diclofenac	"In healthy subjects, omeprazole does not accelerate the healing of pre-existing mucosal	Crossover study with small sample size. Short-term treatments of

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		s	"separate 2-week course of an identical looking placebo." Water-soluble diclofenac (50mg) taken 2nd week.	(median = 6; range 0-6) and omeprazole/ diclofenac (median = 9; range 0-6; p = 0.17) were found.	lesions or prevent the development of small diclofenac-induced mucosal lesions."	unclear clinical significance.
Bianchi Porro 2000 RCT	8.5	N = 104 RA or OA	40mg pantoprazole vs. placebo QD for 12 weeks	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.
Hawkey 2005 RCT	7.5	2 RCTs: N = 608 and N = 556 (NASAI, SPACE 1) Con-tinuous NSAID users free of gastro-duodenal ulcers, erosive esophag-itis, and H pylori	Esomeprazole 20mg, vs. esomeprazole 40mg vs. placebo QD for 4 weeks	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 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).	"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.
Cullen 1998 RCT	6.5	N = 169 Patients taking NSAIDs regularly, chronic-ally, and above defined minimum doses	Omeprazole 20mg vs. placebo, given for up to 6 months	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 RCT	6.5	N = 515 Rheum-atic	Pantoprazole 20mg plus placebo vs. misoprostol	Pantoprazole superior to misoprostol (p = 0.005) for endoscopic failure. Estimated	"Pantoprazole 20 mg o.d. is superior to misoprostol 200 microg b.i.d. in the	Six-month treatment. Study suggests pantoprazole superior to

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		patients likely to take NSAIDs contin-uously for at least 6 months	200µg	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.	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."	misoprostol.
Desai 2008 RCT	6.5	N = 70 Healthy adults aged 50-75 not taking chronic NSAIDs	Naproxen 500mg BID plus omeprazole 20mg QD vs. naproxen 500mg BID plus placebo for a 6.5-day 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.
Bianchi Porro 1998 RCT	6.0	N = 114 Arthritic disorders requiring indometh-acin, diclo-fenac, or keto-profen	Omeprazole 20mg QD vs. placebo for 3 weeks. All patients given indomethacin 100mg, ketoprofen 150mg, and diclofenac 150mg	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 RCT	6.0	N = 12 Healthy volunteer s	Lansoprazole 30mg QD vs. placebo plus aspirin for 1 week	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.
Niwa 2008 RCT	5.5	N = 10 Healthy subjects	Rebamipide 300mg plus diclofenac 75mg plus omeprazole 20mg vs. placebo plus diclofenac 75mg plus omeprazole	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 suggests efficacy for small intestine.

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			20mg QD for 1 week			
Miyake 2005 RCT	5.0	N = 194 RA in patients treated over a long term with NSAIDs	Famotidine 20mg BID vs. lansoprazole 15mg QD for 24 weeks	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.
Scheiman 1994 RCT	4.5	N = 20 Healthy volunteers	Omeprazole 40mg QD vs. placebo plus aspirin 650mg QID for 2 weeks	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.
Pilotto 2000 RCT	4.0	N = 127 H pylori positive patients with no severe gastro-duodenal lesions	Pantoprazole 40mg QD plus amoxicillin 1g BID and clarithromycin 250mg BID for 1 week vs. pantoprazole 40mg QD for 1 month	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.
GI Issues: Misoprostol						
Raskin 1995 RCT	9.0	N = 1,623 Patients with upper gastro-intestinal symptoms during NSAID therapy and no endo-scopic evidence of gastric or duo-denal	Placebo QID vs. misoprostol 200µg BID and placebo BID vs. misoprostol 200µg TID and placebo QD vs. misoprostol 200µg QID	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	Twelve week trial. Data support BID or TID dosing as well as QID.

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		ulcers			600 µg daily. Maximum protection against NSAID-induced duodenal ulcers can be achieved with doses as low as 400 µg daily. Physicians prescribing misoprostol should choose a dosage that best balances the drug's mucosal protective effects with its side effects."	
Bianchi Porro 1997 RCT	7.5	N = 70 RA or OA with endos-copically normal mucosa	Misoprostol TID: misoprostol 200µg and ranitidine placebo after every meal 3 times daily vs. misoprostol BID: Misoprostol 200µg after breakfast and dinner, misoprostol placebo after lunch; ranitidine placebo after every meal vs. ranitidine 150mg after breakfast and dinner, ranitidine placebo after lunch, and misoprostol placebo after each meal for 14 days.	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 gastrointestinal symptoms did not differ between 3 treatment groups. 56% with gastroduodenal ulcer had no gastrointestinal symptoms.	The study confirms that "[M]isoprostol is as effective as ranitidine in the short-term prevention naproxen-induced duodenal lesions, but 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."	RA or OA. Data suggest misoprostol is superior to ranitidine.
Raskin 1996 RCT	7.0	N = 538 Patients on chronic NSAID therapy with NSAID-related upper GI pain without gastric or duodenal ulcers	Misoprostol 200µg QID vs. ranitidine 150mg BID for 8 weeks	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	7.0	N = 638 Patients	Misoprostol 200µg vs.	At 12 weeks, duodenal ulcer in 2/320 (0.6%;	"Misoprostol significantly lowers the	Twelve week trial. Data support

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RCT		with chronic inflamm-atory or nonin-flamatory arthritis taking an NSAID but no gastric or duodenal ulcer	placebo for 12 weeks	95% CI, 0.2% to 3.9%) misoprostol, vs. 15/323 (4.6%; CI, 2.8% to 8%) placebo (p = 0.002).	frequency of both duodenal and gastric ulcer development in patients who require long-term therapy with NSAIDS."	misoprostol efficacious.
Bardhan 1993 RCT	7.0	N = 358 Patients requiring chronic NSAID therapy (Group 1 = normal; Group 2 = non-ulcer lesions)	Misoprostol 400-800µg daily vs. placebo tablets for 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.
Lanza Gastro-enterology 1988 RCT	6.5	N = 90 Normal volunteer s	Misoprostol 200µg QID vs. cimetidine 300mg QID vs. placebo for 7 days	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 RCT	6.5	N = 253 OA patients receiving ibuprofen , piroxica mor napro-xen with abdom-inal pain	Misoprostol 200µg vs. sucralfate 1g QID a day for 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.
Graham 2002 RCT	6.0	N = 537 Patients without H pylori and long-term users of NSAIDs with history of gastric	Placebo plus Misoprostol 200µg QID vs. 15 or 30mg of lansoprazole QD for 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	"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	Not blinded to misoprostol. H pylori negative.

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		ulcer		= 0.04).	considered, proton pump inhibitors and full-dose misoprostol are clinically equivalent."	
Elliot 1994 RCT	6.0	N = 83 Arthritis patients on chronic NSAID therapy	Misoprostol 200µg vs. placebo tablets for 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.
Chandra-sekaran 1991 RCT	5.5	N = 90 Arthritic patients	Diclofenac sodium 150mg a day OA subjects vs. indomethacin 75mg a day for seronegative spondarthro-pathy subjects vs. ibuprofen 1.2g a day and aspirin 2.7g a day for rheumatoid arthritis subjects for 4 weeks	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 Gastroentero l 1988 RCT	5.5	N = 30 Healthy volunteer s	Misoprostol 200µg vs. sucralfate 1g vs. placebo, co-administered with 650mg of aspirin 4 times a day 7 days	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 RCT	5.5	N = 130 Healthy subjects	Misoprostol 50µg vs. 100µg vs. 200µg vs. placebo plus aspirin 975mg (given as three 325mg tablets) for 7 days	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."	
Donnelly 2000 RCT	5.0	N = 32 Healthy volunteer s	Misoprostol 100µg plus aspirin 300mg vs. placebo plus aspirin	Gastric erosion in 52% on aspirin plus placebo vs.17% on aspirin plus misoprostol (OR = 0.18, CI: 0.07-0.48),	"Misoprostol 100 µg daily can prevent low-dose aspirin induced gastric mucosal injury without causing	Misoprostol 100QD vs. placebo plus ASA 300QD for 28 days. Data suggest misoprostol protects

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			300mg once daily for 28 days	averaged over Days 5, 14, and 28. Percent gastric petechiae: 42% and 23% (OR = 0.42, CI: 0.17-0.97).	identifiable adverse effects."	from gastric injury associated with ASA.
Silverstein 1986 RCT	5.0	N = 60 Healthy male volunteers	Misoprostol 200µg vs. placebo for 24 hours	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.
Medina Santillan 1999 RCT	4.5	N = 38 Healthy volunteers	Sodium diclofenac 75mg plus misoprostol 50µg vs. diclofenac for 14 days	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.
Koch 2000 RCT	4.0	N = 8,843 RA	Misoprostol plus NSAID vs. NSAID plus placebo	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.
GI Issues: Sucralfate						
Miglioli 1996 RCT	5.0	N = 107 Patients with arthritis	Diclofenac 200mg a day vs. naproxen 1g a day plus sucralfate gel 1gm BID or placebo for 14 days.	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.
GI Issues: H-2 Blockers						
Ehsanullah 1988 RCT	6.0	N = 297 RA or OA without lesions in the stomach and duo-denum	Ranitidine 150mg twice a day vs. placebo twice a day. NSAID drug treatment: naproxen 750mg a day; piroxicam 20mg a day; diclofenac 100mg a day; indomethacin 100mg a day.	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.
Robinson 1989 RCT	5.5	N = 144 Patients with normal endo-scopic findings	Ranitidine 150mg twice a day vs. placebo plus ibuprofen, indomethacin, naproxen,	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).

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		requiring NSAIDs	sulindac, or piroxicam for 8 weeks			
Robinson 1991 RCT	4.5	N = 673 Patients receiving NSAIDs for arthritic or musculo-skeletal conditions	Ranitidine 150mg twice daily vs. placebo for 4 weeks or 8 weeks.	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 suggests pro-tective for DU not GU.

OPIOIDS

Opioids are widely used to manage acute pain, post-operative pain, and pain associated with malignancy. A systematic review estimated that opioid use results in an average decrease of 30% in pain ratings for musculoskeletal pain.(500) However, these results do not include the approximately 50% of patients who do not tolerate opioids for these conditions (see Chronic Pain chapter and opioid evidence table). Opioids for treatment of non-malignant chronic pain is also increasingly controversial (see Chronic Pain chapter) particularly due to marked estimates of associated mortality risk with approximately equal numbers of deaths on a population-basis from both opioids and motor vehicle accidents now reported in both Utah and West Virginia.(501, 502) This suggests that the relative risks are greater due to lower population exposure to opioids. Additionally, there remains a lack of quality long-term studies demonstrating opioid safety and efficacy, as well as a lack of accompanying improvements in the population despite increasing use.(503-505) Use of opioids for chronic non-malignant pain is detailed in the Chronic Pain chapter including guidance on initiation, maintenance, and discontinuation of opioid therapy, criteria to diagnose addiction and problematic use, and adverse effects, along with sample opioid agreements and ADL, IADL, and Screener and Opioid Assessment for Patients with Pain forms.

Opioids have a wide therapeutic range and dosage and timing may need to be titrated. Commonly prescribed drugs in this drug class include codeine, morphine, oxycodone, hydromorphone, oxymorphone, hydrocodone, fentanyl, tramadol, and with many subtypes of extended, controlled, or immediate release formulations.(506) Adverse effects appear prominent, especially during introduction and/or dose adjustment. These include affects on the central nervous system (drowsiness, somnolence, fatigue, tolerance) and the gastrointestinal tract (constipation, nausea, dyspepsia), although there are other CNS and GI effects, as well as effects on the cardiovascular, respiratory, dermatologic, endocrine, and musculoskeletal systems. Tolerance, addiction, and drug-seeking behaviors are common.(507-512) Approximately 80% of patients experience some adverse effects from opioids and approximately 33 to 66% do not finish a clinical trial with opioids due primarily to these adverse effects (the large range in estimates is due to trial design such as whether a wash-out phase was included, length of treatment, and severity of pain).(500, 513)

1. *Recommendation: Opioids for Post-operative and Acute Hip Pain*
   Judicious use of opioids is recommended for treatment of post-operative hip pain or acute severe hip pain.

Indications – Acute, severe post-operative pain or select use for acute, severe non-operative hip pain.

Dose/Frequency – Per manufacturer recommendations; generally the lowest dose to achieve adequate pain relief in the acute pain setting without overly impairing other functions.

Indications for Discontinuation – Resolution of pain, sufficient reduction in pain to allow for management with other medications or methods, adverse effects.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

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2. *Recommendation: Routine Use of Opioids for Acute, Subacute, or Chronic Non-malignant Hip Pain*
   Routine use of opioids for treatment of acute, subacute, or chronic non-malignant pain conditions is not recommended, although selected patients may benefit from judicious use (see below).

   Strength of Evidence – **Not Recommended, Evidence (C)**

3. *Recommendation: Opioids for Subacute or Chronic Hip Pain Patients*
   Opioids are recommended for select patients with subacute or chronic hip pain.

   Indications – Select patients with subacute or chronic persistent pain that is not well-controlled (as manifested by decreased function attributable to their pain) after non-opioid treatment approaches have been tried. Other approaches that should have been first utilized include non-opioid medications (e.g., NSAIDs, acetaminophen), physical restorative approaches, behavioral interventions, self-applied modalities, and functional restoration. Patients with prior psychological disorders, depression, histories of drug abuse/dependence, and/or a personality disorder are more at risk for a poor outcome and should be very cautiously treated with opioids.

   Frequency/Dose – Low dose of a weaker opioid for initial trials with or without NSAID. Patients should have ongoing clinical visits to monitor efficacy, adverse effects, compliance and surreptitious medication use. A trial of an increased dose would be recommended for patients experiencing improvement in functional outcomes during the trial, but with insufficient benefit.

   Indications for Discontinuation – Failure of initial trial to result in objective functional improvement, resolution, improvement to the point of not requiring this intervention, intolerable adverse effects that are not self-limited, non-compliance, diversion, and/or surreptitious medication use.

   Strength of Evidence – **Recommended, Insufficient Evidence (I) for select patients**

Rationale for Recommendations
There are 14 high- and moderate-quality studies evaluating the use of opioids for treating patients with chronic, non-malignant hip pain (see opioids evidence table) as well as many other studies in other non-malignant pain conditions (see Chronic Pain chapter). However, there is a lack of quality evidence of long-term opioid efficacy or adverse effects (see opioids evidence table) and quality evidence of high risks of mortality. Thus, there are no large scale studies with robust data to definitively address some of these important questions.

There are no quality trials evaluating the use of opioids in post-operative or acute severe hip pain patients, although there are trials of anesthetic approaches that appear to reduce the need for post-operative opioids (see Appendix 1). However, post-operative pain is an acute pain indication for which there is relatively little controversy. Patients should be transitioned to treatments with lower adverse effect profiles (e.g., NSAIDs, acetaminophen, exercise) as soon as possible based on the clinical course.

For patients with chronic hip pain, there is quality evidence that diclofenac is equivalent to tramadol and has a lower adverse effect profile.(348) Diclofenac has also been shown to be superior to dextropropoxyphene/ acetaminophen while having few adverse effects including less interference with work.(349) There are no quality studies that suggest that NSAIDs are inferior for treatment of hip pain patients. Comparable results have been found from studies of LBP patients (see Low Back Disorders chapter). Thus, there is quality evidence that other treatments are superior to opioids, that routine use is not indicated, and that other treatments should be tried first.

Nearly all 9 trials of opioids in patients with hip pain that included a placebo for comparison found the opioid modestly superior for pain relief among those who completed the trial, but there were no trials with moderate or marked benefits (see Figure 10).(514-522) While these studies suggest reductions in pain ratings compared with placebo, they do not document improvements in function; rather most suggest high adverse effects (see below). Half of the trials were of 4 weeks duration, with one of 8 weeks,(521) and two of 90 days duration.(517, 518) Thus, although one trial reported an open-label extension phase including data of up to 18 months,(520) there remain no quality long-term safety and efficacy data. The

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one trial with the open-label extension phase printed a graph with an appearance of a modest increase in dose over time, noted that 5 patients had been hospitalized for possible oxycodone related adverse effects, reported most patients (56.6%) discontinued treatment mostly due to adverse effects, and documented that the dose of oxycodone required titration at 10 to 21% of clinic visits after 8 weeks of treatment. These data suggest intermediate term management of patients on opioids is potentially difficult in hip pain patients.

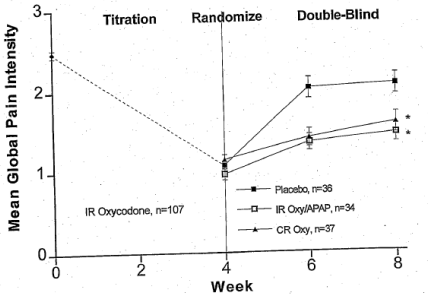
Most of the quality studies were designed for chronic hip pain management, although two trials included a requirement to be treated with an NSAID or COX-2 inhibitor,(518, 521) one evaluated arthritic flares,(514) and one evaluated breakthrough pain.(514, 519) Thus, there is quality evidence of mild efficacy for each of these indications. There is no quality evidence suggesting superiority of short- versus long-duration opioids(523) (see opioid evidence table), although many pain specialists recommend using long-acting or sustained-acting time released opioids to achieve a stable blood level. Pain specialists also recommend that for chronic pain conditions, opioids be used on a regular schedule and not as needed.

Adverse effects from opioids are very high, with estimates of more than 2 adverse effects per patient(524) and other estimates of 20 to 87% of patients with adverse effects (see opioid evidence table). There is a slight trend in the studies for higher adverse effects for more potent opioids and somewhat fewer adverse effects for less potent opioids such as tramadol, although studies are not consistent. Discontinuation rates in the trials ranged widely and also appear to approximately parallel trends in opioid strength.

The decision to treat hip pain with opioids, especially long-term, should be undertaken with care (see Chronic Pain chapter for recommendations on opioid screening, evaluation, and management). Since this decision typically has long-term impacts, if the physician does not have specialized knowledge and/or experience regarding the appropriate use of opioids, it is recommended that a second opinion be obtained from a physician with experience in chronic pain management and/or a psychological evaluation to confirm this decision before the patient is placed on long-term opioids (see Appendix 1, Chronic Pain chapter). Screening patients for prior issues including alcohol and other substance use, depression, psychological and personality disorders, and family history is recommended.(525-530) There is evidence that patients with higher psychological disorder profiles have approximately 3-fold as much placebo analgesia.(531) Opioid agreements and urine screening(532, 533) are also recommended as evidence suggests they are helpful.

Opioids are not invasive, have high adverse effects for a drug including rapid development of tolerance, and are low cost when generic formulations are used (chronic use of brand name medications may be moderate to high cost). **While routine use of opioids for treating patients with chronic hip pain is not recommended, opioids are recommended for select patients in chronic hip pain settings after other treatment options have been exhausted in a manner consistent with the recommendations in this section.**

Figure 9. Mean (SE) Global Pain Intensity in Patients Randomized to Double Blind Treatment with Placebo, Controlled Release (CR) Oxycodone (Oxy), or Immediate Release (IR) Oxycodone-Acetaminophen (APAP)



Pain intensity rated on categorical scale of 0 = none, 1 = slight, 2 = moderate, 3 = severe.

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*Active treatments significantly different from placebo (p≤0.05); not different from one another.

Caldwell JR, Hale ME, Boyd RE, Hague JM, Iwan T, Shi M, Lacouture PG. Treatment of osteoarthritis pain with controlled release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal anti-inflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatology*. 1999;26(4):862-9. Reprinted with permission from the Journal of Rheumatology.

Evidence for Use of Opioids

There are 3 high- and 11 moderate-quality RCTs incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Silverfield 2002 RCT	8.5	N = 308 Hip or knee OA	Tramadol/ acetaminophen (37.5/325mg) vs. placebo 1-2 QID for 10 days	Discontinuation from adverse effects was tramadol/acetaminophen 12.7% vs. 5.4% placebo. Pain intensity scores (baseline/final): Tramadol/ acetaminophen (2.4/1.3) vs. placebo (2.4/1.6), p <0.001. Patients' overall assessments (very good and good): Tramadol (80.0%) vs. placebo (56.4%), p <0.001.	"[A]ddition of tramadol/aceta-minophen to NSAID or COX-2-selective inhibitor therapy was well tolerated and effective in the treatment of OA flare pain."	Short-term trial of 10 days of addition of tramadol for OA flare in addition to NSAID suggests modest efficacy.
Caldwell 1999 RCT	8.0	N = 107 Spine, knee OA	Oxycodone controlled release 10mg q 12 hours vs. oxycodone plus acetaminophen 5/325mg TID vs. placebo. All on NSAID. Open label titration run-in for 30 days then 30 day RCT. Double dummy.	Mean global pain intensity scores increased from open label to DB-RCT [mean (SE)]: placebo +1.0 (0.13) vs. controlled release oxycodone 0.44 (0.13) vs. oxycodone-ASAP 0.49 (0.11), p <0.004 comparing active treatments vs. placebo, NS between active treatments. Overall adverse reactions included 50% somnolence rates in oxycodone group during titration.	"[C]ontrolled release oxycodone q12h and immediate release oxycodone-APAP qid, added to NSAID, were superior to placebo for reducing OA pain and improving quality of sleep. The active treatments provided comparable pain control and sleep quality. Controlled release oxycodone was associated with a lower incidence of some side effects."	Most (60%) taking opioids previously. Dropout rates very high with 35.9% lost during initial open label titration phase; additional 33.6% lost during trial (total 57.5% dropouts). Suggests equivalency of 2 opioids. Modest efficacy vs. placebo, results also only directly applicable to patients previously treated with opioids.
Mullican 2001 RCT	8.0	N = 462 Chronic LBP and/or OA	Tramadol/ acetaminophen 37.5/325mg vs. codeine/ acetaminophen 30/300mg 1-2 Q4-6 hour up to 10 QD for 4 weeks. Double dummy.	Pain scores not different throughout. Total pain relief scores (Day 1/22): Tram/APAP 9.9±6.14/ 11.9±5.83 vs. Cod/APAP 10.1±6.19/11.6±6.24 (NS). Overall efficacy scores 22 days: Tram/ APAP 2.9±1.12 vs. Cod/ APAP 2.8±1.16 (NS). Somnolence (24 vs. 17%), constipation (21 vs. 11%) more common in codeine group. Similar in efficacy for LBP and OA.	"[T]ramadol/APAP tablets (37.5 mg/325 mg) are as effective as codeine/APAP capsules (30 mg/300 mg) in the treatment of chronic nonmalignant low back pain and OA pain and are better tolerated."	No placebo. 79.8% completed study. Comparable efficacy.
Fleischmann 2001	7.5	N = 129 Knee	Titrated doses of tramadol 1-2	Final pain intensity scores: tramadol 2.10±1.06 vs. 2.48±1.13	"Tramadol may be useful as monotherapy in the	High dropout rate (41.3% tramadol vs. 65.2% placebo), limits

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RCT		OA	50mg tablets QID vs. placebo for 91 days; 10-day washout period	placebo, p = 0.082. Patient overall assessment tramadol 0.10±1.41 vs. placebo -0.44±1.3, p = 0.038. Dropout rates were high (41.3% tramadol vs. 65.2% placebo).	treatment of joint pain associated with OA."	strength of conclusions; may limit generalizability. Data statistically negative for main outcome, but positive for others suggesting modest efficacy.
Pavelka 1998 Crossover Trial	7.0	N = 60 Hip or knee OA	Tramadol 50-100mg up to TID vs, diclofenac 25-50mg up to TID for 4 weeks. Doses titrated	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 treatment preference (46.7% tramadol vs. 45.0% diclofenac, p = 0.85). Functionality scores (WOMAC) improved in tramadol group 39.6±16.0 to 32.0±17.4 vs. diclofenac 40.0±17.2 to 30.1±17.0 with 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."	Data suggest tramadol equivalent to diclofenac on average. Study suggests some preferred different medications and results not predictable.
Lloyd 1992 RCT	6.5	N = 86 Severe hip OA	Controlled-release dihydrocodeine 60mg to 120mg BID vs. dextro-propoxyphene/paracetamol 32.5 to 325mg 2 tablets TID-QID for 2 weeks	Average daily pain scores Week 2: dihydrocodeine 39.2±5.3 vs. dextropropoxyphene 39.8±4.6 (NS). Pain on hip ROM better in hydrocodeine group. Adverse effects worse with dihydrocodeine and more dropouts (total dropout rate 33.7%) Overall adverse effects: dihydrocodeine 102AEs/ 43 patients (2.4/patient) vs. dextropropoxyphene (84/43) (2.0/patient).	"[A]fter 2-weeks' treatment CR dihydrocodeine provided superior analgesia to dextropropoxyphene/ paracetamol with no difference in side-effects."	Short-term study. Described as double blind, but different dosing regimens raise questions about blinding success. Data suggest short-term equivalency by most measures, but higher dropouts for dihydrocodeine (43% vs. 21%) and more adverse effects (39.5% vs. 9.3% of dropouts).
Parr 1989 RCT	6.5	N = 846 Mostly hip or knee OA	Diclofenac sodium slow release 100mg QD vs. dextropropoxyphene 180mg plus paracetamol 1.95gm QD for 4 weeks	Pain ratings (change in VAS): diclofenac -27.0 vs. dextropropoxyphene plus paracetamol -22.7, p <0.05 (8% greater reduction with diclofenac). Physical mobility scores: -10.8 vs. -7.4 (p <0.01) (13% better with diclofenac). Work interference less common with diclofenac (3 vs. 11, p <0.05), and time lost (3 vs. 16, p <0.05). Dizziness, lightheadedness less	"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)."	No regular NSAID use in prior 6 months. Dropouts 15.3% diclofenac vs. 17.0%. 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 worktime.

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				common for 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 GI effects not different (63 vs. 60); comparable dropouts.		
Emkey 2004 RCT	6.5	N = 307 Moderate or severe knee or hip OA	Tramadol/ acetaminophen vs. placebo up to 4 tablets a day 10 days, then up to 8 tablets a day for duration as added therapy to celecoxib or rofecoxib for 91 days	Mean VAS scores were (baseline/final) tramadol 69.0±12.5/41.5±26.0 vs. placebo 69.5±13.2/48.3± 26.6. Discontinuations due to lack of efficacy higher in the placebo group (17% vs. 8.5%).	"Tramadol 37.5mg/APAP 325 mg combination tablets were effective and safe as add-on therapy with COX-2 NSAID for treatment of OA pain."	Data suggest modest efficacy of tramadol/ acetaminophen vs. placebo. Overall dropouts 26.1% equal in both groups, but more insufficient pain relief in placebo (66.7% dropouts) and adverse events in active treatment (48.8% dropouts).
Roth 2000 RCT	6.0	N = 133 Moderate to severe spine, knee or other OA	Oxycodone controlled release 10mg Q12 hour vs. 20mg Q 12 hour. vs. placebo for 14 days; 6 month open label extension and optional 12 month extension	Mean pain intensities (baseline/14 days, interpretation of graphic data): oxycodone 10mg (2.5/1.9) vs. oxycodone 20mg (2.5/1.6) vs. placebo (2.4/2.2), p <0.05 compared with placebo.	"Around-the-clock controlled-release oxycodone therapy seemed to be effective and safe for patients with chronic, moderate to severe, osteoarthritis-related pain."	Short term trial. Overall dropouts 47.4% (81.5% of placebo dropouts ineffective, 60.5% oxycodone dropouts with adverse events). Somnolence in 25-27%, dizziness in 20-30%, nausea in 27-41% of active treatment groups. Data suggest modest efficacy. In long-term open-label extension, 10-21% required dose titration at each clinic visit. Dose appeared to trend upwards modestly over 72 weeks.
Schnitzer 1999 RCT	6.0	N = 236 Knee OA	Tramadol 200mg a day vs. placebo over 8 weeks with 5 weeks open label run-in. All treated with Naproxen 500mg BID and those with marked relief excluded	In open-label, tramadol reduced VAS pain scores by 19mm in naproxen non-responders vs. 5mm in responders, p <0.05. Maximum effective naproxen dose for naproxen responders, 221 for tramadol vs. 407 placebo, p = 0.021. For naproxen non-responders, mean effective doses: 419 vs. 396mg, p = 0.71.	"In patients with painful OA of the knee responding to naproxen 1,000mg a day, the additional of tramadol 200mg/day allows a significant reduction in the dosage of naproxen without comprising pain relief."	Overall dropouts in active treatment 19.3%. Main utility of data may be in treatment of patients not responsive to naproxen.
Roth 1998	6.0	N = 63	Tramadol 50mg 1-2 Q	Patient assessments (excellent/very good):	"Tramadol may have a role as adjunctive	20.6% discontinued open-label from

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RCT		OA break-through pain	4-6 hour PRN vs. placebo. Open label run-in for 1 day, then 13 day RCT	tramadol (11/20 = 55%) vs. placebo (5/20 = 25%). Mean resting pain scores at end: tramadol 0.85±0.32 vs. placebo 1.32±0.33, p = 0.46. Cumulative continuation rates 13 days: tramadol 84% vs. 53% (graphic data). Adverse effects in somnolence in tramadol 25% vs. 14%, nausea 35% vs. 14%, vertigo 20% vs. 5%.	treatment for breakthrough pain in patients receiving NSAID therapy for musculoskeletal pain attributed to OA."	adverse effects. Only 36.5% (23/63) of original study population completed RCT. Data suggest limited efficacy for breakthrough pain reduction in OA flares, but dropouts very high.
Kjærsgaard-Andersen 1990 RCT	6.0	N = 158 Hip OA	Codeine plus paracetamol (60mg/1g TID) vs. paracetamol 1g TID for 4 weeks	More use of rescue medication in 1st week paracetamol (21% vs. 5%), Difference disappeared 2nd week (20% vs. 21%). Significantly more adverse reactions with codeine (1st week: nausea n = 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% versus 23.0%.
Peloso 2000 RCT	6.0	N = 66 Hip and/ or knee OA	Control-released codeine vs. placebo. Dose titrated from 100mg/day up to 400mg/day for 4 weeks	WOMAC pain scale 44.8% improved (263.5/145.4) in codeine vs. 12.3% (252.4/ 221.3) controls (p = 0.0004). Rescue medication with acetaminophen averaged 4.2 codeine vs. 9.2 controls. Patient clinical effectiveness CR codeine 2.1±0.9 vs. 0.9±1.0, p = 0.0001.	"Single entity controlled release codeine is an effective treatment for pain due to OA of the hip or knee."	Total 39.2% codeine withdrew vs. 32.7%; 75% codeine withdrawals due to adverse effects; 16.2% of placebo withdrawals due to inadequate pain control.
Caldwell 2002 RCT	5.0	N = 295 Moderat e to severe hip and/ or knee OA	Extended release morphine 30mg QAM vs. ER morphine 30mg QPM vs. morphine controlled release (MS Contin) 15mg BID vs. placebo for 4	Reductions in WOMAC OA index pain by 17% with morphine ER QAM dose vs. 20% QPM vs. 18% MS-controlled release vs. 4% placebo (not different between 3 active treatments). ER morphine had better quality of sleep. Dropouts high at 40% of active treatments, with similar dropout rates	"Controlled release oxycodone q12h and immediate release oxycodone-APAP qid, added to NSAID, were superior to placebo for reducing OA pain and improving quality of sleep. The active treatments provided comparable pain control and sleep	Data suggest modest efficacy. 39.6% (88/222) of active treatment patients dropped out, with 60.2% (53/88) of those due to adverse effects. A subsequent randomized open label trial of 181 of these patients who completed compared QAM and QPM

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			weeks. Double dummy.	across groups, except placebo with more due to lack of efficacy and fewer from adverse effects. Somnolence in 12-16%, dizziness in 10-12% of active treatment patients.	quality." Controlled release oxycodone was associated with a lower incidence of some side effects."	regimens and 52.5% of those patients withdrew with 33.1% experiencing adverse effects.

SKELETAL MUSCLE RELAXANTS

Skeletal muscle relaxants comprise a diverse set of pharmaceuticals designed to produce muscle relaxation through different mechanisms of action generally considered to be effects on the central nervous system (CNS) and not on skeletal muscle.(534, 535) These medications are widely used in primary care to treat painful conditions, most prominently low back pain,(536-542) muscle spasms,(543) and myalgias. They are generally not used for treatment of hip disorders.

1. *Recommendation: Muscle Relaxants for Acute and Subacute Hip Pain with Significant Muscle Spasm*
   Muscle relaxants are recommended for acute and subacute, moderate to severe hip pain from muscle spasm that is unrelieved by NSAIDs, avoidance of exacerbating exposures or other conservative measures.

   Indications – Acute and subacute, moderate to severe hip pain from muscle spasm that is unrelieved by NSAIDs, avoidance of exacerbating exposures or other conservative measures.

   Frequency/Dose – Initial dose in evening (not during workdays or if patient operates a motor vehicle, though daytime use acceptable if minimal CNS-sedating effects). If significant daytime somnolence results, particularly if it interferes with performance of conditioning exercises and other components of the rehabilitation process or treatment plan, discontinue or prescribe a reduced dose. Duration for exacerbations of chronic pain is limited to a couple weeks. Longer term treatment is generally not indicated.

   Indications for Discontinuation – Resolution of pain, non-tolerance, significant sedating effects that carry over into the daytime, other adverse effects.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Muscle Relaxants for Chronic Hip Pain*
   Muscle relaxants are not recommended for chronic hip pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations

There are no quality studies of these agents for treatment of patients with hip pain. Skeletal muscle relaxants have been evaluated in quality studies evaluating chronic back and neck,(544-546) (see Chronic Pain and Low Back Disorders chapters) although there are far more studies on acute low back pain.(547) The quality of the studies comparing these agents to placebo are likely overstated due to the unblinding that would be inherent in taking a drug with substantial CNS-sedating effects. The adverse effect profile is concerning,(548) with CNS sedation rates ranging from approximately 25 to 50% and a low but definite risk of abuse.(549, 550) Thus, prescriptions for skeletal muscle relaxants for daytime use should be carefully weighed against the need to drive vehicles, operate machinery, or otherwise engage in occupations where mistakes in judgment may have serious consequences (e.g., crane operators, air traffic controllers, construction workers, etc.). Skeletal muscle relaxants have beneficial uses, particularly for nocturnal administration to normalize sleep patterns disrupted by skeletal muscle pain, as well as for daytime use among the few patients who do not suffer from the CNS-depressant effects. They are low cost if generic medications are prescribed. Skeletal muscle relaxants are not recommended for continuous management of subacute or chronic hip pain, although they may be reasonable options for select acute pain exacerbations or for a limited trial as a 3rd- or 4th-line agent in more severely affected patients in whom NSAIDs and exercise have failed to control symptoms.

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Evidence for the Use of Skeletal Muscle Relaxants
There are no quality studies evaluating the use of skeletal muscle relaxants for patients with hip and groin pain.

TOPICAL MEDICATIONS AND LIDOCAINE PATCHES
Topical medications include patches, capsaicin and sports creams, NSAIDs, wheatgrass cream, dimethyl sulfoxide (DMSO), N Acetylcysteine (NAC), and Eutectic Mixture of Local Anesthetics (EMLA). Capsaicin is applied to the skin as a cream or ointment and is thought to reduce pain by stimulating other nerve endings (effective through distraction). Rado-Salil ointment is a proprietary formulation of 14 agents, the two most common being menthol (55.1%) and methylsalicylate (26.5%). There are many other commercial products that similarly cause a warm or cool feeling in the skin. All of these agents are thought to work through a counter-irritant mechanism (i.e., feel the dermal sensation rather than the pain). Topical NSAIDs have been used to treat many different MSDs, including arthritis, lateral epicondylitis, and other tendinoses.(551, 552) Many different NSAIDs are compounded, including ibuprofen, naproxen, ketoprofen, piroxicam, and diclofenac.

1. *Recommendation: Capsicum Creams for Acute, Subacute, or Chronic Hip Pain*
   Capsicum is recommended for short-term treatment of acute or subacute hip pain as well as for acute exacerbations of chronic hip pain as a counterirritant.

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

   Frequency/Duration – Duration of use for patients with chronic pain is limited to an acute flare-up period, generally lasting no more than 2 weeks. Not to be used continuously or for more than 1 month as the cost is high compared to alternative treatments of greater or equal efficacy and the patient should be transitioning to an active treatment program. Caution should be exerted to avoid application near the groin.

   Indications for Discontinuation – Resolution of pain, lack of efficacy, development of adverse effects.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Topical NSAIDs, Lidocaine Patches, Eutectic Mixture of Local Anesthetics (EMLA), Other Creams/Ointments for Trochanteric Bursitis*
   There is no recommendation for or against the use of topical NSAIDs, lidocaine patches, eutectic mixture of local anesthetics (EMLA), or other creams/ointments to treat greater trochanteric bursitis pain as it is unclear whether the target tissue is sufficiently superficial to be treated topically.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

3. *Recommendation: Topical NSAIDs, Wheatgrass Cream, Lidocaine Patches, Eutectic Mixture of Local Anesthetics (EMLA), Other Creams/Ointments for Hip Pain Other than Trochanteric Bursitis*
   Topical NSAIDs, wheatgrass cream, lidocaine patches, eutectic mixture of local anesthetics (EMLA), or other creams/ointments are not recommended for hip pain other than trochanteric bursitis as the target tissue is too deep. Counterirritants may be reasonable.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Evidence of efficacy for topical medications and patches is relatively sparse for any disorder and not available for hip pain although there are some quality studies suggesting short- to intermediate-term benefits for some of these agents for more superficial tissues (see Chronic Pain, Elbow Disorders, and Hand, Wrist, and Forearm Disorders chapters). These agents, when demonstrated to have efficacy, appear weakly effective. They might cause deleterious effects if they are used long term. Topical applications of anesthetic agents over large areas are thought to carry significant risk of potentially fatal adverse effects.(553) There are many other commercially available creams and ointments, but no quality studies for the purposes of treating hip pain and the target tissue is very deep to the skin surface

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although greater trochanteric bursitis may be sufficiently superficial to be accessible with these agents. Capsicum is recommended as a counterirritant option for treatment of hip pain based on analogy to treatment of low back pain and other chronic pain conditions.(554, 555)

Evidence for the Use of Topical Medications
There are no quality studies evaluating the use of topical medications, including patches, capsaicin and sports creams, NSAIDs, wheatgrass cream, DMSO, NAC, and EMLA for treatment of hip and groin pain.

TUMOR NECROSIS FACTOR-ALPHA BLOCKERS
A variety of tumor necrosis factor (TNF) alpha blockers, including infliximab (a chimeric monoclonal antibody directed against TNF-alpha), etanercept (a recombinant molecule comprising part of the TNF receptor plus the constant region of human immunoglobulin G1 that binds to TNF-alpha), and adalimumab (an IgG1 monoclonal antibody that binds to TNF-alpha) are in widespread use for rheumatologic and other inflammatory disorders. There may be indications for their use to treatment some patients in the setting of inflammatory rheumatologic disorders. However, this is beyond the scope of this guideline.

1. *Recommendation: Tumor Necrosis Factor-alpha Blockers for Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain, or Other Non-inflammatory Hip Disorders*
   Tumor necrosis factor-alpha blockers are not recommended for treatment of osteoarthrosis or acute, subacute, or chronic hip pain, including other non-inflammatory hip disorders.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
2. *Recommendation: Tumor Necrosis Factor-alpha Blockers for Arthroplasty Patients with Peri-acetabular Osteolysis*
   Tumor necrosis factor-alpha blockers are not recommended for treatment of arthroplasty patients with peri-acetabular osteolysis.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
One quality study evaluated etanercept for treatment of periacetabular osteolysis in arthroplasty patients, but found a lack of efficacy.(556)

Evidence for the Use of Tumor Necrosis Factor-alpha Blockers
There is 1 moderate-quality RCT incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Schwarz 2003 RCT	6.0	N = 20 Arthroplasty patients with periacetabular osteolysis	Etanercept (25mg SQ, twice a week) vs. placebo for 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.

GLUCOSAMINE, CHONDROITIN, AND METHYLSULFONYLMETHANE (MSM)
Glucosamine, chondroitin, and methylsulfonylmethane (MSM) are over-the-counter nutraceuticals, advocated as safe and effective treatment alternatives to NSAIDs for the management of osteoarthrosis. These supplements have also gained additional interest as agents that may potentially modify or slow the progression of osteoarthrosis.

Glucosamine is an amino acid monosaccharide that occurs naturally in the human body and is one of the principle substrates in the biosynthesis of cartilaginous glycosaminoglycans, proteoglycans, and hyaluronic acid.(557) Although the specific cause of osteoarthrosis is unknown, turnover of the cartilage

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matrix is mediated by a multitude of complex autocrine and paracrine anabolic and catabolic factors, leading to loss of articular cartilage, subchondral bone remodeling, and low-level inflammation of the synovial membrane.(558) Glucosamine supplementation is hypothesized to beneficially affect the imbalance between rates of synthesis and degradation of cartilage proteoglycans.(557, 559) Glucosamine reportedly has anti-inflammatory properties.(560, 561) Glucosamine preparations come in two forms – glucosamine sulfate (pill and crystalline powder) or glucosamine hydrochloride – and are often combined with chondroitin sulfate and sometimes with methylsulfonylmethane. Most studies have utilized glucosamine sulfate rather than glucosamine hydrochloride, although there are no quality comparative head-to-head trials. Glucosamine sulfate is also available in suspension for intramuscular and intra-articular injection.(562, 563)

Glucosamine has few adverse effects with safety profiles comparable to placebo in the reviewed trials. However, there are two hypothetical risks that may suggest that select patient groups avoid these supplements. First, there is debate as to whether or not glucosamine, which is an aminoglycan, promotes insulin resistance;(564-566) although no adverse effect has been found in patients who have well-controlled diabetes mellitus or even in persons with glucose intolerance.(567, 568) Second, glucosamine preparations are commonly produced from the shells of shrimp and crabs (chitin), leading to concerns for potential allergic responses in persons with shellfish allergies. In a trial sponsored by the U.S. National Institutes of Health of 15 patients with known systemic allergies to shrimp, administration of glucosamine sulfate was not found to result in any immediate hypersensitivity reactions.(569) Glucosamine products in the U.S. are also commonly synthesized from grains, providing an alternate source for persons concerned with shellfish allergies. Therefore, these hypothetical risks appear to be low. The most common glucosamine dose is 1,500mg per day in single or divided doses.

Chondroitin, a sulfated glycosaminoglycan matrix, provides much of the structural elasticity. Chondroitin is thought to work via anti-inflammatory activity, stimulation of proteoglycans and hyaluronic acid synthesis, and decrease chondrocytic catabolic activity, although the exact mechanisms are unclear.(570) As with glucosamine, there are few reported adverse effects from chondroitin sulfate. This supplement is produced from animal cartilage such as bovine trachea, porcine, and sharks. The most common dose is 1,200mg per day in single or divided dosages. Chondroitin is most commonly combined with glucosamine in commercial preparations, sometimes additionally including MSM.

1. *Recommendation: Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Hip Osteoarthrosis*
   There is no recommendation for or against the use of glucosamine sulfate 1,500mg daily (single or divided dose), chondroitin sulfate, or methylsulfonylmethane for treatment of hip osteoarthrosis.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: Glucosamine Sulfate Intra-Muscular Injections for Hip Osteoarthrosis*
   There is no recommendation for or against the use of glucosamine sulfate intra-muscular injections for the treatment of hip osteoarthrosis.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

3. *Recommendation: Glucosamine Sulfate Intra-articular Injections for Hip Osteoarthrosis*
   There is no recommendation for or against the use of glucosamine sulfate intra-articular injections for the treatment of hip osteoarthrosis.

   Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

4. *Recommendation: Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Osteoarthrosis Prevention*
   There is no recommendation for or against the use of glucosamine sulfate, chondroitin sulfate, or methylsulfonylmethane for prevention of osteoarthrosis.

   Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

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Rationale for Recommendations
There has been some debate over the efficacy of these preparations in reducing pain, improving function, and slowing the progression of the joint space narrowing in osteoarthrosis (see glucosamine evidence table). Four quality studies have followed knee joint spaces with x-rays,(571-574) and one has followed the hip joint.(575) Three studies utilized glucosamine sulfate,(572, 573, 575) while two utilized chondroitin sulfate.(571, 574) Three studies demonstrated preservation of joint spaces compared with placebo, including some suggestions that over 3 years there was no joint space narrowing in the active treatment group.(572-574) The study that was negative was the study of the hip joint,(575) but the data also appeared to trend towards efficacy in both symptoms and x-ray findings. One of the chondroitin sulfate studies(571) found some beneficial x-ray findings, but the joint space was not statistically significant. Thus, while studies that utilized x-rays suggest benefits from treatment of knee osteoarthrosis with either glucosamine sulfate or chondroitin sulfate, quality evidence utilizing x-ray studies of efficacy for treating hip OA is not available.

There are 13 quality studies that included a comparison of glucosamine sulfate with placebo (see glucosamine evidence table). Of the 5 highest quality studies, one(576) was negative but trended toward benefits. There are 4 quality studies that included a comparison of chondroitin sulfate with placebo.(571, 574, 576, 577) The studies on chondroitin are somewhat mixed, as two suggest x-ray benefits as noted above, but symptoms did not improve in 2 studies(574, 576) though one trended toward benefit.(576) One quality study included an assessment of MSM and found it appeared beneficial.(578) Overall, the studies suggest benefits at rates well above chance associations.

Three studies compared these treatments with traditional NSAIDs(577) or acetaminophen.(579) Glucosamine hydrochloride, chondroitin sulfate, or combination thereof, was not superior to celecoxib 200mg per day.(577) However, the combination was successful for treating moderate to severe osteoarthrosis compared with placebo.(577) Two studies found glucosamine sulfate comparable to ibuprofen 1,200mg per day.(580, 581) Acetaminophen was found to be inferior to glucosamine sulfate.(579)

Glucosamine, alone or in combination with chondroitin, appears to provide first- or second-line therapy for patients with osteoarthrosis of the knee. These preparations are not invasive, appear safe and do not result in gastrointestinal erosions or the other common side effects of NSAIDS, are relatively inexpensive, and provide modest relief of knee osteoarthrosis pain, particularly in patients with more advanced pain. These medications may also modify or slow the progression of knee OA as measured by slowing of cartilage destruction and joint narrowing, although the clinical significance of this effect has not be fully identified. There is preferential evidence for the use of the sulfate salt rather than the hydrochloride formulation of glucosamine. There is one quality study involving MSM.(578) There is some evidence that a single daily dose may be more effective than divided doses. Thus, there is quality evidence that glucosamine with or without chondroitin is efficacious for treatment of osteoarthrosis. However, concerns have been raised regarding the use of different glucosamine formulations (hydrochloride versus sulfate), the difference in frequency and dosage strength, and the duration and severity of disease of the study populations.(582) Dose has not been standardized and reportedly ranges widely in available preparations. Therefore, due to lack of uniformity and standardization in preparations, some inconsistency in studies, the fact that most of the studies involved the knee, and that the single study of hip treatment including x-rays was statistically negative,(575) there is no recommendation for or against the use of these preparations for hip OA.

Evidence for the Use of Glucosamine, Chondroitin, and Methylsulfonylmethane
There are 16 high-(254, 557, 562, 571-574, 576-579, 583-587) and 9 moderate-quality(563, 568, 569, 575, 580, 581, 588-590) RCTs incorporated in this analysis. There are 2 low-quality(591, 592) RCTs in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments

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Glucosamine vs. Placebo						
Uebelhart 2004 RCT	10.0	N = 110 Knee OA	Chondroitin sulfate 800mg QD vs. placebo for two 3-month periods during 1 year	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 RCT	9.5	N = 1,583 Knee OA	Oral glucosamine hydrochloride (500mg TID) vs. chondroitin sulfate (400mg TID) vs. both glucosamine and chondroitin sulfate vs. celecoxib 200mg QD vs. placebo in treatment of knee osteoarthritis in 6-month trial	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.
Pavelká 2002 RCT	9.5	N = 202 Knee OA	Oral glucosamine sulfate (1,500mg once daily) vs. placebo for knee osteoarthritis in 3-year trial of disease progression	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 RCT	9.0	N = 318 OA	Oral glucosamine sulfate (1,500mg once daily) vs. acetaminophen (1,000mg TID) vs. placebo using double dummy technique in treatment of knee OA for 6	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%)	"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	Glucosamine appeared superior to acetaminophen as well as placebo.

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			months	than placebo (21.2%) (p = 0.004 and p = 0.047 vs. placebo).	show significant effects on the algofunctional indexes."	
Usha 2004 RCT	9.0	N = 118 OA	Oral glucosamine (Glu) 500mg TID vs. methyl-sulfonylmethane (MSM) 500mg TID vs. both Glu and MSM vs. placebo in osteoarthritis of knee for 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). 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).	"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.
Maziéres 2007 RCT	9.0	N = 307 Knee OA	Chondroitin sulfate 500mg BID vs. placebo for 24 weeks for knee osteoarthritis	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 RCT	8.5	N = 80 Knee OA	Oral glucosamine sulfate (500mg TID) vs. placebo with osteoarthritis of the knee for 6 months	Area under curve (AUC) analysis revealed no significant difference between placebo [mean = 1065.45, SD=398.07] and glucosamine [mean = 1081.28, SD = 577.69]; p = 0.89 in primary outcomes measures. No differences between placebo and glucosamine for treatment response (x^2 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).	"As a symptom modifier in OA patients with a wide range of severities, glucosamine sulfate was no more effective than placebo."	Permitted co-treatment with NSAIDs may have confounded results. Relatively small sample size.
McAlindon 2004 RCT	8.5	N = 205 Knee OA	Oral glucosamine (1,500mg once daily) and placebo in 12 week trial for knee	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,

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			osteoarthritis			resulting in initial use of glucosamine sulfate capsules replaced by glucosamine hydrochloride powder. Study completed through Internet.
Mehta 2007 RCT	8.5	N = 95 OA	Oral glucosamine sulfate (750mg BID) vs. Reparagen (900mg BID) in mild to moderate osteoarthritis of knee for 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) significantly lower in reparagen group ($p < 0.01$).	"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
Messier 2007 RCT	8.5	N = 89 Knee OA	Glucosamine hydrochloride 1,500mg chondroitin sulfate/1,200mg QD vs. placebo for 6 months for knee OA. Both groups received exercise training and instruction.	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 RCT	8.5	N = 252 Knee OA	Oral glucosamine sulfate (500mg TID) vs. placebo for knee osteoarthritis over 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.
Houpt 1999 RCT	8.0	N = 118 Knee OA	Oral flucosamine hydrochloride (500mg TID) vs. placebo for osteoarthritis of the knee for 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.

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Reginster 2001 RCT	8.0	N = 212 Knee OA	Oral glucosamine sulfate (1,500mg QD) vs. placebo for knee OA in 3 year trial of disease progression	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.
Michel 2005 RCT	8.0	N = 300 Knee OA	Oral chondroitin sulfate 800mg QD vs. placebo for 2 years for knee OA	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.
Rozendaal 2008 RCT	7.5	N = 222 Hip OA	Oral glucosamine sulfate (750mg BID vs. placebo for hip osteoarthritis over 2 years	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 RCT	6.5	N = 199 Knee OA	Oral glucosamine sulfate 500mg. TID vs. ibuprofen 400mg TID for 4 weeks treatment of knee osteoarthritis	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.
Rindone 2000 RCT	6.0	N = 98 Knee OA	Oral glucosamine sulfate (500mg TID) vs. placebo for knee OA over	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	"Glucosamine was not better than placebo in reducing pain from osteoarthritis of the knee in this group of	Study details are sparse.

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			2 months	[mean (SD): 4.9 [2.8] glucosamine vs. 4.9 [2.2] placebo, p = 0.90].	patients."	
Scroggie 2003 RCT	6.0	N = 38 Type 2 diabetes mellitus	Glucosamine sulfate 1,500mg/chondroitin sulfate 1,200mg vs. placebo for 90 days in patients with type 2 diabetes mellitus	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 Crossover Trial	5.5	N = 15 Subjects with shrimp allergy and an ImmunoCAP class level of 2 or greater	Glucosamine hydrochloride 1,500mg chondroitin/ 1200mg using shell-fish derived vs. synthetic manufactured glucosamine in patients with confirmed shrimp/shell fish allergies	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 RCT	5.0	N = 40 Uni-lateral knee OA	Glucosamine sulfate (1.5g) vs. ibuprofen (1.2g) daily over 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 continue treatment for a further 6 to 10 weeks or longer with oral glucosamine sulfate."	Comparison is made with OTC strength ibuprofen. Allocation, baseline characteristics and blinding are unclear. There was no control for co-interventions.
Pujalte 1980 RCT	4.0	N = 20 OA	Glucosamine sulfate (500mg TID) vs. placebo for 6-8 weeks for non-specific OA	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	4.0	N = 80 OA	Glucosamine sulfate 500mg TID vs. placebo	Glucosamine sulfate demonstrated decrease in symptoms to a significantly larger extent in significantly shorter time	"The positive effect of hospitalization on the symptoms of	Lack of details. No control for co-interventions.

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RCT			for 30 days for non-specific OA	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.	osteoarthritis may be significantly accelerated, and increased by a factor of almost two, with a simple oral treatment with glucosamine sulfate."	Patients in hospital for unclear reasons. Multiple joint locations included (back, neck, generalized).
Invasive Preparations						
Reichelt 1994 RCT	8.5	N = 155 Knee OA	Intramuscular injection glucosamine sulfate (400mg twice a week) vs. placebo for knee osteoarthritis over 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.
Vajaradul 1981 RCT	5.0	N = 54 Gonarth-rosis	Intra-articular injection of glucosamine sulfate (dose not reported) vs. saline placebo in affected knee	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.
Glucosamine vs. Placebo Discontinuation Trial						
Cibere 2004 RCT	8.5	N = 137 Knee OA	Oral glucosamine sulfate (up to 1,500mg a day) vs. placebo 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.	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.

COMPLEMENTARY OR ALTERNATIVE TREATMENTS OR DIETARY SUPPLEMENTS

Many interventions have been attempted to treat chronic pain conditions, sometimes including patients with hip pain. Some of these interventions might be classified as dietary supplements or as complementary or alternative treatments.(593-596) A few of these include homeopathic treatments, naturopathic treatments, vitamins, herbal remedies (certain exceptions discussed below), spiritual healing, touch for healing, craniosacral therapy, aromatherapy, energy healing, and neural therapy. Most of these interventions do not have any quality evidence of efficacy. Some controversy surrounds the

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issue of the value of placebo effects in healing.(597) As there are many interventions shown to be efficacious for the treatment of acute, subacute, and/or chronic pain, it is strongly recommended that patients be treated with therapies proven to be efficacious, whether the intervention is considered complementary or not.

Recommendation: Complementary or Alternative Treatments or Dietary Supplements for Acute, Subacute, or Chronic Hip Pain

Complementary or alternative treatments or dietary supplements, etc. are not recommended for treatment of acute, subacute, or chronic hip pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

As there is no evidence of efficacy and they have not been shown to produce meaningful benefits or improvements in functional outcomes, complementary and alternative treatments including dietary supplements, etc., are not recommended.

Evidence for the Use of Complementary or Alternative Treatments or Dietary Supplements, etc.

There are no quality studies evaluating the use of complementary or alternative treatments, dietary supplements, etc., for hip and groin pain.

HERBAL AND OTHER PREPARATIONS

There are many treatments that have been attempted to treat chronic hip pain, especially due to osteoarthrosis, including herbal treatments.(598) Some interventions that might be classified as complementary or alternative methods or dietary supplements, etc.,(271, 593) are reviewed above. A few of these interventions include homeopathic, herbal, and naturopathic treatments. Besides the complementary and alternative methods, vitamins or dietary supplements have also been attempted as treatments for chronic pain conditions. Most of these do not have any quality evidence of efficacy,(599) and there is some controversy surrounding the issue of the value of placebo effects on healing.(597)

There are some remedies for which there is evidence with regards to the management of acute low back pain and osteoarthrosis. White willow bark (Salix) extract has been studied in low back pain. A principal ingredient is salicin, with salicylic acid as the principal metabolite. Daily doses of 240mg salicin, approximately equivalent to 50mg of acetylsalicylate (which was sufficiently low as to suggest that this may not be the sole reason for its analgesic effect), have been shown to be more effective than placebo in alleviating pain and improving physical impairment scores in patients with acute low back pain, with gastrointestinal complaints occurring no more frequently than with placebo. Topical copper salicylates have also been used for treatment of arthritis.(600, 601) Extract of *Harpagophytum procumbens* (devil's claw root) has been used in Europe to treat musculoskeletal symptoms with some evidence that it may relieve acute low back pain, acute episodes of chronic low back pain, and osteoarthrosis more effectively than placebo in doses that have consisted of the equivalent of 50 to 100mg of harpagoside daily. Mild gastrointestinal upset has been reported at higher doses. Other treatments include ginger extract,(602-609) rose hips,(610-619) s-adenosylmethionine,(620-628) Camphora molmol, Maleluca alternifolia, Angelica sinensis, Aloe vera, Thymus officinalis, Menthe peperita, Arnica Montana, Curcuma longa, Tancaetum parthenium, avocado soybean unsaponifiables,(629-634) willow bark extract,(635, 636) copper salicylate,(600) and oral enzymes.(637-641)

Figure 10. Knee pain on standing as measured by 100-mm visual analog scale after 2 and 6 weeks in patients with osteoarthritis receiving placebo (n = 123) or ginger extract (n = 124), in the intent-to-treat analysis. Bars show the mean pain rating (in mm) and 95% confidence intervals.

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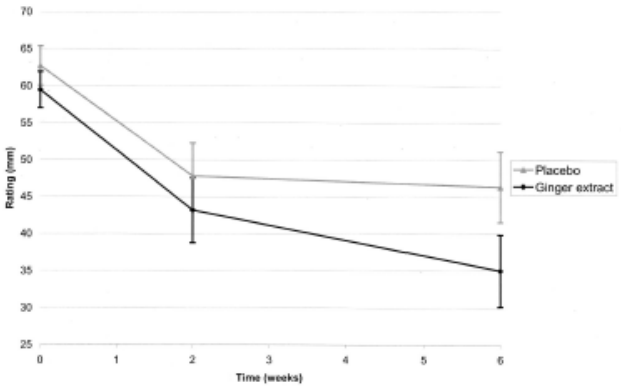

Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum*. 2001;44(11):2531-8. Reprinted with permission from John Wiley and Sons.

Recommendation: 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, and Zingiber Officinicalis, Avocado Soybean Unsaponifiables, Oral Enzymes, Topical Copper Salicylate, S-Adenosylmethionine, and Diacerein Harpagoside for Acute, Subacute, or Chronic Hip Pain

There is no recommendation for or against use of 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, and zingiber officinicalis, avocado soybean unsaponifiables, oral enzymes, topical copper salicylate, S-Adenosylmethionine, and diacerein harpagoside for treatment of acute, subacute, or chronic hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation

Most of these agents have no quality evidence available (e.g., Camphora molmol, Maleluca alternifolia, Angelica sinensis, Aloe vera, Thymus officinalis, Menthe peperita, Arnica Montana, Curcuma longa, Tancaetum parthenium, Harpagoside) for acute, subacute, and chronic hip pain. Some have conflicting results (e.g., willow bark (Salix), rose hips, avocado soybean unsaponifiables, and ginger extract). Still others have no quality studies comparing the active ingredient with placebo (e.g., S-Adenosylmethionine, harpagoside, oral enzymes) and one agent appears ineffective (copper salicylate).

However, none of these agents has had a standardized dose, resulting in a lack of clarity of patient dosing. All of the studies comparing the agent to a standard NSAID dose found the NSAID superior; only those with lower doses of NSAIDs sometimes found evidence suggesting equivalency (see herbal and other preparations evidence table). These agents are not invasive, have unclear adverse effect profiles, and over time are moderate to high cost. Thus, there is no recommendation for or against use of these agents.

Evidence for the Use of Herbal and Other Preparations

There are 9 high- and 10 moderate-quality RCTs or crossover trials incorporated in this analysis. There is 1 low-quality RCT(616) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
S-Adenosylmethionine						
Najm 2004 Crossover Trial	9.0	N = 61 Knee OA	SAMe 600mg BID vs. celecoxib 100mg BID for 8 weeks each. Double dummy.	Celecoxib superior for pain relief in first month (p = 0.024). During 2nd month, no differences in pain. Total COOP score:	"SAMe has a slower onset of action but is as effective as celecoxib in the management of	No placebo comparison. Data suggest SAMe is equally effective, although

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				baseline 48.7±8.7 vs. SAMe 39.9±9.3 vs. celecoxib 39.8±11.3. SF-36 scores did not differ.	symptoms of knee osteoarthritis. Longer studies are needed to evaluate the long-term effectiveness of SAMe and the optimal dose to be used."	celecoxib 100mg BID has faster onset of pain relief.
Glorioso 1985 RCT	7.5	N = 150 Hip or knee OA	SAMe 400mg vs. ibuprofen 400mg TID for 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.
Vetter 1987 RCT	4.5	N = 36 OA knee, hip or spine	S-Adenosylmethionine 400mg TID vs. indomethacin 50mg TID for 4 weeks.	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 RCT	4.0	N = 36 OA of hip, knee or spine	S-Adenosylmethionine 400mg TID vs. ibuprofen 400mg TID for 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.
Willow Bark (Salix)						
Biegert 2004 2 RCTs	9.0	N = 127 Hip or knee OA plus RA (n = 26)	Willow bark extract (240mg salicin a day) vs. diclofenac 100mg a day vs. placebo for 6 weeks. Two RCTs, one for OA and one for RA.	WOMAC pain scores: diclofenac -23±20 vs. willow bark -8±21 vs. placebo -5±23. (NS between willow bark and placebo but $p = 0.003$ between diclofenac and placebo). Other WOMAC subscores and total scores had similar results. Most improvement was achieved after 2 weeks of treatment.	"[N]o evidence of relevant analgesic or antiinflammatory efficacy in willow bark extract for patients with OA and RA."	Two RCTs both suggest diclofenac superior to willow bark extract or placebo for OA or RA. Some baseline differences; 12 % of willow bark group, 40 % diclofenac group and 27% in placebo group received physical therapy, $p = 0.01$).

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Schmid 2001 RCT	8.0	N = 86 Hip or knee OA	Willow bark extract (240mg salicin a day) vs. placebo for 2 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.
Ginger Extract						
Bliddal 2000 Randomized Crossover Trial	7.5	N = 75 Hip or knee OA	Ginger extract 170mg EV.ext-33 TID vs. ibuprofen 400mg TID vs. placebo TID. Double dummy.	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.
Wigler 2003 Crossover Trial	7.0	N = 29 Knee OA	Zintona EC vs. placebo QID for 3 months each treatment	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 RCT	6.5	N = 247 Knee OA	Ginger extract (255mg EV.EXT 77 extracted from 2.5-4.0gm dried ginger rhizomes plus 0.5-1.5gm dried galanga rhizomes) vs. placebo for 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.
Haghighi 2005 RCT	4.0	N = 120 Hip or knee OA	Ginger extract 30mg BID vs. ibuprofen 400mg TID vs. placebo for 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	Methodological issues including blinding not well described. Baseline data demonstrate statistically significant differences in disease severity measures yet appear to represent these

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					comparison."	as "P>0.05." If methodological issues overcome, data suggest comparable efficacy between ginger and OTC ibuprofen and superiority to placebo.
Rose Hips						
Winther 2005 Crossover Trial	9.0	N = 94 Knee or hip OA	Rose-hip powder 5g a day vs. placebo for 3 weeks	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.
Rein 2004 Crossover Trial	8.5	N = 112 OA in hip, knee, hand, shoulder, neck	Rose-hip powder 5g a day vs. placebo for 3 months each treatment arm	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.
Copper Salicylate						
Shackel 1997 RCT	9.5	N = 116 Hip and/ or knee OA	Topical copper-salicylate gel vs. placebo gel 1.5g to the forearm BID for 4 weeks	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.
Oral Enzymes						
Akhtar 2004 RCT	7.5	N = 98 Knee OA	Enteric-coated Phlogenzym® (bromelain 90mg, trypsin 48mg and rutosid 100mg) TID vs. diclofenac 50mg BID. Double dummy.	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.

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Klein 2006 RCT	6.5	N = 90 Hip OA	Enteric-coated Phlogenzym® 2 TID vs. EC diclofenac 50mg BID. Double dummy.	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 RCT	6.0	N = 63 Knee OA	Enteric-coated Phlogenzym® 6 per day vs. Diclofenac 50mg TID for 1 week then BID for 3-week treatment. Double dummy.	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.
Avocado Soybean Unsaponifiable						
Maheu 1998 RCT	9.5	N = 164 Knee or hip OA	Avocado/Soybean Unsaponifiables (ASU) 300mg daily for 6 months vs. placebo for symptomatic efficacy	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.
Lequesne 2002 RCT	9.0	N = 163 Hip OA	Avocado/soybean unsaponifiables (ASU) 300mg daily for 2 years vs. placebo for joint space narrowing	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 differences in regard to symptomatic effects in each of subpopulations, and NSAID use similar in both groups.	"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-hoc analysis in the subpopulation of more severely affected patients, compared with those receiving placebo."	High withdrawal rate over 2-year period (41%), although ITT and per-protocol analyses were similar.
Blotman	9.0	N = 164	Avocado/soybean	Mean cumulative dose of	"Over 6 weeks, ASU	Phase III trial.

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1997 RCT		Primary femoro-tibial or hip OA	unsaponifiables (ASU) 300mg daily for 3 months vs. placebo for symptomatic efficacy	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.	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."	Unclear if this is preliminary report of same study (Maheu).

DIACEREIN (Diacerhein)

Diacerein is an alternative pharmaceutical therapy developed to treat osteoarthrosis which has purported inhibitory action on interleukin-1, metalloproteases, and other inflammatory mediators which are involved in cartilage destruction in *in vivo* and animal models including inflammatory arthropathies.(642-650) It also stimulates prostaglandin E_2 synthesis and does not affect phospholipase A_2, cyclooxygenase (COX), or lipooxygenase, and thus does not affect the gastric mucosa as do NSAIDs.(651) Diacerein has been used as a disease-modifying agent in patients with moderately progressive joint narrowing.(652-655) It is available by prescription in only a few Asian and European countries, and is not currently available in the U.S. The adverse effect profile is generally significantly higher than placebo, most commonly due to higher incidence of diarrhea(643, 656) and darkening of the urine and the magnitude of its effects on pain are small.(644) Diacerein may not be a treatment option for most patients. Optimal dose has been suggested to be 50mg twice daily.(643) It may be an alternative to NSAIDs as a second- or third-line treatment particularly for patients with a history of upper gastrointestinal bleeding as it appears to be potentially associated with lower rates of gastric lesions.(651) However, one quality study suggests NSAIDs are superior to diacerein for relief of pain.(656)

Recommendation: Diacerein for Treatment of Osteoarthrosis

There is no recommendation for or against the use of diacerein for the treatment of osteoarthrosis.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation

Diacerein is not currently available in the U.S. There are a few quality studies of diacerein specific to the knee joint or combining hip and knee osteoarthrosis patients included in this analysis.(643, 657-666) Five high- or moderate-quality studies that compared diacerein against placebo demonstrated modest pain relief from diacerein.(643, 652, 658, 667, 668) A study to establish dose-response showed statistically significant improvement of symptoms with 50, 100, and 150mg daily dose, but with fewer side effects and best efficacy with the 100 mg per day group.(643) There is evidence suggesting the effects of diacerein last weeks to months after cessation of therapy,(656, 658) which is not found among those on an NSAID.(656) In addition to the symptomatic relief qualities reported, there is one moderate quality study that demonstrated a significant difference in joint space narrowing versus placebo.(652) A 2x2 factorial study comparing diacerein, tenoxicam, diacerein with tenoxicam and placebo demonstrated early efficacy of tenoxicam. However, after 4 weeks, the diacerein plus placebo also reached statistically significantly better symptomatic relief than placebo alone.(656) There was no added synergistic effect, such that the diacerein plus tenoxicam group was no better or worse than by themselves.

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Examination of diacerein efficacy in two studies that used diacerein as one of the control arms rather than the main active research arm were not as conclusive in favor of diacerein. A comparison of diacerein to hyaluronic acid intra-articular injections over 1 year did not demonstrate diacerein to be more effective than an oral placebo, but the study had significant methodological weaknesses to make conclusions uncertain, as a possible placebo effect of intra-articular injection may have masked oral diacerein treatment.(669) Two studies comparing diacerein to Harpagophytum procumbens (Devil's Claw Root) demonstrated both to be effective in improving scores over baseline, but there was no placebo group for comparison.(670, 671)

Evidence for the Use of Diacerein

There are 6 high- and 4 moderate-quality RCTs or randomized crossover trials incorporated in this analysis. There are 2 low-quality RCTs(672, 673) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Diacerein vs. Placebo						
Dougados 2001 RCT	9.0	N = 507 Hip OA	Diacerein 50mg twice daily vs. placebo for 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 RCT	9.0	N = 168 Knee OA	50mg diacerein BID vs. placebo for 3 months, followed by 3 month off-treatment period	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 Randomized Crossover Trial	8.5	N = 20 Hip or knee OA	Placebo x 2 weeks, diacerein 25mg BID x 4 weeks x 50mg BID for 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 significantly decreased on diacerein.	"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. Comparisons with no/low dose intervals.
Pelletier 2000 RCT	6.0	N = 484 Knee OA	Placebo BID vs. diacerein 25mg BID vs. diacerein 50mg BID vs. diacerein 75mg BID for 4 months	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	"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.

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				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).		
Kay 1980 Crossover Trial	5.0	N = 12 Hip or knee OA	Diacerein 50mg a day for 4 weeks preceded and followed by 4 weeks of placebo	Data not in aggregate. Overall improvements on Diacerein marked in 3/12 (25%) and slightly improved in 3/12 (25%). Remainder 4/12 (33.3%) unchanged; 2/12 worse.	"Improvement was not apparent for several weeks after starting active treatment and remission lasted for 2 weeks to 3 or more months after the drug was withdrawn."	Sparse details and limited analyses. Appears a crossover trial, however randomization and blinding unclear.
Diacerein vs. NSAID						
Nguyen 1994 RCT	7.5	N = 280 Hip OA	2x2 factorial design: diacerein placebo + tenoxicam placebo vs. tenoxicam 20mg and diacerein placebo vs. diacerein 50mg BID and tenoxicam placebo vs. diacerein 50mg BID and tenoxicam 20mg for 8 weeks	Patient overall assessments rated good or very good: 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.	"Both tenoxicam and diacerein appear to be 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)."	Allocation method unclear. Results 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%).
Diacerein vs. Other Interventions						
Pham 2004 RCT	8.5	N = 301 Medial knee OA	Three courses of 3 intra-articular (IA) injections of 2.5mL hyaluronic acid (HA) +oral placebo vs. IA injections of saline solution + diacerein 50mg BID vs. IA injections of saline solution + oral placebo, 1 year	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.
Diacerein vs. Harpagophytum						
Leblan 2000 RCT	8.5	N = 122 Hip and knee OA	Diacerein 50mg BID vs. harpagophytum (2,610mg a day) for 4 months. Double dummy.	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.
Chantre 2000 RCT	8.0	N = 122 Hip and knee OA	Diacerein 50mg BID vs. Harpadol (6 capsules a day, each containing 435mg	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 =	"The results confirm that the two drugs are equally effective in the treatment of osteoarthritis of the knee or the hip. Improvements in all	No placebo comparison group. Suggests harpagophytum at least comparable

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			of powder Harpagophytum procumbens) for 4 months. Double dummy.	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.	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."	to diacerein, if not superior based on NSAIDs consumed.
Gastric Erosions						
Petrillo 1991 2 RCTs in 1 report	4.5	Study 1: N = 23 with normal or minor endo-scopic findings Study 2: N = 30 with grade 2 or 3 gastric lesions	Study 1: diacetylrhein 50mg BID vs. naproxen 250mg TID for 4 weeks. Study 2: diacetylrhein 50mg BID vs. placebo for 4 weeks.	Study 1: 1/10 (10%) developed gastric lesions on endoscopy vs. 5/10 (50%), p >0.05. Study 2: 11/13 (85%) of diacerein group improved at 4 weeks vs. 9/15 (60%), p >0.05.	"[D]iacetylrhein possesses a good degree of gastric tolerability and may be used in antirheumatic maintenance treatment even when gastric lesions are present."	Some details sparse. Underpowered. Suggests higher gastric erosions in naproxen than diacerein.

REFERRAL TO ALLIED HEALTH PROFESSIONALS AND OTHER PHYSICAL METHODS

Devices

Some patients with hip pain might benefit from limited use of devices, particularly as an assistive aid towards regaining improved or full function. These aids include crutches, walkers, and canes. However, aids might also be detrimental in individuals whose function declines with the aid. In general, devices are recommended when there is either: 1) improvement expected and the device is part of a plan to regain better or normal function; or 2) the device is essential to achieve the maximum function possible within the limits of fixed defects.

CANES AND CRUTCHES

Recommendation: Canes and Crutches for Moderate to Severe Acute, Subacute, or Chronic Hip or Groin Pain

Canes and crutches are recommended for moderate to severe acute hip or groin pain or subacute and chronic hip or groin pain where the device is used to advance the activity level.

Indications – Moderate to severe acute hip or groin pain or subacute or chronic hip or groin pain.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

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). Other than such circumstances, use of assistive devices including wheelchairs, canes, and crutches is not recommended. For chronic hip or groin 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 the Use of Canes and Crutches

There are no quality studies evaluating the use of canes and crutches for hip and groin pain.

MAGNETS AND MAGNETIC STIMULATION

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High-intensity magnetic stimulation purportedly causes depolarization of nerves and has been found to result in an anti-nociceptive effect in rats.(674) As electromagnetic fields have been known to increase osteoblastic activity, proponents believe that magnetic fields have therapeutic value in the treatment of musculoskeletal disorders.

Recommendation: Magnets and Magnetic Stimulation for Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

Magnets and magnetic stimulation is not recommended for treatment of osteoarthrosis or acute, subacute, or chronic hip pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

There is no significant evidence from which to draw conclusions on the utility of magnets as a treatment modality for osteoarthrosis or acute, subacute, or chronic hip pain. However, there is evidence for lack of efficacy in the treatment of low back pain.(675) Magnets are not invasive, have no adverse effects, and are low cost. Other treatments have proven efficacy.

Evidence for the Use of Magnets and Magnetic Stimulation

There are no quality studies evaluating the use of magnets and magnetic stimulation for osteoarthrosis or acute, subacute, or chronic hip pain.

ORTHOTICS, SHOE INSOLES, AND SHOE LIFTS

Orthotics, shoe insoles, and shoe lifts commonly prescribed for low back pain (see Low Back Disorders chapter), and more specifically for individuals who have lower extremities that are substantially different in length, referred to as “leg length discrepancies” – generally defined as more than 2 to 3cm. These discrepancies are theoretically linked to increased risk of LBP, and may be of consequence with hip pain. In theory, shoe lifts may ameliorate this leg length discrepancy and thereby reduce LBP or hip pain.

Recommendation: Orthotics, Shoe Insoles, or Shoe Lifts for Hip Pain

Orthotics, shoe insoles, or shoe lifts are recommended for patients with significant leg length discrepancy with hip pain felt to be a consequence of that discrepancy.

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

Strength of Evidence **– Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

There are no quality studies of these devices for hip pain patients. These devices are not invasive, have few adverse effects, and are low cost. Thus they are recommended for select patients with significant leg length discrepancies felt to be producing or contributing to symptoms.

Evidence for the Use of Orthotics, Shoe Insoles, or Shoe Lifts

There are no quality studies evaluating the use of orthotics, shoe insoles and shoe lifts for hip pain.

Allied Health Therapies

ACUPUNCTURE

Acupuncture has been used to treat many musculoskeletal conditions including spine pain and osteoarthrosis, particularly of the knee (see Chronic Pain and Knee Disorders chapters), with some evidence that patients seek this treatment if they have more severe pain.(676) There is a paucity of quality literature on applications for hip arthritis.(677-679) Multiple techniques have been used, including manual needle stimulation, electrical needle stimulation (electroacupuncture), superficial dry needling, and deep dry needling.(680) Acupuncture administrations may involve moxibustion and cupping. Moxibustion is a traditional Chinese therapy involving burning of an herb (mugwort) to stimulate blood flow and balance “Qi.” Cupping is another ancient Chinese practice involving placement of a cup on the skin with negative pressure induced either through heat or suction and tension is placed on the

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underlying tissue. Besides traditional acupuncture, there are many other types of acupuncture that have arisen, including accessing non-traditional acupuncture points.(681) High-quality evidence has documented that use of traditional acupuncture locations is not necessary to derive equivalent benefits from treatment of low back pain (see Chronic Pain and Low Back Disorders chapters).(682-684)

1. *Recommendation: Acupuncture for Chronic Osteoarthrosis of the Hip*
   Acupuncture is moderately recommended for select use for 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/Duration – A limited course of 6 appointments(685) with 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. There is quality evidence that traditional acupuncture needle placement is unnecessary.(686)

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

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

2. *Recommendation: Acupuncture for Acute or Subacute Hip Pain*
   There is no recommendation for or against the use of acupuncture for acute or subacute hip pain.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations

There are a few quality studies that evaluate acupuncture for treatment of hip osteoarthrosis; more studies address knee osteoarthrosis.(687-700) Some have concluded that evidence suggests there is no effect of acupuncture on pain.(632) One trial evaluated gluteal trigger points;(701) otherwise, there are no other quality studies for other hip conditions. Some trials have combined acupuncture with electrical currents and others have applied electrical currents to acupuncture sites. For treatment of musculoskeletal conditions, there are no quality studies to show clear benefit of electroacupuncture over needling. There continue to be some questions about efficacy of acupuncture,(702, 703) with concerns about biases, e.g., attention and expectation bias in these study designs as well as adequacy of placebo acupuncture treatments.(679, 704)

All four quality studies that included hip osteoarthrosis patients suggest benefits from acupuncture, although the techniques used vary widely.(686, 687, 705, 706) These trials included comparisons with no acupuncture,(687) routine care,(705) and exercise and advice.(685) One trial compared electroacupuncture, hydrotherapy, and education, finding electroacupuncture superior.(706) The fourth quality study found that traditional needle placement is unnecessary,(686) which is similar to the evidence-based conclusion for acupuncture for low back pain (see Low Back Disorders chapter). Studies reporting results after the cessation of acupuncture have nearly all found lasting benefits,(685, 687, 706) although there are no long-term follow-up studies reported. High-quality studies for all of these potential indications with sizable populations and long follow-up periods are needed. Acupuncture when performed by experienced professionals is minimally invasive, has minimal adverse effects, and is moderately costly. Despite significant reservations regarding its true mechanism of action, a limited course of acupuncture may be recommended for treatment of hip osteoarthrosis as an adjunct to a conditioning and weight loss program. Acupuncture is recommended to assist in increasing functional activity levels more rapidly. Primary attention should remain on the conditioning program. Acupuncture is not recommended for those not involved in a conditioning program or who are non-compliant with graded increases in activity levels.

Evidence for the Use of Acupuncture

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There are 5 moderate-quality RCTs incorporated in this analysis. There are 2 low-quality RCTs(685, 707) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Hip Osteoarthrosis						
Witt 2006 RCT	6.0	N = 712 Hip or knee OA	Acupuncture (up to 15 sessions) vs. no acupuncture (delayed treatment for 3 months). Acupuncture individualized.	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.	"[A]cupuncture 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 RCT	6.0	N = 67 Hip OA	Traditional needle placement and manipulation (20 minutes) vs. needles away from classic positions, not manipulated. All needles within L2-L5 dermatomes; 10 treatments 3 weeks.	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)].	"[N]eedle 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 RCT	5.0	N = 45 Hip OA	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) vs. hydrotherapy (warm-up, mobility, strengthening) plus education vs. education alone for 30 minute appointments, 10 times over 5 weeks.	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	"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.

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				group alone.		
Reinhold 2008 RCT	5.0	N = 489 Hip or knee OA	Acupuncture plus routine care (10-15 appointments) vs. routine care for 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.
Gluteal Muscle Trigger Points						
Huguenin 2005 RCT	7.5	N = 60 Male soccer runners	Dry needling of gluteal trigger points (most upper outer buttocks, 3-5 points each, 0.3mm diameter, 25mm long acupuncture needles) vs. placebo needling (blunted needle to 1 minute)	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.

HOT AND COLD THERAPIES

It has been proposed that cold and heat have actual therapeutic benefits to modify the disease processes (e.g., cold to allegedly reduce acute inflammation and swelling and heat to speed healing through increased blood supply).(708, 709) However, it has been proposed that these various modalities are distractants that apparently do not materially alter the clinical course.(710) Still it is postulated that the distractants allow increased activity levels, thus even though distractants might not directly modify the disease processes, this theory supports using these modalities through indirect mechanism(s) of action.(711) Many patients with chronic pain report a temporary soothing effect from the application of heat or the use of ice packs in the home setting.

Cryotherapies

Cold or cryotherapies involve applications of cold or cooling devices to the skin. They have been used for treatment of non-operative pain and post-operative pain.(712)

1. *Recommendation: Home Use of Cryotherapies for Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain*
   Cryotherapies are recommended for home use if efficacious for the temporary relief of osteoarthrosis or acute, subacute, or chronic hip pain.

   Frequency/Duration – Education regarding home cryotherapy application may be part of the treatment if cold is effective in reducing pain.

   Indications for Discontinuation – Non-tolerance, including exacerbation of hip pain.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Cryotherapy for Treatment of Hip Arthroplasty and Surgery Patients*
   Cryotherapy is recommended for treatment of hip arthroplasty and surgery patients.

   Frequency/Duration – Pain relief with cold therapy for the first four post-operative days(712) (see Figure 11). This includes cold-compression.

   Indications for Discontinuation – Non-tolerance, including exacerbation of LBP.

   Strength of Evidence – **Recommended, Evidence (C)**

Rationale for Recommendations

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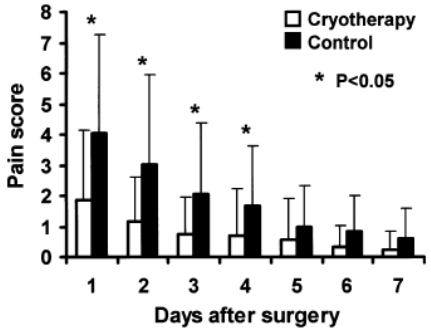
There is one moderate-quality trial that addresses cryotherapies; however, it addressed post-operative arthroplasty patients and suggested benefits with significantly lower pain scores.(712) There are no quality trials that evaluate cryotherapy for treatment of other hip conditions. Among post-operative patients, earlier reductions in pain scores and improved mobility may assist in reducing post-operative complications including DVTs, thus cryotherapies including more expensive cryotherapy delivered by machines which are moderately costly appear justifiable and are recommended for these post-operative patients. For other patients, self applications of cryotherapies using towels or reusable devices are non-invasive, minimal cost, and without complications. While cryotherapy is generally not helpful in patients with osteoarthrosis, a small minority may find benefit, thus, cryotherapy is recommended as a potential distractant or counter-irritant. Other forms of cryotherapy can be considerably more expensive, including chemicals or cryotherapeutic applications in clinical settings and are not recommended.

Figure 11. Comparison of Pain Relief between Cryotherapy and Control Groups after THA. Pain Scores Measured Postoperatively from day 1 to day 4 were Significantly Lower for the Cryotherapy Group than for the Control Group.



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Evidence for the Use of Cryotherapy for Hip Arthroplasty
There is 1 moderate-quality RCT incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Saito 2004 RCT	4.5	N = 46 Cementless THA	Cryotherapy (cold compress) vs. no cryotherapy for 4 days post-op	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.

Heat Therapies

Many forms of heat therapy have been used to treat musculoskeletal pain including hot packs, moist hot packs, sauna, warm baths, infrared, diathermy, and ultrasound. The depth of penetration of some heating agents is minimal since transmission is via conduction or convection, but other modalities have deeper penetration.(713) A particular methodological problem with most studies of heat therapy is that despite occasional attempts at, and claims of, successful blinding, it is impossible to blind the patient from these interventions as they produce noticeable, perceptible tissue warming. Not surprisingly, some of these heat-related modalities have been shown to reduce pain ratings more than placebo for patients with low back pain. It is less clear whether there are meaningful, long-term benefits. Heat therapies are passive treatments. In chronic pain settings, use of heat should be minimized to self-treatments of flare-ups with primary emphasis on functional restoration elements (e.g., exercises).

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Recommendation: Self-application of Heat Therapy for Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

Self-application of low-tech heat therapy is recommended for treatment of osteoarthrosis or acute, subacute, or chronic hip pain.

Indications – 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.

Frequency/Duration – Self-applications may be periodic. Education regarding home heat application should be part of the treatment plan if heat has been effective for reducing pain.

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

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

Self-application of heat-using towels or reusable devices is non-invasive, minimal cost, and without complications. While they are generally not helpful in patients with osteoarthrosis, heat therapy may be helpful in a small minority, and thus is recommended as potential distractant or counter-irritant. Other forms of heat can be considerably more expensive, including chemicals or cryotherapeutic applications in clinical settings and are not recommended.

Evidence for the Use of Heat Therapy

There are no quality studies evaluating heat therapy for osteoarthrosis or acute, subacute, or chronic hip pain.

DIATHERMY, INFRARED THERAPY, AND ULTRASOUND

There are many other commercial modalities to deliver heat; these generally differ on how deeply the heat is felt. None of these modalities have demonstrated major efficacy for any disorder; however, there have been limited uses for treatment of specific disorder with a specific intervention (see Hand, Wrist, and Forearm Disorders; Elbow Disorders; Low Back Disorders; and Chronic Pain chapters).

Recommendation: Diathermy, Infrared Therapy, or Ultrasound for Hip Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

There is no recommendation for or against the use of diathermy, infrared therapy, or ultrasound for treatment of hip osteoarthrosis or for patients with acute, subacute, or chronic hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations

There are no quality studies evaluating the use of diathermy, infrared, or ultrasound for patients with hip pain. Ultrasound and diathermy are reportedly ineffective for treatment of knee arthritis patients.(253, 714) While not invasive and have low complication rates, these modalities are moderate to high cost depending on the number of treatments.

Evidence for the Use of Diathermy, Infrared, or Ultrasound

There are no quality studies evaluating the use of diathermy, infrared, or ultrasound for treatment of hip osteoarthrosis or acute, subacute, or chronic hip pain.

LOW-LEVEL LASER THERAPY

Low-level laser treatment usually involves laser energy that does not induce significant heating. It is theorized that the mechanism of action is through photoactivation of the oxidative chain.(715)

Recommendation: Low-level Laser Therapy for Hip Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

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There is no recommendation for or against the use of low-level laser therapy for treatment of osteoarthrosis or acute, subacute, or chronic hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
The few available studies that have evaluated low-level laser therapy for treatment of osteoarthrosis conflict on the efficacy.(716) There are no quality studies evaluating low-level laser therapy for treatment of osteoarthrosis of the hip, a particularly deep joint. Low-level laser therapy is not invasive, has few adverse effects, but is costly.

Evidence for the Use of Low-Level Laser Therapy
There are no quality studies evaluating the use of low-level laser therapy for hip osteoarthrosis or acute, subacute, or chronic hip pain.

MANIPULATION AND MOBILIZATION
Manipulation and mobilization are two types of manual therapy. Manipulation has been used to treat hip disorders.(717, 718) There is quality evidence of efficacy of manipulation particularly for treatment of acute low back pain (see Low Back Disorders chapter) and neck pain. There is a controlled comparative clinical study suggesting hip arthroplasty patients might ambulate greater distances if manipulated in the early post-operative period.(719)

1. *Recommendation: Manipulation or Mobilization for Acute Hip Pain, Hip Osteoarthrosis, or Surgical or Hip Fracture Patients*
   There is no recommendation for or against the use of manipulation or mobilization for treatment of acute hip pain, hip osteoarthrosis, or for surgical or hip fracture patients.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: Manipulation or Mobilization for Subacute or Chronic Hip Pain*
   The use of manipulation or mobilization is recommended for patients with subacute or chronic hip pain.

   Strength of Evidence – **Recommended, Evidence (C)**

Rationale for Recommendations
There is quality evidence of efficacy for manipulation or mobilization in treating hip osteoarthrosis, acute, subacute, or chronic hip pain patients,(233) but further quality studies are needed. There is one high-quality study of manipulation in hospitalized hip patients that found a lack of efficacy.(720) However, this study did not include treatment to the hip or knee. Manipulation is not invasive, has low adverse effects, but is moderately costly depending on the number of treatments. There is no recommendation for or against use in these patients with the exception of patients with subacute or chronic hip pain.

Evidence for the Use of Manipulation or Mobilization
There is 1 high- and 1 moderate-quality RCT incorporated in this analysis. There is 1 low-quality RCT in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Licciardone 2004 RCT	8.5	N = 60 Hospital-ized knee or hip OA surgery or hip fracture	Osteopathic manipulative treatment protocol (OMT) vs. sham treatment protocol. Manipulation was individualized (myofascial release, strain/counterstrain, muscle energy, soft tissue, high-velocity low amplitude	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

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			mobilization, craniosacral). All received standard care.			limit generalizability. At face value, OMT was not effective.
Hoeksma 2004 RCT	7.5	N = 109 Hip OA	Manual therapy program (stretching, hip joint traction, traction manipulation in each limited position-high velocity thrust, repeated until optimal results) vs. Exercise therapy program.	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."	Use of multiple techniques limits ability to interpret or generalize results.

MASSAGE

Massage is a commonly used treatment for chronic muscular pain administered by multiple health care providers as well as family or friends. It is most typically used for treatment of spine and torso pain (see Chronic Pain and Low Back Disorders chapters).

Recommendation: Massage for Hip Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

There is no recommendation for or against the use of massage for hip osteoarthrosis or acute, subacute, or chronic hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation

Massage is a commonly used treatment for musculoskeletal pain, but few studies evaluated disorders other than LBP.(721-723) While massage is not invasive and has few adverse effects, it is moderate to high cost (when professionally administered) depending on the number of treatments. Other treatments are available with documented efficacy.

Evidence for the Use of Massage

There are no quality studies evaluating the use of massage to treat hip osteoarthrosis or acute, subacute, or chronic hip pain.

REFLEXOLOGY

Reflexology is a complementary or alternative treatment. It entails the physical act of applying pressure to the feet and hands with specific thumb, finger, and hand techniques without the use of oil or lotion. Reflexology is based on a system of zones and reflex areas that reflect an image of the body on the feet and hands with a premise that such work effects a physical change to the body.

Recommendation: Reflexology for Hip Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

Reflexology is not recommended for treatment of hip osteoarthrosis or acute, subacute, or chronic hip pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

There are no quality studies of reflexology for hip pain. It also has not been shown to be efficacious for the treatment of chronic LBP in a moderate-quality study.(724) Other treatments have been shown to be efficacious.

Evidence for the Use of Reflexology

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There are no quality studies evaluating the use of reflexology for hip osteoarthrosis or acute, subacute, or chronic hip pain.

Electrical Therapies

There are multiple forms of electrical therapies used to treat musculoskeletal pain. These include high-voltage galvanic, H-wave stimulation, interferential therapy (IFT or IT), iontophoresis, microcurrent, percutaneous electrical nerve stimulation (PENS), sympathetic electrotherapy, and transcutaneous electrical stimulation (TENS). The mechanism(s) of action, if any, are unclear.

ELECTRICAL STIMULATION THERAPIES

Recommendation: Electrical Stimulation Therapies for Treatment of Hip Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain

There is no recommendation for or against the use of electrical therapies outside of research settings for the treatment of hip osteoarthrosis or acute, subacute, or chronic hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation

There are no quality studies for any of these therapies in occupational populations with hip pain. There is one quality study suggesting efficacy of iontophoresis with sodium salicylate for hip pain in children with sickle cell disease;(725) however, applicability to occupational populations and others is unclear. Some of these electrical therapies are thought to be of greater benefit for certain types of disorders, such as iontophoresis with glucocorticosteroid for trochanteric bursitis and gluteus medius tendinopathy; however, there are no quality studies available. These therapies are mostly non-invasive with low adverse effects, but are moderate to high cost when examined in aggregate. There is no recommendation for or against the use of these therapies. There are other treatments that are effective.

Evidence for the Use of Electrical Therapies

There are no quality studies evaluating the use of electrical therapies for hip osteoarthrosis or acute, subacute, or chronic hip pain.

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

TENS is a modality to control pain through electrical stimulation delivered by pads placed on the surface of the skin for the treatment of many painful conditions, including both non-inflammatory and inflammatory disorders, although it has most typically been used for spine disorders (see Chronic Pain and Low Back Disorders chapters).(726-732)

1. *Recommendation: TENS for Hip Osteoarthrosis or Acute, Subacute, or Chronic Hip Pain*
   There is no recommendation for or against the use of TENS for hip osteoarthrosis or acute, subacute, or chronic hip pain.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: TENS for Emergency Transport of Patients with Hip Fracture*
   TENS is moderately recommended for emergency transport of patients with hip fracture.

   Indication – Hip fracture.

   Duration – During emergency transport.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendations

There are no quality studies of TENS that directly address hip osteoarthrosis or other hip conditions. However, a high-quality study suggests TENS reduces pain during emergency transport,(733) thus there is evidence to suggest TENS might be successful for this limited indication. TENS is not invasive, has low adverse effects, and is moderately costly. There is currently no recommendation for TENS as a treatment for hip disorders.

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Evidence for the Use of TENS
There is 1 high-quality RCT incorporated in this analysis. There is 1 low-quality RCT(734) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Lang 2007 RCT	8.0	N = 72 Hip fractures	TENS vs. sham TENS during emergency transport	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.

INJECTIONS

There are a several types of injections that have been used for patients with hip pain. These include: intraarticular glucocorticosteroid injections, viscosupplementation, prolotherapy and botulinum injections.

INTRAARTICULAR GLUCOCORTICOSTEROID INJECTIONS

Intraarticular glucocorticosteroid injections are sometimes performed to attempt to deliver medication with minimal systemic effects to the hip joint.(735-741) Their usual purpose is to gain sufficient relief to either resume conservative medical management or to delay operative intervention. These injections are generally, although not always, performed under fluoroscopic or ultrasound guidance.

Recommendation: Intraarticular Glucocorticosteroid Injections for Hip Osteoarthrosis
Intraarticular glucocorticosteroid injections are moderately recommended for the treatment of hip osteoarthrosis.

Indications – Hip joint pain from osteoarthrosis sufficient that control with NSAID(s), acetaminophen, weight loss and exercise is unsatisfactory.

Frequency/Dose/Duration – An injection should be scheduled, rather than a series of 3. Medications used in the RCTs were triamcinolone hexacetonide 40mg or triamcinolone acetonide 80mg, or methylprednisolone 40mg or 80mg (see glucocorticosteroid injection table). Anesthetics have most often been bupivacaine or mepivacaine. Multiple doses have been utilized with no head-to-head comparisons in trials; however, a comparative clinical trial found greater efficacy for methylprednisolone 80mg over 40mg.(741)

Indications for Discontinuation – A second glucocorticosteroid injection is not recommended if the first has resulted in significant reduction or resolution of symptoms. If there has not been a response to a first injection, there is less indication for a second. If the interventionalist believes the medication was not well placed and/or if the underlying condition is so severe that one steroid bolus could not be expected to adequately treat the condition, a second injection may be indicated (a second injection is particularly recommended to be performed under ultrasound or fluoroscopic guidance). In patients who respond with a pharmacologically appropriate several weeks of temporary, partial relief of pain, but who then have worsening pain and function and who are not (yet) interested in surgical intervention, a repeat steroid injection is an option. There are not believed to be benefits beyond approximately 3 of these injections in a year. Patients requesting a 4th injection should have reassessment of conservative management measures and be counseled for possible surgical intervention.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation
There are 4 high- or moderate-quality RCTs evaluating efficacy of glucocorticosteroid injections for treatment of hip OA. Both of the highest quality trials had positive results (see Figure12).(735, 736) The lowest quality study did not clearly document efficacy, but also was underpowered with small numbers of subjects per treatment arm.(740) Thus, the quality evidence documents efficacy of these injections. The

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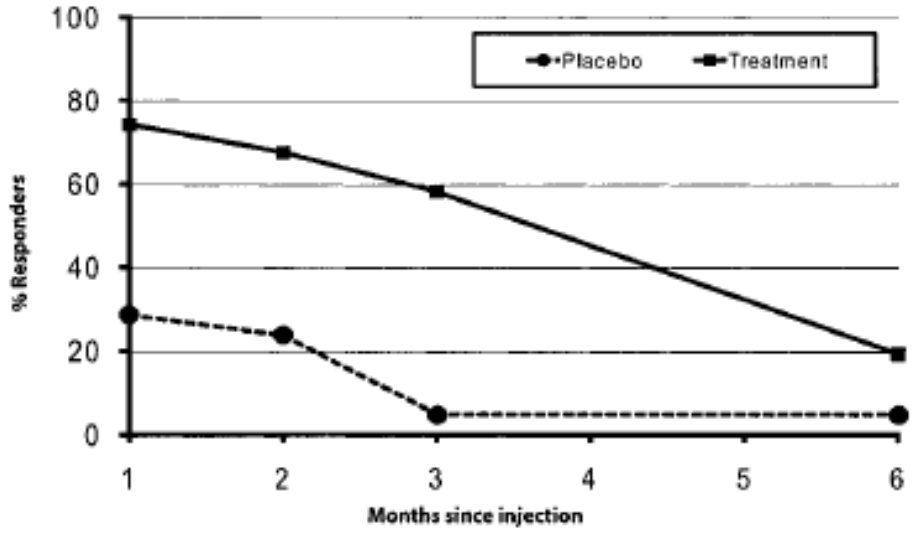
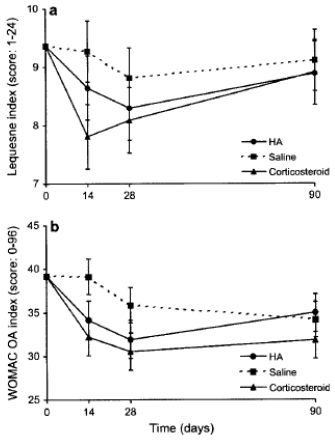
length of benefits is somewhat unclear with approximately 3 months of benefit and no quality evidence of long-term efficacy. There are no head-to-head medication or dose comparisons to identify the optimal combination. A non-randomized study suggested methylprednisolone 80mg was superior to 40mg; however, the results need to be replicated in a quality trial.(741) The primary use of the injections appears to be to improve symptoms and delay, but not prevent, surgical intervention in most patients. There is no quality evidence to support, or require, a series of 3 injections and no quality evidence of a limit to the number of injections. There is some evidence to suggest steroid injections may be superior to hyaluronic acid injections (see Figure 13).(737) Hip injections may require ultrasound or fluoroscopy, as there are no quality trials of blind injections and all quality trials utilized it, although some physicians perform these injections without the use of fluoroscopy or ultrasound.(737, 741) Hip injections are invasive, have a low risk of adverse effects, but are relatively costly. They are an option for treatment of hip patients particularly after inadequate results from NSAID trials, exercise, or other conservative interventions.

Figure 12. Percentage of patients receiving either placebo or intraarticular corticosteroid injection who showed a response from baseline up to 6 months as defined by a 20% decrease in the summed score for the Western Ontario and McMaster Universities Osteoarthritis Index pain subscale



Lambert RGW, Hutchings EJ, Grace MGA, Jhangri GS, Conner-Spady B, Maksymowych WP. Steroid injection for osteoarthritis of the hip. A randomized, double-blind, placebo-controlled trial. *Arth Rheum*. 2007;56(7):2278-87. Reprinted with permission from John Wiley and Sons.

Figure 13. Values of (a) The Lequesne Index and (b) The WOMAC Scores Given as Mean ± SE



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Reprinted from *OsteoArthritis and Cartilage* , 14, Qvistgaard E, Christensen R, Torp-Pedersen S, Bliddal H, Intra-articular treatment of hip osteoarthritis: a randomized trial of hyaluronic acid, corticosteroid, and isotonic saline, 163-170, Copyright (2006), with permission from Elsevier.

Evidence for the Use of Glucocorticosteroid Injections

There are 3 high- and 1 moderate-quality RCT incorporated in this analysis. There is 1 low-quality study in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Intraarticular Injections						
Lambert 2007 RCT	10.0	N = 52 Hip OA	Triamcinolone hexacetonide 40mg plus bupivacaine 10mg vs. bupivacaine. Fluoroscopy used.	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 RCT	9.0	N = 101 Hip OA	Intraarticular Hyaluronic acid 3 2mL injections vs. methylprednisolone 40mg (and 2 placebo injections) vs. saline; 3 injections given at 14 day intervals; ultrasound-guidance	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 RCT	8.5	N = 80 Hip OA	Triamcinolone acetonide 80mg vs. mepivacaine 1% 2mL; fluoroscopy used	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.
Flanagan 1988 RCT	5.0	N = 36 Hip OA awaiting THA	Triamcinolone 20mg vs. bupivacaine 0.5% 10mL vs. saline; fluoroscopy used	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.

VISCOSUPPLEMENTATION INJECTIONS

Viscosupplementation has been performed particularly for knee osteoarthrosis, but hip osteoarthrosis patients have also been studied.(738, 742-745)

Recommendation: Intraarticular Hip Viscosupplementation Injections for Hip Osteoarthrosis

Intraarticular hip viscosupplementation injections are recommended for treatment of hip osteoarthrosis.

Indications – Hip joint pain from osteoarthrosis to the extent that control is unsatisfactory with NSAID(s), acetaminophen, weight loss, and exercise strategies. Patient should generally have failed treatment with

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glucocorticosteroid injection which has been shown in one study to be superior particularly considering difference between 1 injection and 3 injections required for viscosupplementation.(737) Similar to glucocorticosteroid injections, the purpose is to gain sufficient relief to either resume conservative medical management or to delay operative intervention. Injections are recommended to be performed under either ultrasound or fluoroscopic guidance.(742, 743, 746-750)

Dose – There is no apparent difference in outcomes for high versus low molecular weight preparations.(743)

Frequency/Duration – One injection approximately every 7 to 14 days; up to 3 injections.(737, 743)

Indications for Discontinuation – A second (or third) injection is not recommended if there are adverse effects or the clinical results have been a significant reduction or resolution of symptoms.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
There have been suggestions that viscosupplementation of the hip joint may be beneficial for patients with hip osteoarthrosis;(742, 743, 746-751) however, there are no reported trials including a placebo. Most systematic reviews have concluded the evidence is suggestive, but weak.(738, 744, 745, 750) Open-label trials show an approximately 50% response rate and there is some evidence of results lasting 6 months.(743, 746-750) No long-term treatment trials have been reported. There were no differences seen between low- and high-molecular weight hyaluronan visco-supplementation injections.(743) Both resulted in approximately 40% reductions in pain ratings with benefits lasting 6 months. However, a high-quality trial showed glucocorticosteroid injections are superior, thus they should generally be used initially(737) and these injections are recommended although with insufficient evidence.

Injections have mostly been done under ultrasound,(746-748) although they can be done under fluoroscopy.(743) These injections are invasive, have a low risk of adverse effects, but are relatively costly. They are an option for treatment of hip patients particularly after inadequate results from NSAID trials, exercise, or other conservative interventions generally including glucocorticosteroid injection.

Evidence for the Use of Intraarticular Hip Viscosupplementation Injections
There is 1 high- and 2 moderate-quality RCTs(737, 743, 752) incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Glucosaminoglycan Injections						
Qvistgaard 2006 RCT	9.0	N = 101 Hip OA	Intraarticular hyaluronic acid 3 2mL injections vs. methyl-prednisolone 40mg (and 2 placebo injections) vs. saline. 3 injections given at 14 day intervals; ultrasound-guidance	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.

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Gramajo 1989 RCT	7.0	N = 62 Hip or knee OA	Glycosaminoglycan-peptide complex (GPC) ("Rumalon") injections vs. placebo injections. 3 injections a week for 8 week course, 3 courses per year.	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.
Tikiz 2005 RCT	6.0	N = 48 patients with 56 hips Hip OA	Lower molecular weight hyaluronan (LMW HA) (Ostenil) 2mL vs. higher molecular weight viscosupplement (hylan G-F 20, Synvisc) 2ML; 1 intra-articular injection Q week for 3 weeks	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.
Glucosaminoglycan Injections						
Gramajo 1989 RCT	7.0	N = 62 Hip or knee OA	Glycosaminoglycan-peptide complex (GPC) ("Rumalon") injections vs. placebo injections; 3 injections a week for 8 week course, 3 courses per year.	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.

PROLOTHERAPY INJECTIONS

Prolotherapy injections attempt to address a theoretical cause or mechanism for chronic pain. This therapy involves repeated injections of irritating, osmotic, and chemotactic agents (e.g., dextrose, glucose, glycerin, zinc sulphate, phenol, guaiacol, tannic acid, pumice flour, sodium morrhuate) combined with an injectable anesthetic agent to reduce pain, into back structures, especially ligaments, with the theoretical construct that it will strengthen these tissues.

Recommendation: Prolotherapy Injections for Acute, Subacute, or Chronic Hip Pain

Prolotherapy injections are not recommended for treatment of acute, subacute, or chronic hip pain.

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Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
There are no quality studies of prolotherapy injections for treatment of patients with hip pain. The highest quality evidence for treatment of other conditions has shown no benefit of prolotherapy injections.(753) Prolotherapy injections are invasive and have a stated purpose of causing irritation and have reported adverse consequences (see Chronic Pain chapter). These injections are invasive, have adverse effects, and are costly. There are other treatments with documented efficacy available for treatment of these patients.

Evidence for the Use of Prolotherapy Injections
There are no quality studies evaluating the use of prolotherapy injections for hip pain.

BOTULINUM INJECTIONS
Botulinum injections have antinociceptive properties and have been used to produce muscle paresis.(754-757) These injections have primarily been used for non-occupational conditions such as cervical dystonia,(758) strabismus, blepharospasm,(759) and severe primary axillary hyperhidrosis.(759, 760) In the hip region, there are treatments that have been used mainly for children with spasticity due to cerebral palsy.(761-763) These injections are thought to directly treat a taut muscle band and to have analgesic properties.(755-757)

Recommendation: Botulinum Injections for Hip Osteoarthrosis or Other Hip Disorders
There is no recommendation for or against the use of botulinum injections for hip osteoarthrosis or other hip disorders.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
These costly injections have resulted in deaths.(764) There are other treatment strategies with documented efficacy.

Evidence for the Use of Botulinum Injections
There are no quality studies evaluating the use of Botulinum toxin A for treating hip osteoarthrosis or other hip disorders.

PRE-OPERATIVE AUTOLOGOUS BLOOD DONATION
Autologous blood donation has been used to attempt to reduce risks of bloodborne pathogen transmission in the event a blood transfusion is required.(765-775)

Recommendation: Pre-operative Autologous Blood Donation
There is no recommendation for or against the use of pre-operative autologous blood donation.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
There is one moderate-quality trial suggesting autologous blood donation is ineffective in healthy patients undergoing hip arthroplasty.(766) More transfusions are required for those who have donated blood pre-operatively and the costs are higher without measurable benefits. However, there are certain clinical scenarios in which pre-operative autologous blood donation may be beneficial, and the patient's age and health status needs to be considered. Therefore, there is no recommendation for or against the use of pre-operative autologous blood donation.

Evidence for the Use of Pre-operative Autologous Blood Donation
There is 1 moderate-quality RCT incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Billote 2002	7.0	N = 96 Patients	Autologous blood donation (2 units, last donation at	Hemoglobin levels lower on admission (129±13g/ L vs.	"Preoperative autologous donation provided	Results suggest autologous blood donation ineffective

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		scheduled for primary THR	least 2 weeks before surgery) vs. no donation pre-arthroplasty. All treated with FeSO4 325mg BID.	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.	no benefit for nonanemic patients undergoing primary total hip replacement surgery."	as conducted in this trial and costs were $758 higher per patient for this population.

GLUTEUS MEDIUS TENDINOSIS AND TEARS ("ROTATOR CUFF OF THE HIP"), TROCHANTERIC BURSITIS AND GREATER TROCHANTERIC PAIN SYNDROME

Gluteus medius tendinosis or tears, trochanteric bursitis, and greater trochanteric pain syndrome are a constellation of symptoms and signs that have overlap. They parallel shoulder tendinoses and subacromial bursitis, although they have not been shown to have a direct mechanistic parallel between the hip and shoulder. These entities are increasingly recognized as significant causes of hip pain and morbidity.(49, 182, 186, 192, 193, 776-778) However, similar to the shoulder, many cases of bursitis may actually be manifestations of gluteus medius tendinosis.(182) As with the shoulder, it appears that bursitis does not generally occur without some tendinosis also present.(182) The gluteus medius tendon is the structural analog of the supraspinatus tendon; the degenerative pathophysiology is comparable. Thus, the entity has been considered analogous to "rotator cuff" of the hip.(182, 194, 779-781)

Risk factors are not defined. Purported factors associated with tendon ruptures have generally included age, trauma, fractures, diabetes mellitus, obesity, anabolic steroid use, renal failure, hyperparathyroidism, dystrophic calcification, rheumatoid arthritis, systemic lupus erythematosus, and gout.(40, 777) Also comparable with the shoulder, most cases appear to be partial tears and not related to acute specific trauma.(182, 782, 783)

There are no quality studies of diagnostic testing and diagnostic strategies are somewhat unclear.(47, 69, 191) Patients with trochanteric bursitis are usually treated without diagnostic testing. Tests for gluteus medius tears usually involve x-rays and MRI. There are no quality studies of gluteus medius tendinosis, tears or trochanteric bursitis other than for glucocorticosteroid injections.

1. *Recommendation: Glucocorticosteroid Injections for Acute, Subacute, or Chronic Trochanteric Bursitis, Greater Trochanteric Pain Syndrome and Gluteus Medius Tears with Accompanying Clinical Bursitis*

   Trochanteric glucocorticosteroid injections are 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.

   Dose – The two quality studies used either: 1) methylprednisolone 60mg plus 2.5mL 0.5% bupivacaine;(784) or 2) betamethasone plus lidocaine and suggested better outcomes with higher doses.(785) The higher quality study had no placebo control. However, there are multiple glucocorticosteroid medications and no head-to-head comparisons between different medications.

   Frequency/Duration – Each injection should be scheduled separately and the effects of each evaluated before additional injections are scheduled rather than scheduling a series of 3 injections. The most tender location is recommended be targeted(784) and fluoroscopic guidance is not necessary for an initial injection,(784) although it may be a more reasonable option for a second injection if the first injection is unsatisfactory.

   Indications for Discontinuation – Resolution of symptoms, decrease in symptoms to a tolerable level or failure to gain significant benefits.

   Strength of Evidence – **Recommended, Evidence (C)**

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2. *Recommendation: NSAIDs or Acetaminophen for Acute, Subacute, or Chronic Trochanteric Bursitis, Greater Trochanteric Pain Syndrome and Gluteus Medius Tears with Accompanying Clinical Bursitis*
NSAIDs or acetaminophen are recommended for treatment of acute, subacute, or chronic trochanteric bursitis, greater trochanteric pain syndrome and gluteus medius tears with accompanying clinical bursitis (see NSAID frequency, dose discontinuation).

Strength of Evidence **– Recommended, Insufficient Evidence (I)**

3. *Recommendation: Limitations for Greater Trochanteric Bursitis/Greater Trochanteric Pain Syndrome*
Limitations may be helpful in the acute phase of greater trochanteric bursitis/greater trochanteric pain syndrome.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

4. *Recommendation: Progressive Exercise for Acute, Subacute, Chronic Trochanteric Bursitis, Greater Trochanteric Pain Syndrome and Gluteus Medius Tears with Accompanying Clinical Bursitis*
Progressive, eccentric exercise is recommended for gluteus medius tendinosis and tears, particularly to strengthen the lateral hip musculature (see exercise frequency, dose, discontinuation information).

Strength of Evidence **– Recommended, Insufficient Evidence (I)**

5. *Recommendation: Surgical Repair for Gluteus Medius Tears*
Surgical repair is recommended for gluteus medius tears that are non-responsive to medical management.

Strength of Evidence **– Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Trochanteric bursitis has been treated with glucocorticosteroid injections.(784-790) There are only two quality studies of glucocorticosteroid injection for trochanteric bursitis. The high quality study had no placebo control; however, it provided quality evidence that fluoroscopic guidance was not necessary for an initial injection. The moderate-quality trial compared 3 different doses of betamethasone, however, without a placebo control. As the probability of clinical response was higher in the higher dose group,(785) there is some evidence these injections are likely effective compared with placebo and are recommended. These injections are invasive, have a low risk of adverse effects, but are relatively costly. They are an option for treatment of hip patients particularly after inadequate results from NSAID trials, exercise or other conservative interventions.

Evidence for the Use of Glucocorticosteroid Injection for Trochanteric Bursitis
There is 1 high- and 1 moderate-quality RCT incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Trochanteric Bursal Injections						
Cohen 2009 RCT	8.5	N = 65 Greater trochanteric pain syndrome	Fluoroscopic vs. blind glucocorticoid injections with 60mg depomethylprednisolone plus 2.5mL 0.5% bupivacaine into most tender location	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.
Shbeeb	4.0	N = 83	Betamethasone 6mg	Percentages improving	"Corticosteroid and	No placebo control.

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1996 RCT		Trochanteric bursitis	vs. 12mg vs. 24mg all mixed with 4mL 1% lidocaine. Fluoroscopy not used.	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).	lidocaine injection for trochanteric bursitis is an effective therapy with prolonged benefit."	Range of doses used corresponding to dose-response relationship suggests trochanteric bursal injections at least somewhat efficacious.

FEMOROACETABULAR IMPINGEMENT, "HIP IMPINGEMENT," AND LABRAL TEARS

Impingement, a pathophysiological theoretical construct, is thought to involve either abnormalities of the femoral head ("cam impingement") or acetabulum ("pincer impingement"), depending on the appearance of the hip joint.(47) Developmental abnormalities are thought to result in the condition, including a mild slipped capital femoral epiphysis.(166, 791-796) The condition is also believed to develop and cause hip pain in athletes, e.g., hockey players(797) and those involved in kicking activities such as martial arts.(48, 798) The rationale behind an athletic injury to the labrum is thought to involve a slipped capital femoral epiphysis and/or repeated deep flexion, abduction and internal rotation.(166) Slipped capital femoral epiphysis, fractures and osteonecrosis are thought to be causes due to altered anatomical orientation.(47, 791, 792, 795) A second group of patients have this condition after arthroplasty.(166, 799)

Femoroacetabular impingement has been theorized to increase risk for hip osteoarthrosis.(38-48) This theory includes a corollary that early identification could lead to successfully surgically intervention, e.g., clearing hip motion and alleviating femoral abutment.(166, 800, 801) Thus the process of osteoarthrosis delayed or aborted(38, 185) with some estimates of delaying arthroplasty by 20 years.(69) However, there is no quality epidemiological evidence in support of this theory or corollary.(45) More data are being collected to support these theories beginning with large case series.(38)

Labral tears could be considered as distinct entities. Some authors believe these are the most common cause of mechanical hip joint symptoms including popping, catching and locking.(153, 802, 803) Yet, labral tears are present in over 58-90% of middle-aged to older hips studied,(804-806) most often in conjunction with other degenerative phenomenon,(153, 804, 807, 808) including degenerative joint disease and tendinosis/ impingement.(44, 48, 69, 809-811) Most tears are reportedly in the anterosuperior part of the labrum.(158, 181, 805, 812) The pathophysiology of labral tears is controversial, particularly as these appear to be more analogous to a disease where precipitating events are either seemingly minor or absent.(48, 153) Theories for potential causes include age-related degeneration similar to other cartilaginous structures, degenerative articular surfaces, acute trauma, and stereotypical use.(48, 813)

Patients with hip impingement typically present with anterior groin pain exacerbated by hip flexion.(48, 166) Pain usually increases with prolonged sitting, difficulty getting in and out of an automobile or chair, and walking up slopes.(48, 166, 182) An antalgic gait may be present, along with severe trochanteric tenderness, reduced range of motion and weak abduction for acute significant tendon tears.(777) Lateral hip pain with radiation to the thigh may occur, as well as buttock or groin pain.(182, 782, 783) Passive hip range of motion is normal, but internal rotation of a 90º flexed hip is painful and the lateral trochanter is tender.(182, 814) Pain may also be reproduced with figure-four or flexed-abducted externally rotated (FABER) position. The distance between the lateral genicular line and the examination table is usually increased.(166) There may be limitation in internal rotation in the affected hip.(48) Resisted abduction provokes pain as does pain when standing on the affected leg for at least 30 seconds.(182) A minority of patients may be mistakenly diagnosed with "low back pain"(182) as that clinical "diagnostic" categorization has frequently aggregated lumbar, lumbosacral and gluteal pain.

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There are no quality studies comparing diagnostic testing and thus diagnostic strategies are somewhat unclear. Diagnostic tests for chronic hip pain thought to be femoroacetabular impingement or labral tears usually include x-rays and MR arthrography.(183, 196, 815-817)

1. *Recommendation: NSAIDs, Local Glucocorticosteroid Injections and/or Physical or Occupational Therapy for Treatment of "Hip Impingement" or Labral Tears*
   NSAIDs, local glucocorticosteroid injections, and/or physical or occupational therapy are recommended for treatment of "hip impingement" or labral tears(37, 38, 45, 818, 819) (see NSAID frequency, dose discontinuation information, as well as exercise frequencies and information inferred from treatment of osteoarthrosis).

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
A chronic or relapsing course is more common in elderly patients.(182) There are no quality studies that address treatment for femoroacetabular/hip impingement. A trial of conservative therapy has been recommended.(46, 158, 795, 800, 802, 820) Reduction, modification, or elimination of activities that significantly provoke symptoms is also recommended.(45, 46, 48, 795, 800, 818)

2. *Recommendation: Surgical Repair for "Hip Impingement" or Labral Tears*
   Arthroscopic surgery or open repair is recommended for "hip impingement" or labral tear cases that fail conservative management.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
Surgical repairs have been attempted with reportedly successful results in case series.(182, 193, 779, 821) Arthroscopic surgery(69, 151, 156, 158, 160, 166, 802, 809, 818, 822-827) or open repair(800, 801, 809, 828, 829) are recommended for cases that fail conservative management.(45, 818, 830)

There are many different surgical procedures that have been utilized to attempt to address the hip pathology that is thought to be producing symptoms,(800) including debridement(801, 818) and or osteoplasty of the femoral head(800) acetabular osteoplasty,(800) resection or repair of labral tears,(165, 166, 791, 809, 820) labral debridement(795) limbectomy,(162) trochanteric flip osteotomy; peri-acetabular osteotomy,(831) triple osteotomy.(162, 165, 166, 791, 795, 800, 801, 809, 818, 820, 831) Surgical procedures for hip dysplasia have included shelf osteoplasty, femoral varus osteotomy, and acetabular osteotomy.(46, 69, 831, 832) There are no quality studies to address efficacy of either open or arthroscopic repairs, or comparative studies between these approaches.(45) There is controversy regarding which approach is preferred.(45, 46, 800) A case series reported better results from arthroscopy among patients with mechanical symptoms and without osteoarthrosis.(160) Arthroscopy has been used to diagnose and potentially plan subsequent mini or open surgical repair.(46, 48, 833)

OSTEONECROSIS

Osteonecrosis or avascular necrosis is a complex pathological process involving increased bone marrow pressure, ischemia with loss of vascular supply to the bone with subsequent bone death initiated by vascular occlusion (see Table 8 for stages).(174, 834, 835) It tends to occur in areas of the body with more tenuous blood supply, including the heads of the femur, humerus, or other ends of long bones, although it can occur in any bone. As the process advances, the bone collapses. 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.(174) Whether stereotypical, forceful use of the joint as a risk factor is unknown. Other risks appear to include diabetes mellitus, glucocorticosteroid use(124, 836-840) or endogenous excess,(840) arteriovascular disease,(124, 174, 841) hyperlipidemia sickle cell anemia,(838) coagulopathies,(840) Gaucher's disease,(124, 174, 837,

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838) HIV,(839, 842) post-irradiation,(124, 174, 838) alcoholism,(124, 174, 838-841) and smoking.(124, 174, 836-842) Many cases are idiopathic.(174, 843) In the quality RCTs, alcoholism is often the predominant cause.(177, 844)

Table 8. Steinberg Stages of Osteonecrosis

Stage Descriptor	Clinical Features	X-ray Findings	Bone Scan
0	0	Normal	Normal
I	0	Normal	Abnormal
II	+	Sclerosis and/or cyst formation	Abnormal
III	++	Subchondral collapse (crescent sign) without flattening	Abnormal
IV	++	Flattening of femoral head without joint narrowing, or acetabular involvement	Abnormal
V	+++	Flattening of femoral head with joint narrowing and/or acetabular involvement	Abnormal
VI	+++	Advanced degenerative changes	Abnormal

Adapted from Ficat RP. Idiopathic bone necrosis of the femoral head. Early diagnosis and treatment. *J Bone Joint Surg [Br]*. 1985;67(1):3-9 and Steinberg ME. Chapter 5: Management of Avascular Necrosis of the Femoral Head – An Overview. *Instr Course Lect*. 1988;37:41-50.

There appears to be a clinically silent, pre-clinical state that is most frequently identified in the asymptomatic hip.(174, 845) Patients present with either acute or insidious onset of persistent, hip pain that may radiate to the thigh. Pain is often worse at night and may be somewhat worse with activity. Hip range of motion is typically limited. Pain and range of motion worsen as the degree of impairment progresses. The stages are not inexorable, rather there appears to be potential for recovery at any of the early stages.(174)

The focus on early treatment of a mild to moderate case 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. Multiple surgical procedures have been used to treat osteonecrosis including core decompression,(846-849) rotational or simple varus osteotomy,(846, 850, 851) vascularized and devascularized bone grafting,(849, 852) cementation,(853-856) muscle pedicle grafting,(857) trabecular rod implementation, autologous bone marrow transplantation,(858) femoral head resurfacing,(859, 860) hemiarthroplasty and arthroplasties.(843, 846-867) Electrical stimulation is also used, although there are no quality studies of the procedure.(868)

1. *Recommendation: Avoidance of Dysbaric Exposures or Other Symptom-provoking Activities or Other Risk Factors for Treatment of Osteonecrosis*
   Reduction or elimination of activities that significantly provoke osteonecrotic symptoms, including avoidance of dysbaric exposures, or control of diabetes mellitus, elimination or reductions in glucocorticosteroid use, and/or elimination of alcohol and tobacco products is recommended.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Non-weight-bearing Activities for Treatment of Osteonecrosis*
   There is no recommendation for or against the institution of non-weight-bearing activities for patients with osteonecrosis.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

3. *Recommendation: Aggressive Targeting of Coronary Artery Disease Risk Factors for Treatment of Osteonecrosis*

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Aggressive targeting of all coronary artery disease risk factors is recommended for treatment of osteonecrosis.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

4. *Recommendation: Bisphosphonates for Mild to Moderate Cases of Osteonecrosis*
   Bisphosphonates are recommended particularly for mild to moderate cases of osteonecrosis (see dose, frequency, discontinuation information).

   Strength of Evidence – **Recommended, Evidence (C)**

5. *Recommendation: NSAIDs for Treatment of Osteonecrosis*
   NSAIDs are recommended for treatment of osteonecrosis.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

6. *Recommendation: Glucocorticosteroids for Treatment of Osteonecrosis*
   Glucocorticosteroids, including by injection, are not recommended in early disease stages for treatment of osteonecrosis.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

7. *Recommendation: Hyperbaric Oxygen for Treatment of Osteonecrosis*
   There is no recommendation for or against the use of hyperbaric oxygen for treatment of osteonecrosis.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

8. *Recommendation: Core Compression Surgery for Treatment of Osteonecrosis*
   Core compression surgery is recommended for treatment of osteonecrosis.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

9. *Recommendation: Arthroplastic Surgery for Treatment of Osteonecrosis*
   Arthroplasty is strongly recommended for treatment of osteonecrosis with collapse or unresponsive to non-operative treatment.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale for Recommendations

There are few quality studies evaluating treatments for osteonecrosis. There is no quality evidence regarding non-weight-bearing status which is sometimes instituted for months(844, 865, 869) and thus, there is no recommendation for or against its use. Control of diabetes mellitus, elimination or reductions in glucocorticosteroid use, and elimination of alcohol and tobacco products are all recommended at the time the diagnosis is considered. As there is evidence statins reduce risk,(836) the composite data suggest aggressive targeting of all coronary artery disease risk factors is needed and recommended.

Bisphosphonates have been evaluated in one quality study. Results suggest large differences between bisphosphonates and no treatment with an approximately 60% difference in need for surgery over 28 months (see Figure 14),(870, 871) thus bisphosphonates are recommended particularly for mild to moderate cases. Other treatments have included nonsteroidal anti-inflammatory medications which are recommended (see NSAIDs for dose, frequency, discontinuation information). Glucocorticosteroids including by injection are not recommended in early disease stages as there is evidence that systemic glucocorticoid exposures increase risk for the disorder, but there may be indications in selected patients with more advanced disease. Hyperbaric oxygen has been used to treat osteonecrosis of the jaw,(872) but a study following osteonecrosis of the hips of children from chemotherapeutics found no improvements with hyperbaric oxygen; thus, there is no recommendation for or against its use. Careful observation of patients for results of treatment with a bisphosphonate is necessary and threshold for prompt surgical intervention is low, particularly among those with failure of bisphosphonate, contraindications, intolerance, progression or development of collapse.

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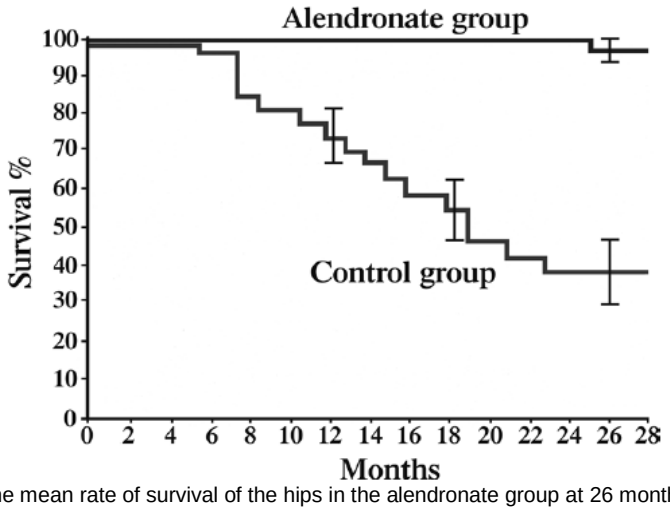
Core decompression with or without bone grafts is the surgical procedure that has been most utilized to attempt to treat osteonecrosis.(174, 847, 873-876) However, the two moderate-quality studies that are applicable to adult populations(177, 876) conflict(847) (see Figures 15 and 16). The primary purpose of the procedure is to relieve the elevated intramedullary pressure that stagnates the microvascular circulation.(174) In a case series, results were good in 94% of Stage I and 82% in Stage II. However, a case series cannot prove superior results with earlier treatment as results may mislead through spectrum and other biases. Though the two quality studies of a coring procedure conflict, core decompression is recommended.

Once the head of the femur collapses, the treatment has often included arthroplasty, although early case series reported high revision rates of up to 37% that have more recently declined to approximately 2 to 9%(855, 877-887) with improvements initially attributed to cementation techniques with subsequent reductions in revisions attributed to cementless techniques.(843) A few of the quality studies regarding arthroplasty were performed for osteonecrosis, although none solely included those patients.(855, 888, 889) The prognosis appears to be reasonably good in more recent studies of these patients and arthroplasty is strongly recommended.

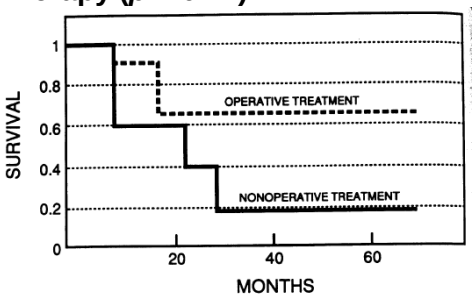
Figure 14. The Kaplan-Meier survivorship curves, with total hip replacement as the end point, show the survival rate of hips with Steinberg stage-II and stage-III osteonecrosis in the alendronate group and the control group versus observation time.



The mean rate of survival of the hips in the alendronate group at 26 months was 93.3% (95% confidence interval, 86.9% to 99.7%). The mean rate of survival of the hips in the control group at 12, 18, and 26 months was 72% (95% confidence interval, 63% to 81%), 51.8% (95% confidence interval, 42.2% to 61.4%), and 35.8% (95% confidence interval, 25.8% to 45.8%), respectively. At 24 months, 29 hips (20 patients) in the study group and nine hips (seven patients) in the control group had survived. Of the five hips (four patients) in the alendronate group that were observed for 28 months, four hips (three patients) had survived. Of the four hips in the control group that were observed for 28 months, two hips had survived.

Lai K-A, Shen W-J, Yang C-Y, Shao C-J, Hsu J-T, Lin R-M. The use of alendronate to prevent early collapse of the femoral head in patients with nontraumatic osteonecrosis. A randomized clinical study. *J Bone Joint Surg Am.* 2005;87:2155-9. Reprinted with permission from the Journal of Bone and Joint Surgery American.

Figure 15. Survival Estimates for Hips with Stage I ON: Core Decompression versus Conservative Therapy (*p* = 0.14)



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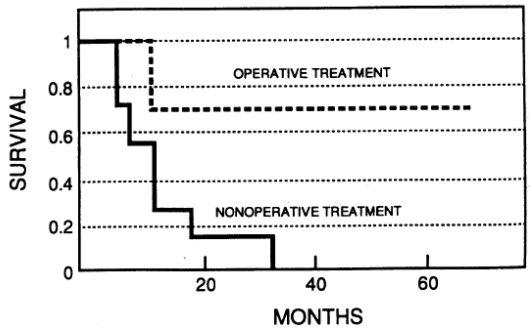
Median survival: operative > 27 months; nonoperative = 11 months.

Stulberg BN, Davis AW, Bauer TW, Levine M, Easley K. Osteonecrosis of the femoral head. A prospective randomized treatment protocol. *Clin Orthop Related Res*. 1991;268:140-51. Reprinted with permission from Lippincott Williams & Wilkins.

Figure 16. Survival Estimates for Hips with Stage II ON: Core Decompression versus Conservative Therapy (*p* = 0.048)



Median survival: operative > 46 months; non-operative = six months.

Stulberg BN, Davis AW, Bauer TW, Levine M, Easley K. Osteonecrosis of the femoral head. A prospective randomized treatment protocol. *Clin Orthop Related Res*. 1991;268:140-51. Reprinted with permission from Lippincott Williams & Wilkins.

Evidence for Hip Osteonecrosis

There are 6 moderate-quality RCTs or randomized crossover trials(177, 870, 876, 890-892) incorporated in this analysis. There are 2 low-quality RCTs(844, 893) in Appendix 2. See also evidence table of studies of arthroplasties.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Coring Procedures						
Stulberg 1991 RCT	4.5	N = 36 patients with 55 affected hips Mainly Stages I, II or III osteonecrosis (2 with stage IV)	Coring procedure (partial weight bearing) vs. conservative treatment (nonweight bearing for 6 plus weeks)	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 [8(100%)/1(10%)].	"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.
Koo 1995 RCT	4.5	N = 33 with 37 hips Most Stage I osteonecrosis	Core decompression (partial weight bearing) vs. conservative treatment (nonweight bearing with crutches until pain resolved and analgesics)	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.

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Neumayr 2006 RCT	4.5	N = 46 patients with 46 hips Stages I, II, or III osteo-necrosis; all sickle cell anemia	Core decompression plus physical therapy vs physical therapy alone (limited weight bearing, stretching, adductor and other muscle strengthening).	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 three years after treatment."	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 sickle cell anemia to working populations or others unclear.
Arthroplasty						
Kim J Bone Joint Surg Am 2005;87(8): 1769-76 Randomized Crossover Trial	6.5	N = 52 All osteonecrosis; all bilateral arthroplasties	Zirconia femoral head vs. cobalt-chromium head.	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 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.	"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. the 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 (despite advice to avoid high impact).
Seyler 2006 RCT	4.0	N = 210 OA or osteonecrosis	Stratified enrollments for OA and osteonecrosis. Compared alumina-on-alumina vs. cobalt-chromium-on-polyethylene surfaces.	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-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.	"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.
Bisphosphonates for Osteonecrosis						
Lai 2005	5.0	N = 40 with 54 hips	Alendronate 70mg Q week	Progression 1+ stage alendronate 4/29	"Alendronate appeared to	Not placebo controlled. Results suggest

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RCT		Stage II or III nontraumatic osteonecrosis	vs. no treatment for 25 weeks.	(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.	prevent early collapse of the femoral head in the hips with Steinberg stage-II or IIIC nontraumatic osteonecrosis."	treatment prevents collapse of femoral head.

HAMSTRING and HIP FLEXOR STRAINS

Hamstring and hip flexor strains are thought to be true muscular strains (i.e., disrupted myotendinous junctions).(87, 894-896) These problems are usually precipitated by a high force maneuver, including sports injuries in sprinting, football, or soccer,(897-899) with near maximum voluntary contraction capabilities. Prior injury is likely the greatest predictor of future risk. Patients have pain exacerbated by use, stiffness and weakness. The examination findings are tenderness usually at either the muscle origin or insertion (e.g., high versus low hamstring strains) with swelling or large ecchymoses in more severe cases. Some cases involve complete ruptures and require surgical repair. Clinical tests are generally not necessary, although in the more severe cases, evaluation with x-rays and/or MRI are used to evaluate the underlying bony structure as well as the degree of muscle tear as severe, rare cases may require surgery. Treatments may include NSAIDs, heat or cold, ace wraps, work limitations, physical or occupational therapy, and progressive agility, trunk stabilization and icing (PATS).

1. *Recommendation: X-rays or MRI to Diagnose Hamstring or Hip Flexor Strains*
   X-rays or MRI are recommended to diagnose hamstring or hip flexor strains in more severe cases.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: NSAIDS for Treatment of Hamstring or Hip Flexor Strains*
   NSAIDS are recommended for treatment of hamstring or hip flexor strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: Work Limitations for Treatment of Hamstring or Hip Flexor Strains*
   Work limitations are recommended for patients with hamstring or hip flexor strains who perform high-physical jobs or cannot avoid job tasks thought to have resulted in the strain. There is no recommendation for or against work limitations for treatment of most hamstring or hip flexor strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I) – High-physical demands**

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I) – Most cases**

4. *Recommendation: Ice or Heat or Wraps for Treatment of Hamstring or Hip Flexor Strains*
   Ice or heat or ace wraps are recommended for treatment of hamstring or hip flexor strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

5. *Recommendation: Bed Rest for Treatment of Hamstring or Hip Flexor Strains*
   Bed rest is not recommended for treatment of hamstring or hip flexor strains.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

6. *Recommendation: Physical or Occupational Therapy for Treatment of Hamstring or Hip Flexor Strains*
   Physical or occupational therapy is recommended for treatment of hamstring or hip flexor strains.

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Strength of Evidence – **Recommended, Insufficient Evidence (I)**

7. *Recommendation: Progressive Agility, Trunk Stabilization and Icing (PATS) for Treatment of Hamstring or Hip Flexor Strains*
   Progressive agility, trunk stabilization, and icing (PATS) are recommended for treatment of hamstring or hip flexor strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
There is one quality study of treatment options for hamstring or hip flexor strains; however, it only addresses exercise; thus nearly all treatment recommendations are empiric.(87, 894) Nonsteroidal anti-inflammatory medications are recommended (see NSAIDs for dose, frequency, discontinuation information). Work limitations may be necessary depending on the severity of the condition and the required job demands. Those performing high-physical demand tasks or who have no ability to avoid repeating physically demanding job tasks thought to have resulted in the condition are recommended to have work limitations, but in other cases, there is no recommendation for or against these limitations. Ice and/or heat are recommended as are ace wraps. Bed rest is not recommended due to concern regarding deep venous thrombosis and other adverse effects, although relative rest may be required for many patients. Patients with persisting pain are recommended to have a course of physical or occupational therapy, although compliance long term is a noted problem.(87) Quality evidence suggests stretching and isolated progressive resistance training are not successful compared with progressive agility, trunk stabilization, and icing (PATS),(900) thus PATS is recommended (see exercise for dose, frequency, and discontinuation information).

Evidence for the Use of PATS for Hamstring Strains
There is 1 moderate-quality RCT incorporated in this analysis. There are 2 low-quality RCTs(87, 901) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
STST vs. PATS						
Sherry 2004 RCT	5.0	N = 24 Athletes with acute hamstring strains	STST (static stretching, isolated progressive hamstring resistance exercise, icing) vs. PATS (progressive agility, trunk stabilization and icing)	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.

GROIN STRAINS AND ADDUCTOR-RELATED GROIN PAIN

Groin strains are generally thought to be true strains with disrupted myotendinous junction(s) that involve the adductor muscles in the upper thigh.(87, 894) The problem is precipitated by a high-force maneuver, including sports injuries, that is usually near maximum voluntary contraction capabilities. As with other true strains, prior injury is thought to be predictive of future risk. Patients have pain exacerbated by use, stiffness, and weakness. The examination findings are tenderness at the muscular origin, and there may be swelling in more severe cases. Clinical tests are generally not necessary, although in the more severe

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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.

1. *Recommendation: X-rays or MRI to Diagnose Groin Strains or Adductor-related Groin Pain*
   X-rays or MRI are recommended to diagnose groin strains or adductor-related groin pain in more severe cases.

   Strength of Evidence **– Recommended, Insufficient Evidence (I)**

2. *Recommendation: NSAIDS for Treatment of Groin Strains or Adductor-related Groin Pain*
   NSAIDS are recommended for treatment of groin strains or adductor-related groin pain.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: Work Limitations for Treatment of Groin Strains or Adductor-related Groin Pain*
   Work limitations are recommended for patients with groin strains or adductor-related groin pain who perform high-physical jobs or cannot avoid job tasks thought to have resulted in the strain. There is no recommendation for or against work limitations for treatment of groin strains or adductor-related groin pain in most cases.

   Strength of Evidence – **Recommended, Insufficient Evidence (I) – High-physical demands**

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I) – Most cases**

4. *Recommendation: Ice or Heat or Wraps for Treatment of Groin Strains or Adductor-related Groin Pain*
   Ice or heat or ace wraps are recommended for treatment of groin strains or adductor-related groin pain.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

5. *Recommendation: Bed Rest for Treatment of Groin Strains or Adductor-related Groin Pain*
   Bed rest is not recommended for treatment of groin strains or adductor-related groin pain.

   Strength of Evidence **– Not Recommended, Insufficient Evidence (I)**

6. *Recommendation: Physical or Occupational Therapy for Treatment of Groin Strains or Adductor-related Groin Pain*
   Physical or occupational therapy is recommended for treatment of groin strains or adductor-related groin pain.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations

X-rays aide avulsion fracture diagnosis and MRI aide sprain, strain, and tear diagnoses. There are two quality studies of treatment options for groin strains or adductor-related groin pain; however, they only address exercise, thus nearly all treatment recommendations are empiric.(87, 894) Nonsteroidal anti-inflammatory medications are recommended (see NSAIDs for dose, frequency, and discontinuation information). Work limitations may be necessary depending on the severity of the condition and the required job demands. Those performing high-physical demand tasks or who have no ability to avoid repeating physically demanding job tasks thought to have resulted in the condition are recommended to have work limitations, but in other cases, there is no recommendation for or against work limitations. Ice and/or heat are recommended as are Ace wraps which may be helpful. Bed rest is not recommended due to concern regarding deep venous thrombosis and other adverse effects, although relative rest may be required for many patients. Patients with persisting pain are recommended to have a course of physical or occupational therapy, likely to include gentle stretching, but suggested to primarily focus on progressive strengthening exercises and include an aerobic exercise prescription(87, 894) (see exercise dose, frequency, discontinuation information).

Evidence for the Use of Physical or Occupational Therapy for Groin Strains

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There is 1 moderate-quality RCT incorporated in this analysis. There is 1 low-quality RCT in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Physical Therapy						
Holmich 1999 RCT	7.0	N = 8 Male athletes with long-standing groin pain (median 40 weeks)	Active training program (12 exercises) with physical therapy (laser, friction massage, stretching TENS) vs. no active training for 8 to 12 weeks	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 future, randomised, clinical trials."	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.

MERALGIA PARESTHETICA

Meralgia paresthetica is a peripheral entrapment neuropathy of the lateral femoral cutaneous nerve that is a sensory nerve supplying the upper lateral aspects of the thigh. While a nerve entrapment may occur at any point along the nerve, the condition is most commonly from a localized pressure in the area of the inguinal ligament, generally in obese, middle aged adults in whom the obesity is presumed to produce the pressure on the nerve either directly or through tight clothing. The disorder has also occurred among athletes including gymnasts. Onset may be relatively acute, e.g., after one night's sleep or insidious. A tight, heavy tool belt may produce an occupational cause. Other causes include trauma, scarring from prior trauma, 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.

1. *Recommendation: Weight Loss/Avoidance of Aggravating Exposures/Loose Clothing for Treatment of Meralgia Paresthetica*
   Weight loss for patients who are overweight or obese, avoidance of aggravating exposures, and the wearing of loose clothing is recommended for treatment of meralgia paresthetica.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: NSAIDS for Treatment of Meralgia Paresthetica*
   There is no recommendation for or against the use of NSAIDS to treat meralgia paresthetica.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

3. *Recommendation: Topical Lidocaine Patches for Treatment of Meralgia Paresthetica*
   There is no recommendation for or against the use of topical lidocaine patches to treat meralgia paresthetica.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

4. *Recommendation: Glucocorticosteroid Injections for Treatment of Meralgia Paresthetica*
   Glucocorticosteroid injections are recommended for treatment of meralgia paresthetica if more conservative treatments are not efficacious.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

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5. *Recommendation: Nerve Conduction Study to Confirm Diagnosis of Meralgia Paresthetica and Localize Entrapment*
   A nerve conduction study is recommended to confirm the diagnosis of meralgia paresthetica and localize the entrapment.

   Indications – Question regarding accuracy of diagnosis or in patients for whom surgery is contemplated.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

6. *Recommendation: Surgical Release for Treatment of Meralgia Paresthetica*
   Surgical release is 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.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

7. *Recommendation: Spinal Cord Stimulator for Treatment of Meralgia Paresthetica*
   There is no recommendation for or against the use of spinal cord stimulators 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.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations
There are no quality studies to evaluate, diagnose, or treat the condition, thus treatments are empiric. The diagnosis is usually made on clinical grounds and imaging is generally not indicated. Weight loss is recommended for those who are overweight or obese. Patients should also avoid aggravating exposures and wear loose clothing. As this is a peripheral neuropathy and NSAIDs appear ineffective for other entrapment neuropathies in quality studies such as for treatment of carpal tunnel syndrome, there is no recommendation for or against the use of NSAIDs for meralgia paresthetica. Topical lidocaine patches have been used;(902) however, for most patients, the pain is insufficient to warrant treatment; there is no recommendation for or against the use of these patches. Glucocorticosteroid injections have been tried and are recommended if the above more conservative treatments do not resolve the condition (see local diagnostic injection for dose, frequency, and discontinuation information).

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.(903) Particularly among persistent cases, consideration may be given to therapy referral for evaluation of potential movement system impairments that may be contributory. 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. A spinal cord stimulator has been implanted in one case with reported good short- to intermediate-term results;(904) however, the intervention is highly invasive compared with a peripheral entrapment neuropathy; there are no quality studies of efficacy. Therefore, there is no recommendation for or against the use of spinal cord stimulators.

LOWER ABDOMINAL STRAINS

Lower abdominal strains are frequent occurrences in sports and occupational populations particular that involve heavy lifting.(87) The pathophysiological abnormality is unclear. Pain onset is usually acute and in the context of a heavy lift or sports-related forceful exertion. Pain occurs most typically in the lower abdominal muscles often along the inguinal canal, however, there is no hernia. Whether abdominal strain is either a risk or a precursor to an indirect inguinal hernia is also unknown. Some have thought the disorder represented urine reflux into the vas deferens during heavy lifting or strain (see epididymo-

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orchitis below). There are no quality studies to evaluate, diagnose or treat the condition, thus treatments are empiric. Patients should be evaluated for hernias and referred for consideration of surgical repair if found.(30)

1. *Recommendation: Culturing Urine to Diagnose Lower Abdominal Strains*
   There is no recommendation for or against culturing urine to diagnose lower abdominal strain unless other symptoms are present.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: NSAIDS for Treatment of Lower Abdominal Strains*
   NSAIDs are recommended for treatment of lower abdominal strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: Work Limitations for Treatment of Lower Abdominal Strains*
   Work limitations are recommended for patients with lower abdominal strains who perform high-physical jobs or cannot avoid job tasks thought to have resulted in the strain. There is no recommendation for or against work limitations for treatment of lower abdominal strains in most cases.

   Strength of Evidence – **Recommended, Insufficient Evidence (I) – High-physical demands**

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I) – Most cases**

4. *Recommendation: Bed Rest for Treatment of Lower Abdominal Strains*
   Bed rest is not recommended for treatment of lower abdominal strains.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

5. *Recommendation: Ice or Heat for Treatment of Lower Abdominal Strains*
   Ice or heat is recommended for treatment of lower abdominal strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

6. *Recommendation: Physical or Occupational Therapy for Treatment of Lower Abdominal Strains*
   Physical or occupational therapy is recommended for treatment of lower abdominal strains.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
Unless other symptoms are present, there is no recommendation for or against culturing of urine (evaluation and treatment of epididymo-orchitis follows). Nonsteroidal anti-inflammatory medications are recommended (see NSAIDs for dose, frequency, and discontinuation information). Work limitations may be necessary depending on the severity of the condition. Those performing high physical demand tasks or those who have no ability to avoid repeating physically demanding job tasks thought to have resulted in the condition are recommended to have work limitations, but in other cases, there is no recommendation for or against the use of work limitations. Other treatments have included ice, heat, bed rest and physical or occupational therapy. Bed rest is not recommended due to concern regarding deep venous thrombosis and other adverse effects. Ice and heat are recommended. Those with persisting pain are recommended to have a course of physical or occupational therapy, likely to include gentle stretching, but suggested to primarily focus on progressive strengthening exercises and include an aerobic exercise prescription (see exercise for dose, frequency, and discontinuation information).

EPIDIDYMO-ORCHITIS

Epididymitis is an acute or chronic inflammation of the epididymis – the coiled tube that collects sperm from the testicle and passes it to the vas deferens. Orchitis is an inflammation of the testicle. Epididymo-orchitis is an inflammation of both the epididymis and testicle. The vast majority of cases of epididymitis

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or combined epididymito-orchitis are infectious in origin.(7-10, 12-18) Those patients under age 35-45 reportedly have Chlamydia trachomatis infections in more than 80% of cases.(8, 19) Older patients tend to have gram-negative rod infections(7, 16) as do those who have had vasectomies, other urological procedures, a history of prostatitis, or have engaged in anal intercourse.(8, 20, 21) A few cases have been attributed to amiodarone.(22, 23)

There is a small but not insignificant minority of patients who report a history of a heavy lift or strain that precipitated the symptoms,(24-27) which gives rise to the possibility that this entity may sometimes be an occupational disease or injury(28-32) outside of the obvious setting of direct work-related trauma.(33) Mechanisms have thought to involve either reflux of urine in the course of the strain(27, 29, 34-36) or eliciting symptoms from a latent infection.(24) One industrial plant survey showed no difference in the frequency of epididymitis between wage and salary workers.(20) A case report noted a history of epididymal pain after lifting heavy lumber which was evaluated with a largely negative workup until on aspiration of the epididymis, Chlamydia trachomatis was isolated.(7) There is no quality study that has documented negative infectious disease work-ups in these patients, thus there is no definitive method to solve this question of work-relatedness.

Patients should be evaluated for testicular torsion, tumor and genitourinary infections.(30) Those with evidence suggesting any of these other conditions should be referred to a primary health care provider or urologist. Criteria have been published for potentially occupational cases:

1. Recent history of lifting within 48 hours
2. No fever
3. Negative urinalysis
4. Vague pain in the lower abdomen
5. Tenderness of epididymis to palpation(28)

1. *Recommendation: Culturing Urine to Diagnose Epididymitis or Epididymito-orchitis*
   Urine cultures are recommended for select patients to diagnose epididymitis or epididymito-orchitis.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

2. *Recommendation: Needle Aspiration for Treatment of Epididymito-orchitis*
   There is no recommendation for or against the use of needle aspiration to treat epididymito-orchitis.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

3. *Recommendation: NSAIDS or Age-appropriate Antibiotics for Treatment of Epididymitis or Epididymo-orchitis*
   NSAIDS or age-appropriate antibiotics are recommended for treatment of epididymitis or epididymo-orchitis.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

4. *Recommendation: Work Limitations for Treatment of Epididymitis or Epididymo-orchitis*
   There is no recommendation for or against the use of work limitations for patients with epididymitis or epididymo-orchitis, although limitations may be necessary depending on the severity of the condition and the physical job demands.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

5. *Recommendation: Bed Rest for Treatment of Epididymitis or Epididymo-orchitis*
   Bed rest is not recommended for treatment of epididymitis or epididymo-orchitis.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

6. *Recommendation: Ice or Intermittent Elevation for Treatment of Epididymitis or Epididymo-orchitis*

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There is no recommendation for or against the use of ice or intermittent elevation for treatment of epididymitis or epididymo-orchitis.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

7. *Recommendation: Physical or Occupational Therapy for Treatment of Epididymitis or Epididymo-orchitis*
   Physical or occupational therapy is recommended for treatment of epididymitis or epididymo-orchitis.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
There are no quality trials that address treatments for epididymitis or epididymo-orchitis. For this subset of patients, urine cultures are recommended, but there is no recommendation for or against the use of needle aspiration. Empiric treatment with age-appropriate and other risk factor appropriate antibiotics (e.g., Chlamydial coverage under 35 years, gram negative over 35 years) is recommended,(24, 28) as is treatment with NSAIDs (see NSAIDs for dose, frequency, and discontinuation information). Work limitations may be necessary depending on the severity of the condition and the physical job demands, but have not been uniformly required, thus there is no recommendation for or against the use of work limitations.(24) Other treatments have included ice, intermittent elevation, and bed rest.(28) Bed rest is not recommended due to concern regarding deep venous thrombosis and other adverse effects. There are no quality studies that address ice or intermittent elevation to treat epididymitis or epididymo-orchitis; therefore, there is no recommendation for or against their use. Patients with a clinical course that does not resolve rapidly should be evaluated by a urologist.

SURGICAL CONSIDERATIONS

HIP FRACTURES

Hip fractures are the most severe fracture among the elderly.(905-910) Approximately 25% of these patients are deceased 6 months after hip fracture,(911-914) although risk varies widely largely depending on age and pre-morbid conditions. These fractures also occur in working populations, usually as a result of a high-impact injury such as a fall from a height, crush injury, or motor vehicle accident. Approximately half of hip fractures are intracapsular femoral neck fractures;(915) the rest are trochanteric, intertrochanteric, or subtrochanteric for which internal fixation is traditionally recommended.(916) Intracapsular fractures include femoral neck, subcapital and intracapsular fractures. Traction has been used for treatment,(911, 917-919) as have surgical approaches which have included internal fixation, external fixation, and hemiarthroplasty.(920, 921) Various appliances have been utilized for fixation including screws,(911, 922) nails,(923) hook-pins,(924) sliding plates,(912, 922, 925) intramedullary devices (Curtin), external fixation,(926) and percutaneous compression plates.(927, 928) Hip fractures are the third most common reason for arthroplasty.(929-931) The cause of these fractures and work-relatedness is determined based on the mechanism of the fracture.

1. *Recommendation: Surgical Treatment for Hip Fractures*
   Surgical treatment for hip fractures is recommended compared with traction for hip fractures.

   Strength of Evidence – **Recommended, Evidence (C)**

2. *Recommendation: Surgical Treatment for Hip Fractures*
   Surgical intervention for hip fractures is recommended as soon as the patient is medically stable.

   Strength of Evidence **– Recommended, Insufficient Evidence (I)**

3. *Recommendation: Arthroplasty for Hip Fractures*
   Arthroplasty is strongly recommended for older patients with displaced femoral neck and subcapital fractures.

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Strength of Evidence – **Strongly Recommended, Evidence (A)**

4. *Recommendation: Acupressure for Transporting Hip Fracture Patients*

Acupressure is moderately recommended for transporting patients with hip fracture to the hospital.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

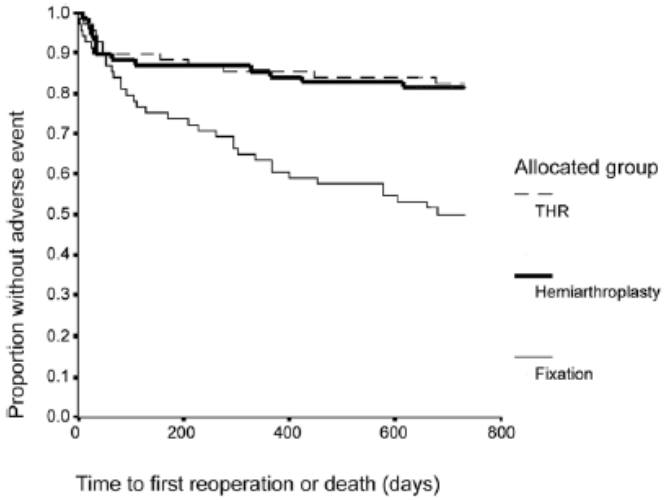
Rationale for Recommendations

There are reports, including quality studies, of fractures healing conservatively with traction,(911, 917-919) yet death rates are also reportedly higher for that method of treatment.(918) A Cochrane review concluded that quality trials comparing conservative and surgical treatment for hip fractures are needed.(932) However, as one quality study found longer hospital stays and deaths particularly in the elderly,(911) the current quality evidence suggests that surgical results are superior to traction for treatment of these fractures, thus surgery is recommended particularly in the elderly.

The speed with which treatment is considered early or delayed is somewhat controversial with estimates of 6 to 12 hours.(834, 835, 933-935) There are no quality studies, but a retrospective review of cases and a large case series suggest better outcomes for earlier intervention(935) or shorter hospitalizations and fewer complications.(936) Generally, early intervention is recommended once the patient is medically stable. Skin sterilization issues have been studied and are important considerations.(937-941)

There are several quality studies evaluating arthroplasty and hemiarthroplasty results compared with internal fixation for treatment of displaced fractures. Three evaluated displaced intracapsular fractures,(916, 942, 943) one evaluated unstable intertrochanteric fractures,(944) two were of displaced femoral neck fractures,(945, 946) and another two were of displaced subcapital fractures(947, 948) (see Figure 17(942)). Nearly all of these studies suggest arthroplasty or hemiarthroplasty result in superior outcomes including lower complication rates, lower reoperation rates, lower pain ratings, and/or superior ambulatory function at 6 to 24 months (see Figure 18). One of the studies concerned younger patients with displaced intracapsular fractures and found total hip arthroplasty resulted in better outcomes.(943) In contrast, a Cochrane review of arthroplasty for hip fractures concluded there was insufficient evidence of superiority of arthroplasty to internal fixation.(949) Regardless, the quality evidence is in favor of arthroplasty or hemiarthroplasty for treatment of displaced femoral neck, displaced intracapsular and displaced subcapital fractures in the older patient is strongly recommended (see arthroplasties) as a preferred treatment option. In the young patient, it is desirable to save the femoral head, so internal fixation should be strongly considered.

Figure 17. Time to the First Reoperation or Death in the Three Groups



THR = total hip replacement

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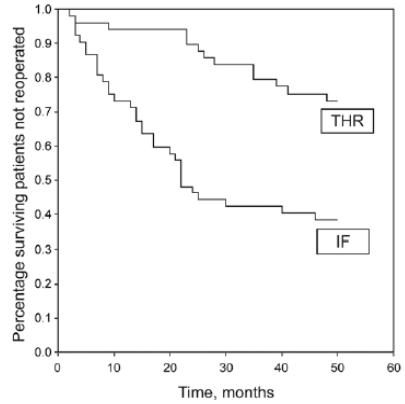
Keating JF, Grant A, Masson M, Scott NW, Forbes JF on behalf of the Scottish Orthopaedic Trials Network. Randomized comparison of reduction and fixation, bipolar hemiarthroplasty, and total hip arthroplasty. Treatment of displaced intracapsular hip fractures in healthy older patients. *J Bone Joint Surg Am*. 2006;88:249-60. Reprinted with permission from the Journal of Bone and Joint Surgery American.

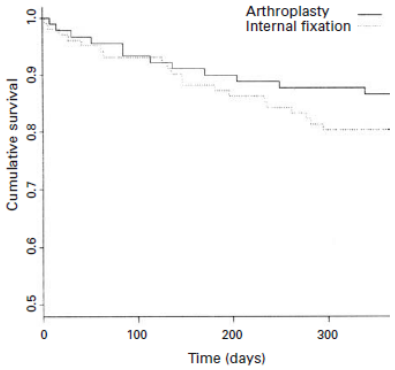
Figure 18. Percentage of Patients who were Still Alive and Had Not Undergone a Reoperation (among all 102 patients who had been included in the study) in Relation to Time



THR = total hip replacement, and IF=internal fixation.

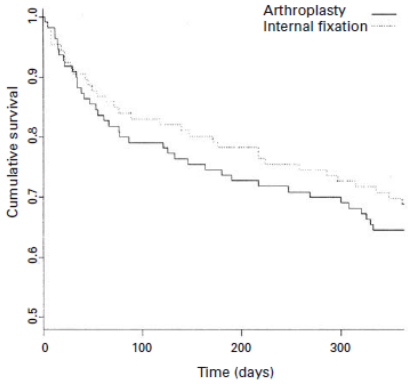
Blomfeldt R, Törnkvist H, Ponzer S, Söderqvist A, Tidermark J. Comparison of internal fixation with total hip replacement for displaced femoral neck fractures. Randomized, controlled trial performed at four years. *J Bone Joint Surg Am*. 2005;87:1680-8. Reprinted with permission from the Journal of Bone and Joint Surgery American.

Figure 19. Survival Curve for Patients aged 70 to 79 years in Both Groups



Reproduced with permission and Copyright© of the British Editorial Society of Bone and Joint Surgery. Parker MJ, Khan RJ, Crawford J, Pryor GA. Hemiarthroplasty versus internal fixation for displaced intracapsular hip fractures in the elderly. A randomised trial of 455 patients. *J Bone Joint Surg Br*. 2002;84(8):1150-5.

Figure 20. Survival Curve for Patients aged from 80 to 89 years in Both Groups



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There are many different surgical approaches and products used for fixation. There also are numerous biomechanical studies on these various approaches;(950-955) however, while yielding sometimes useful information, they are unable to definitively test efficacy or superiority in humans. Pins are sometimes hydroxyapatite-coated,(956) although quality evidence of efficacy or superiority of these products in these patients is lacking.

Fixation failures have been thought to be particularly due to either inadequate reduction or suboptimal fixation.(910, 957, 958) In the elderly, additional factors influencing adverse outcomes include comorbid medical conditions and ability to bear weight.(910, 959-961) These reports suggest technical issues as well as post-operative management are necessary to achieve optimal outcomes.

Two authors have published multiple Cochrane reviews.(962-964) One of these reviews concluded the sliding hip screw was superior to nails for extracapsular hip fractures, but that there is insufficient evidence to ascertain meaningful differences between different intramedullary nails.(963) A sliding hip screw was also thought to be superior to fixed nail plates for extracapsular hip fractures.(964) The sliding hip screw is thought to have a lower complication rate than intramedullary nails for treatment of trochanteric fractures.(962) Another literature review concluded there was a preference for surgical fixation among intertrochanteric hip fracture patients if the patient was medically stable. Stable fractures were felt to be better treated with plate and screw implants and intramedullary devices. Unstable fractures were thought to be better treated with load-sharing intramedullary implants; however, the literature was not felt to have demonstrated this belief.(959)

There are two studies using minimally invasive techniques, but no clear conclusions in favor of these approaches.(965, 966) Osteonecrosis and nonunion rates are high in post-hip fracture patients, and with inadequacy of reduction reportedly a significant factor,(910) successful reduction becomes an important consideration. External fixation devices have been studied in one quality study and suggested external fixation was superior for operative time, blood loss and pain for treatment of pertrochanteric fractures.(956) This study needs replication.

There are many quality RCTs evaluating various products, particularly including dynamic hip screws, dynamic condylar screws, compression hip screws, intramedullary hip screws, gamma nails, gliding nails, proximal femoral nails, Pugh nails, percutaneous compression plates, nail plates, and Medoff sliding plates (see hip fracture evidence table). A majority of the studies failed to find one approach superior to another(912, 913, 922, 927, 967-972) and some provide conflicting results. Additionally, the variability of the types of fractures provides additional uncertainty regarding optimal intervention(s). Thus, there is no recommendation for or against the use of a specific product.

There is quality evidence that acupressure reduced pain for hip fracture patients during transportation (see Figure 21).(973) It is not invasive, has essentially no adverse effects, is low cost and is recommended.

Figure 21. Visual Analog Scale Values for Pain. True Intervention Differs from Sham Intervention Significantly (p<0.001)

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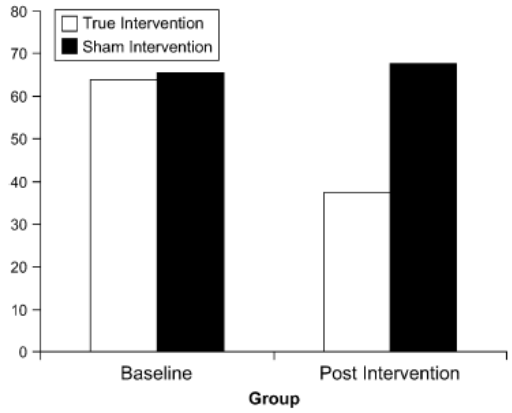

Barker R, Kober A, Hoerauf K, Latzke D, Adel S, Kain ZN, Wang S-M. Out-of-hospital auricular acupressure in elder patients with hip fracture: a randomized double-blinded trial. *Acad Emerg Med*. 2006;13(1):19-23. Reprinted with permission from John Wiley and Sons.

Evidence for Hip Fractures

There are 4 high(305, 916, 973, 974)- and 64 moderate-quality(911-914, 917, 922, 927, 942-948, 956, 965-972, 975-1015) RCTs incorporated in this analysis. There are 21 low-quality(919, 1016-1035) RCTs in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Wound Drainage Systems						
Varley 1995 RCT	6.0	N = 177 Patients undergoing AO dynamic hip screw or hemiarthro-plasty	Closed suction surgical wound drainage for 48 hours (1 deep to fascia lata alongside implant, 1 superficial to fascia lata) vs. no wound drainage	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.
Medications						
Huusko Calcif Tissue Int 2002 RCT	8.5	N = 260 Acute hip fracture	Intranasal salmon calcitonin 200 IU daily vs. placebo nasal spray for 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 -	"Intranasal calcitonin might be useful for hip fracture patients but the clinical significance of this finding needs to be confirmed by studies with more participants, alonger treatment period, a longer follow-up, and perhaps a higher dose of calcitonin."	Data trend towards suggesting weak efficacy.

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				0.001) in the calcitonin group and -0.007 (95% CI -0.012 to -0.003) in the placebo group (P = 0.28)."		
Wilkinson 2001 RCT	5.0	N = 47 THA	Single-dose infusion of 90mg of pamidronate vs. placebo	Pamidronate reduced bone loss vs. placebo for both the proximal femur and the pelvis (p = 0.001 and p = 0.01, respectively). Pamidronate associated with suppression of all biochemical markers of bone turnover compared with placebo (p <0.05), with the exception of urinary free deoxypyridinoline.	"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."	Data support reduction in bone loss and less bone turnover. However, no differences in clinical outcomes.
Surgical Approach including Minimally Invasive						
Starr 2006 RCT	6.5	N = 34 Subtro-chanteric, intertro-chanteric or ipsilateral femoral neck/shaft fracture from high energy injury	Russell-Taylor Recon Nail (piriformis fossa starting point) vs. Howmedica Long Gamma Nail (trochanteric starting point)	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: recon nail: 12 vs. long gamma nail 12, p = 1.0.	"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.
Alobaid 2004 RCT	6.0	N = 48 Intertro-chanteric fractures	Minimally invasive vs. conventional surgical technique for placing dynamic hip screw (DHS)	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.
Surgery vs. Traction						
Hornby 1989 RCT	6.0	N = 106 Trochanteri c fractures	AO dynamic hip screw vs. traction	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.
Hip Screw/Nail vs. Other Approaches						
Hoffman 1996 RCT	7.5	N = 67 Intertro-chanteric	Gamma nail vs. Ambi hip screw	Blood loss 42% greater in Gamma nail group (p = 0.006). Mobility ranked worse in Gamma nail	"Gamma nail is not recommended for routine use by inexperienced orthopaedics due to	No advantage of either technique at 6 months.

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		fractures		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.	findings of longer intensifier screening times, greater blood loss, increased numbers of technical complications and perhaps a poorer rehabilitation."	
Adams 2001 RCT	7.0	N = 400 Intertro-chanteric fractures	Gamma nail vs. dynamic hip screw and plate	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.
Ekström 2007 RCT	7.0	N = 203 Unstable tro-chanteric and sub-tro-chanteric fractures	Proximal femoral nail vs. Medoff sliding plate	Mean operative time for subtrochanteric group for MSP longer: 82±25 vs. 62±29 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.	"No major differences in functional outcome or major complications between proximal femoral nail or Medoff sliding plate. Walking ability in early rehabilitation period was slightly better for the proximal femoral nail group."	One year mortality rate 33/203 (16%). 40% lost/dropout rate at 1 year. Data suggest comparable efficacy.
Moroni 2005 RCT	7.0	N = 40 Pertro-chanteric fractures	Dynamic hip screw vs. external fixation device	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.
Miedel 2005 RCT	7.0	N = 217 Unstable trochanteric	Gamma nail vs. Medoff sliding plate	Mean operating times SGN 61 (22 to 127) vs. MSP 65 minutes in the MSP group. Blood loss	"[U]se of the SGN gave good results in both trochanteric and subtrochanteric fractures.	Combined mortality rate at 1 year=55/217 (25.3%). Mean

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		and subtrochan-teric fractures		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).	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.”	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.
O'Brien 1995 RCT	7.0	N = 102 Intertro-chanteric fractures	Gamma nail vs. dynamic hip screw	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.
Sadowski 2002 RCT	7.0	N = 39 Oblique and transverse intertro-chanteric fracture	Dynamic condylar screw vs. proximal femoral nail	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.
Saudan 2002 RCT	7.0	N = 206 Peri-trochanteric fractures	Sliding compression hip screw vs. intramedullary nailing.	No differences between treatment groups in operation duration, fluoroscopy time, requirement of reduction	“There is no advantage to an intramedullary nail versus a sliding compression hip screw for low-energy	Both treatments were equally effective.

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				of fracture before fixation, and technical problems with implants. No difference in post-operative data. At 1 year 29/206 (14%) had died.	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."	
Vossinakis 2002 RCT	7.0	N = 100 Peri-trochanteric fractures	Pertrochanteric fixator vs. sliding hip screw	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.
Brandt 2002 RCT	6.5	N = 71 Peri-trochanteric fractures	Percutaneous compression plating vs. dynamic hip screw	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 transfusions vs. 6 in PCCP (p <0.001).	"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 complications in DHS.
Baum-gaertner 1998 RCT	6.5	N = 135 Inter-trochanteric fractures	Intramedullary hip screw vs. compression hip screw	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 <0.01), and operating room charges ($2105 vs. $2520, p <0.01). No difference between stable and unstable fracture patterns with intramedullary hip	"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 orthopaedic surgeon's first experience with the device, and do not necessarily reflect the true potential of this intramedullary hip screw."	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 surgeons were less familiar with, providing possible bias against new implant if experience

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				screw. Intramedullary hip screw patients had intra-operative complications exclusively.		would mitigate complications.
Harrington 2002 RCT	6.5	N = 102 Unstable inter-trochanteric fractures	Compression hip screw vs. intramedullary fixation with an intramedullary hip screw	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.
Olsson 2001 RCT	6.5	N = 114 Inter-trochanteric fractures	Medoff sliding plate vs. compression hip screw	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.
Pajarinen 2005 RCT	6.5	N = 108 Peri-trochanteric fracture	Dynamic hip screw vs. proximal femoral nail	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.
Kosygan 2002 RCT	6.5	N = 111 Inter-trochanteric fractures	Percutaneous compression plate vs. classic hip screw	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.
Ahrengart 2002 RCT	6.0	N = 426 Inter-trochanteric fractures	Compression hip screw vs. gamma nail	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) minutes, p <0.05; type 4 59 (22-240) min, p <0.05. CHS EBL	"Surgical treatment should be chosen according to the type of intertrochanteric fracture. Compression hip screw method may be faster and safer for less comminuted fractures.	23% drop out (mortality, complication). Study used two types of compression hip screws (dynamic hip

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				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 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."	screw and Richards classic) without details of how many or related outcome measures.
Bridle 1991 RCT	6.0	N = 100 Inter-trochanteric fractures	Dynamic hip screw vs. gamma nail	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
Janzing 2002 RCT	6.0	N = 115 Inter-trochanteric fractures	Percutaneous compression plate vs. dynamic hip screw	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.
Lunsjö 2001 RCT	6.0	N = 569 Unstable inter-trochanteric fractures	Medoff sliding plate vs. DHS vs. DHS/stabilizing plate vs. dynamic condylar screw	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.

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Leung 1992 RCT	6.0	N = 225 Peri-trochanteric fractures	Dynamic hip screw vs. gamma nail	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 (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.	"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 higher operative complications (14% vs. 10%, p <0.05).
Schipper 2004 RCT	6.0	N = 424 Unstable trochanteric fractures	Gamma nail vs. proximal femoral nail	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.
Vidyadhara 2007 RCT	6.0	N = 73 Unstable trochanteric fractures	Single femoral neck screw vs 2 femoral neck screws (gamma nail vs. ace nail)	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.
Mattsson 2004 RCT	5.5	N = 26 Unstable trochanteric fracture	Sliding screw augmented with calcium phosphate cement	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	"Augmentation with calcium phosphate cement significantly improved the stability of unstable trochanteric fractures fixed with a sliding screw device. In	Study had no clinical outcomes measures to determine if treatment was of benefit to

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				around sagittal axis as varus angulation. Average varus angulation for controls was larger when compared with augmented fractures at all time points.	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."	patients. Small sample size.
Hardy 1999 RCT	5.5	N = 160 Inter-trochanteric fractures	Intramedullary hip screw (IMIS) vs. compression hip screw plate (CHSP)	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.
Goldhagen 1994 RCT	5.5	N = 75 Peri-trochanteric fractures	Compression hip screw vs. Gamma nail	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.
Fornander 1994 RCT	5.5	N = 209 Trochanteric fractures	Gamma nail vs. sliding hip screw	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. 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.	"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).
Dujardin 2001	5.5	N = 60 Trochanteri	Dynamic hip screw vs. experimental	Trochanteric hip screw had longer procedure time 46±9 vs. 24±7 minutes for	"The experimental nail had shown advantages but not all possible	Experimental nail group had disproportionate

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RCT		c fractures	intramedullary nail with 2 non-parallel cervicocephalic screws	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). 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).	disadvantages were able to be evaluated."	number of unstable fracture compared to the hip screw (p <0.01), which further strengthened data suggesting strengthens that experimental nail superior.
Papasimos 2005 RCT	5.0	N = 129 Unstable trochanteric fractures	AMBI dynamic hip screw vs. gamma nail (TGN) vs. proximal femoral nail (PFN)	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 RCT	5.0	N = 100 Inter-trochanteric fractures	Pugh nail vs. dynamic hip screw	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.
Watson 1998 RCT	5.0	N = 160 Inter-trochanteric fractures of which 114 are unstable	Compression hip screw with 4-hole side plate (Dynamic Hip Screw) vs. Medoff sliding plate	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	"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	Pseudo-randomization on medical record number. Substantial difference in group sizes apparently a

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		fractures		ambulatory status, or post-op pain. Medoff plate had higher blood loss (350 vs. 213mL, p = 0.0001) and operating time (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).	fractures."	consequence. Some data support each approach.
Hardy 2003 RCT	5.0	N = 80 Inter-trochanteric fractures	Two screws transfixing the nail in 2 separate holes (Group A) vs. nail locked with 1 screw passing through slot (Group B)	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 femur at level of tip of nail when compared to 6 patients in Group A.	"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)
Utrilla 2005 RCT	4.5	N = 210 Trochan-teric fractures	Trochanteric gamma nail vs. compression hip screw	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.
Esser 1986 RCT	4.5	N = 98 Trochanteri c fractures	Jewett nail-plate (JNP) vs. Dynamic hip screw (DHS) (both 135°)	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	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	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.

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				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.	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."	
Davis 1988 RCT	4.5	N = 230 Inter-trochanteric fractures	Küntscher-Y nail vs. sliding hip screw	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). Total 1-year mortality rates 40% vs. 35% (NS). High complication rates both groups.	"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 significantly lower mortality for patients with good preoperative walking ability compared to Küntscher-Y nail."	High mortality at 1 year (40% vs. 35% SHS), p >0.05. Study did not exclude severely debilitated or demented patients (frequently excluded in other comparison studies).
Bong 1981 RCT	4.0	N = 150 Unstable inter-trochanteric fractures	Skeletal traction with tibial pin vs. medial displacement osteotomy vs. valgus osteotomy	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.
Park 1998 RCT	4.0	N = 60 Inter-trochanteric fracture	Gamma AP nail vs. compression hip screw	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.
Fritz 1999 RCT	4.0	N = 80 Unstable trochanteric fractures	Gliding nail vs. gamma nail	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.
Butt 1995 RCT	4.0	N = 95 Peri-trochanteric fractures	Dynamic hip screw vs gamma nail	Operative times: GN mean 53 minutes vs. 62 minutes DHS. Hospital stays averaged 22 vs. 23 days. Times to union	"We do not recommend the gamma nail for the treatment of peri-trochanteric femoral fractures."	Sparse details of statistical analysis weakens conclusion

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				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.		regarding complications. Study suggests DHS is superior to Gamma nail.
Hemi/Arthroplasty vs. Other Approaches						
Frihagen 2007 RCT	8.0	N = 222 All displaced intracapsular femoral neck fractures with angular displacement	Closed reduction and two parallel screws vs. bipolar cemented hemiarthroplasty. Charnley-Hastings bipolar, cemented vs. Olmed, DePuy/Johnson and Johnson screws.	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 RCT	7.5	N = 48 Displaced femoral neck fractures over 65 years	Unipolar vs. bipolar arthroplasties	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.
Blomfeldt 2005 RCT	7.5	N = 102 Displaced femoral neck fractures	Total hip replacement (Exeter modular stem and Ogee cup) vs internal fixation with two cannulated screws (Olmed)	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 48 months 4% vs. 47% (p < 0.001). Death rates both 25%.	"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.
Macaulay 2008 RCT	7.0	N = 40 Displaced femoral neck fracture	Total hip arthroplasty (≥28mm femoral head implant) vs. hemi-arthroplasty (uni- or bi-polar)	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	"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.

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				favored THA at 24 months.		
Keating 2006 RCT	7.0	N = 299 Displaced intra-capsular fractures	Bipolar hemi-arthroplasty vs. total hip arthroplasty	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 RCT	6.5	N = 455 Intra-capsular fractures	Hemiarthroplasty (Austin Moore) vs. internal fixation (3 AO Stratec screws)	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 RCT	6.5	N = 81 Displaced intra-capsular fractures	THR vs. hemiarthroplasty	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	"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.

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				revision with 14.6% (6/41) hemiarthroplasty vs. 2.5% (1/40) total hip arthroplasty, p = 0.058.		
Kim J Bone Joint Surg Am 2005;87(10):2186-92 RCT	6.5	N = 58 Unstable inter-trochanteric fractures	Cementless Calcar-replacement prosthesis vs. proximal femoral nail	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.
Lamadé 1995 RCT	6.5	N = 30 Cemented hip arthro-plasty	Antihistamines (H1 and H2) vs. placebo	No significant difference for drop in blood pressure between the groups at time of prosthesis insertion.	"There does not seem to be any prophylactic indication for histamine-receptor-blocking agents in cemented hip arthroplasty. Thus recommended means to prevent BCIS should still focus on operative technique."	Time from antihistamine blockers to prosthesis implant not defined. Data suggest lack of efficacy.
Calder 1996 RCT	6.0	N = 250 Displaced intracapsular fractures	Unipolar uncemented vs. cemented bipolar prothesis	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 RCT	5.5	N = 115 Displaced femoral neck fractures ages 65+	Uni- (Unitrax) vs. bi-polar (Centrax) hemi-arthroplasties	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.
Field 2005 RCT	5.0	N = 50 Displaced subcapital fractures	All used Cambridge cup vs. Cambridge cup with hydroxyapatite coating removed. All Thompson hemiarthroplasties and	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	"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	Experimental study. Data suggest hydroxyapatite coated acetabular cups may have less migration and require fewer revisions. However,

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			Palacos-R cement.	different (p = 0.48).	known to provide long-term osseointegration may be advantageous."	functional scores not different.
Sikorski 1981 RCT	5.0	N = 218 Displaced subcapital fracture	Internal fixation vs. Thompson hemi-arthroplasty through a McKee anterolateral approach vs Thompson hemiarthroplasty through a Moore internal fixation.	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.
Dorr 1986 RCT	5.0	N = 89 Femoral neck fractures	THR vs. noncemented bipolar hemiarthroplasty vs. cemented hemiarthroplasty	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 Quasi-randomized RCT	4.5	N = 122 Displaced subcapital hip fractures >70 years	Uncemented hemiarthroplasty (Austin Moore) vs. dynamic hip screw (AO Synthes)	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.
Emery 1991	4.5	N = 53	Cemented vs. uncemented	No pain present in 13/19 (68.4%) cemented vs.	"After a mean follow-up of 17 months,	Details sparse. Data suggest

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RCT		Subcapital fracture	Moore stems	4/20 (25%) uncemented, p = 0.002. More dependency on walking aids after injury in 16 uncemented vs. 8 cemented, p = 0.015.	significantly more of the uncemented group were experiencing pain in the hip and using more walking aids than the patients in the cemented group."	cemented stem outperformed uncemented.
Skinner 1989 RCT	4.5	N =278 Displaced subcapital fractures	Internal fixation vs. Moore hemi-arthroplasty vs. Howse II total hip replacement	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."	Hemiarthroplast y had lower revision but comparable mortality rates for displaced subcapital fractures. No control for physician experience was mentioned.
Santini 2005 RCT	4.5	N = 106 Femoral neck fractures	Cemented vs. uncemented hemiarthroplas ty	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.
Femoral Shaft Fractures						
Cameron 1992 RCT	7.0	N = 88 Femoral shaft fractures	Grosse-Kempf vs. Russell-Taylor vs. Synthes (intermedullary)	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.
Other Surgical Studies						
Mattsson 2005 RCT	7.0	N = 112 Unstable trochanteric fractures	Dynamic hip screw with vs. without cement augmentation	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 differences at 6 months in pain or walking scores. SF-36 scores also superior at 6 months for	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 conventional fixation with a sliding screw device alone.	Results suggest cement augmentation superior especially at 6 weeks, but also at 6 months in some measures.

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				cemented.		
Surgical Drapes						
Lilly 1970 RCT	4.5	N = 22 Nail plating of neck of femur	Adhesive drape covering wound (Steridrape) vs. no adhesive drape	No differences in bacterial counts. Mean viable counts per 100ml washings (beginning of operation/end): adhesive drapes (28.1±9.2/20.4±6.2) vs. no drape (25.3±9.6/19.6±4.4).	"…no evidence of an increase in bacteria on normal skin covered by steridrape for up to four hours…[A]dhesive drapes probably give no protection against bacterial contamination of operation wounds."	Data suggest no differences in outcomes.
Acupressure for Transporting Patients						
Barker 2006 RCT	8.5	N = 38 Acute hip fractures	Acupressure vs. sham acupressure (3 locations each) during transport	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.
Usichenko 2005 RCT	8.0	N = 61 THA	Auricular acupuncture (hip joint, shenmen, lung, thalamus) vs. sham (4 helix points) up to 3 post-op 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 RCT	7.5	N = 64 THA	Auricular acupuncture (lung, shenmen, forehead, hip) vs. sham (4 helix points)	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.

HIP ARTHROPLASTY

Hip arthroplasty has been used for several decades for treatment of hip degenerative joint disease and osteonecrosis.(105, 1036-1053) Many if not most patients who were active pre-operatively are able to return to work or restart sports activities(1054-1060) and cardiovascular fitness improves postoperatively.(1053) Twenty-five-year arthroplasty survival rates of 80% have been reported,(1046, 1047) although the survival data are based on approximately 10 to 25% of the originally replaced joints due to intervening deaths. Quality evidence from controlled trials directly comparing arthroplasty with other treatments is absent likely due to the many decades the procedure has been successfully performed. More recently, hip resurfacing has been used particularly in younger patients with osteoarthrosis or osteonecrosis primarily to attempt to hopefully preserve more bone for subsequent, successful arthroplasty at an older age.(1061-1067)

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The most common reasons for hip arthroplasty vary from one report to the next, but include idiopathic coxarthrosis (70.6%), rheumatoid arthritis (3.1%), sequela after fracture (12.2%), and sequela after dysplasia (6.8%). Women undergo these procedures approximately 70% more frequently than men.(929) Surgical incidence peaks in a population-based registry from Norway among those 70 to 79 years old(1040) (see Figure 22), although the overall risk for hip arthritis continues rising beyond age 80. Arthroplasty rates have been projected to increase sharply over the coming decades due to aging populations (see Figure 23).(5, 929, 930)

Figure 22. Incidence of primary total hip replacement, by age and gender in Norway in 1997. Calculations are based on data from the Norwegian Arthroplasty Register and the Norwegian Population Register.

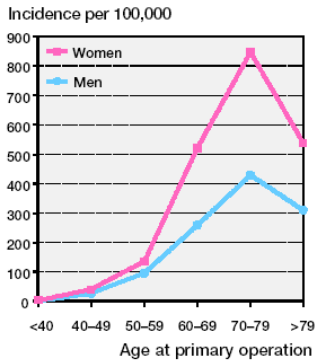

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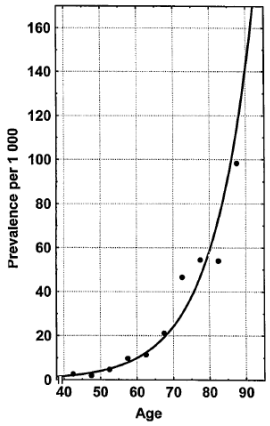
Figure 23. Prevalence of Primary Coxarthrosis as seen on Radiographs in 12,051 Subjects who have had a Normal Radiographic Examination of the Colon. Data from 1966, 1984, and the Current Study were Pooled.



Reprinted with permission from Lippincott Williams & Wilkins. Danielsson L, Lindberg H. Prevalence of coxarthrosis in an urban population during four decades. *Clin Orthop Relate Res*. 1997;342:106-10.

Pain has been shown to be a predictor of total hip arthroplasty ($p < 0.0001$), as have visual analog scale (VAS) handicap ratings, and degree of joint space narrowing.(1068) The primary reason for failure of prosthesis is loosening. Infections occurred in large case registries in 6.1%,(1040) although more recent estimates are under 1% with improved antibiotic prophylaxis. Improvements in cement technique have been incorporated (see below) as well as development of cementless systems. Prosthetic surfaces have also been modified to improve prosthetic survival.(1069) Predictors of complications and poorer functional status at 1 year include female gender, single marital status, less than high school education, nonwhite ethnicity, and the Index of Co-Existent Disease (which measures asymptomatic controlled, uncontrolled and life-threatening diseases).(1070) Some studies have suggested higher rates of osteolytic loosening among younger patients.(1049)

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Analyzing this literature is particularly challenging as the technologies have evolved rapidly, often without any accompanying moderate- or high-quality studies. Further, literature reports are often incomplete, without a comprehensive description that includes the population treated, surgical approach, prostheses utilized, operative site preparation, instrumentation, medications or other treatments utilized (see hip arthroplasty evidence table). At times, this requires reasonable assumptions to be made regarding the predominant techniques in use at the time of the report. Still, provided there is only one variable being tested in a given study, assumptions regarding the generalizability of the results between those two sets of assumptions would appear to remain solid.

The vast majority of patients described in quality studies who undergo hip arthroplasty have been diagnosed with osteoarthrosis. Another large group has rheumatoid arthritis. Other sizable groups have had fractures, osteonecrosis, dysplasia, and ankylosing spondylitis(931) (see hip arthroplasty evidence table). Some studies have included simultaneous, bilateral arthroplasties as crossover trials.(855, 889, 1071)

Recommendations in this guideline are derived from careful review of available high- or moderate-quality studies(1072) (see evidence table below). Alternative procedures that are not recommended may result in superior patient outcomes in experienced surgical hands. Thus, rather than immediately changing surgical technique to implement these recommendations without adequate training and practice, caution is suggested.

1. *Recommendation: Hip Arthroplasty for Moderate to Severe Arthritides, Osteonecrosis, or Substantially Symptomatic Hip Dysplasia*
   Hip arthroplasty is strongly recommended for severe arthritides, osteonecrosis with collapse or unresponsive to non-operative treatment or substantially symptomatic hip dysplasia.

   Strength of Evidence **– Strongly Recommended, Evidence (A)**

2. *Recommendation: Hip Arthroplasty for Bilateral Disease*
   For bilateral disease, carefully selected patients may safely undergo simultaneous bilateral hip replacement.

   Strength of Evidence – **Recommended, Evidence (C)**

3. *Recommendation: Total Hip Arthroplasty*
   Total hip arthroplasty is strongly recommended as an effective operation to speed improvements in patient's symptoms and functional status in those with moderate to severe hip disease.

   Indications – All of the following present: 1) severe hip degenerative joint disease, osteonecrosis with collapse or unresponsive to non-operative treatment, or hip dysplasia (x-rays may indicate moderately severe, but function may be severely impaired); 2) sufficient symptoms and functional limitations such as impairments of activities of daily living or occupational tasks, and 3) failure to successfully manage symptoms after a prolonged period of a conservative management plan that included NSAIDs, exercise, physical or occupational therapy, and where appropriate, weight reduction.(1072) (Altman 04) Also consider intraarticular corticosteroids. Carefully selected patients may be candidates for bilateral arthroplastic procedures.(855, 889, 1071) However, particular attention should be paid to pre-operative medical fitness and psychological fortitude.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

4. *Recommendation: Metal on Metal Hip Resurfacing Arthroplasty*
   Metal-on-metal hip resurfacing arthroplasty is recommended for select patients.

   Strength of Evidence – **Recommended, Evidence (C)**

5. *Recommendation: Acupuncture for Hip Arthroplasty Patients*
   Acupuncture is moderately recommended for hip arthroplasty procedures.

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Indication – Hip arthroplasty patients.

Frequency/Duration – Up to 3 post-operative days.(974, 1015)

Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendations

There is quality evidence of long-term benefits of total hip arthroplasty among patients with moderate to severe hip degenerative joint disease (osteoarthrosis or inflammatory), osteonecrosis of the hip or hip dysplasia (see hip arthroplasty evidence table).(1036, 1038-1053, 1073) Long-term outcomes have included resumption of occupational activities. Since there are operative failures, it is important even with a highly successful operation to assure that non-operative means have failed to sufficiently control symptoms. The primary consideration for operative candidacy should be symptoms and functional status, rather than severity of x-ray findings. There is some evidence from moderate quality studies suggesting bilateral arthroplasties may be safe in carefully selected patients.(855, 889, 1071) There has been enthusiasm for hip resurfacing particularly in younger patients,(1061-1063, 1074, 1075) and 3-year survival rates have been reportedly 99.1%;(1076) however, while there is quality evidence of radiological superiority in the immediate post-operative period,(1077) there is no quality evidence of superiority of the metal-on-metal hip resurfacing arthroplasty procedure over intermediate or longer timeframes(1063, 1067, 1078) (see hip arthroplasty evidence table). Nevertheless, survival rates over the near term suggest the procedure is successful; it is recommended as an option particularly for younger patients(1061-1063, 1067, 1077, 1079) or those with osteonecrosis.(1065, 1066)

Anterior, direct lateral, modified direct lateral, and posterior approaches to hip arthroplasty have been attempted.(127, 931, 1080-1094) There is a quality study comparing different approaches,(1095) (Widman 01) and one study evaluated surgical drapes.(939) There are multiple uncontrolled studies regarding minimal incisional techniques;(1087-1093) one is moderate-quality study.(1096)

Femoral and acetabular components differ by composition, coatings and design. The various surfaces that are used on femoral and acetabular components, “stems,” are often described as smooth, porous and hydroxyapatite coatings.(1042, 1097) Some arthroplasties are inserted with cement, some uncemented and some “hybrid” or combinations of typically uncemented cups and cemented stems.(1051)

Cement or medullary restrictors (or “plugs”) are prosthetic devices inserted into the distal femoral shaft after reaming out the canal prior to placement of the cement and prosthesis.(1098-1109) The purpose of the plug is to seal off the distal canal which allows for higher pressurization of cement,(1098, 1100, 1105, 1110-1113) thus facilitating a thicker and more uniform layer of cement between the prosthesis and the bone.(1111) This is thought to result in better survival of the prosthesis(1100, 1105, 1106) (see hip arthroplasty evidence table).

Complications of hip arthroplasty include bone cement implantation syndrome (BCIS), fat emboli, intraoperative fractures, infected prostheses, dislocations and prothesis failure. BCIS is a constellation of hypotension, hypoxemia, cardiac dysrhythmias, and/or cardiac arrest with a mortality rate of up to 1%.(1114-1117) Intraoperative fractures are a source of morbidity during hip arthroplasties.

Two quality trials demonstrated efficacy of acupuncture for hip arthroplasty patients, including reducing opioid needs.(974, 1015) Acupuncture is minimally invasive, has essentially no adverse effects, is low cost, and thus is recommended.

Evidence for the Use of Hip Arthroplasty

There are 6 high-(974, 1036, 1037, 1039, 1074, 1096, 1118-1120) (one with four reports) and 51 moderate-quality(855, 888, 889, 891, 892, 939, 1015, 1038, 1067, 1071, 1075, 1077, 1095, 1097, 1100, 1104-1106, 1121-1153) RCTs and randomized crossover trials incorporated in this analysis. There are 2 low-quality RCTs(1079, 1154) in Appendix 2.

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Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Surgical Approaches						
Widman 2001 RCT	6.5	N = 74 OA	Lateral position vs. supine position for surgery	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 RCT and crossover for simultaneous	6.5	N = 156 50 bilateral simultaneous; 106 unilateral	Cemented (Elite Plus, Simplex-P cement) vs. uncemented (Profile) hip arthroplasty. All cups Duraloc cementless.	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.
Chiu 1993 RCT	4.5	N = 120 Acute hip fractures	Drape group (operative site was covered with plastic adhesive drape after operation) vs. no-drape group (operation site was left uncovered).	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.
Minimal Incisions						
Ogonda 2005 RCT	8.0	N = 219 Unilateral THA	Surgery through a short incision of ≤10cm vs. standard incision of 16cm	Estimated intra-operative blood loss (ml) mini-incision vs. standard-incision group (mean ± SD): 314±162 vs. 366±190 (p = 0.03). Morphine usage (mg) 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.
Hip Resurfacing vs. Arthroplasty						
Lavigne 2010 RCT	8.5	N = 48 All with OA and <65yrs, included 14	Hip resurfacing (Durom) vs. large-head total hip arthroplasty	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/	"(Hip Resurfacing) did not provide better clinical function over large-head THA."	Younger, active population. Data suggest comparable efficacy.

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		healthy controls	(CLS stem). Durom acetabula both groups; 1 year follow-up.	1.73) (NS). No difference in walking speed, step length, cadence, postural balance. Functional reach favored HR.		
Garbuz 2010 RCT	6.5	N = 104 Patients required to be suitable for hip resurfac-ing	Hip resurfacing (Durom) vs. large-head arthroplasty (Metasul). Durom acetabula both groups; 2 years follow-up.	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.
Femoral Components						
Rasquinha 2004 RCT	8.0	N = 237 88.2% OA	Ranawat-Burstein prosthesis with smooth vs. rough finish for cemented femoral stems. Over 60 years, cemented and under age 60 hybridized prostheses (more criteria in article). Single surgeon. Post-erolateral approach; 3rd generation cement.	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 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.	"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.
MacDonald 2010 RCT	7.5	N = 388 OA	Proximally porous-coated tapered cementless femoral component (Synergy) vs. fully porous-coated cementless femoral component (Prodigy). All 28mm head. Acetabulum usually Reflection and Duraloc respectively. Minimum 2 years follow-up (mean 6.7 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.
Östgaard 2001	7.0	N = 123 OA	Original vs. new Charnley stem	Original instrumentation with AP x-ray views	"The femoral stems were less often in the varus position with the	Authors suggest manufacturer should respond to

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RCT			instrumentation	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).	new instrumentation. However, the worst malposition, with implant-inner cortex contact, especially seen on the lateral radiograph, was not addressed at all."	the problem. Long-term implications vis-à-vis clinical outcome are unclear, but suggest suboptimal results with new instrumentation.
Kim J Bone Joint Surg Am 2005;87(8): 1769-76 Randomized Crossover Trial	6.5	N = 52 All osteo-necrosis, all bilateral arthroplasties	Zirconia femoral head vs. cobalt-chromium head	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 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.	"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 (despite advice to avoid high impact).
Lachiewicz 2008 RCT	5.5	N = 201 THA	Polished (Ra, 0.18 to 0.3 nanometer) vs. precoated roughened (Ra, 1.8 to 2.3 nanometer) cemented femoral component with similar geometry	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.
Garellick 1999 RCT	5.5	N = 372 THA	Charnley vs. Spectron prosthesis	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	"[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.

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				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).		
Nivbrant 1999 RCT	5.0	N = 40 OA	Cemented Scientific Hip Prosthesis (SHP) vs. Lubinus SP2 prosthesis	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.
Kärrholm 1994 RCT	4.5	N = 60 OA	Cemented vs hydroxyapatite coated vs. porous coated. All titanium (Tifit)	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 RCT	4.5	N = 22 THR	CPS stem cemented conventionally using 3rd generation cementation technique vs. TRIOS cemented using transprosthetic drainage system	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.
Incavo 1998	4.0	N = 91 81% OA,	Surface coating in profile femoral	Good/excellent results 19/26 (73%) vs. 20/28 (71%) vs. 22/25	"Clinical differences exist and are attributable to the type	HA coated had superior Harris Hip Scores and

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RCT		9.9% ON, 5.5% trauma	prostheses: 1) smooth; 2) porous coated vs. 3) hydroxyapatite (HA) coated. Multi-center. Full weight-bearing allowed immediately post-op.	(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%.	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.
Kärrholm 2002 RCT	4.0	N = 65 OA	Epoch reduced stiffness stem vs. anatomic stem, both porous coated	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 sclerotic lines surrounding stem (p ≤ 0.002) at 2 years post-operatively. No difference for Harris hip score evaluated at same hospital.	"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 stem with a stiffer design."	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.
Seyler 2006 RCT	4.0	N = 210 OA or osteonecrosis	Stratified enrollments for OA and osteonecrosis. Compared alumina-on-alumina vs. cobalt-chromium-on-polyethylene surfaces.	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.
Femoral Canal Preparation						
Christie 1995 RCT	5.0	N = 24 All femoral neck	Minimal washout of the medullary canal before	Grade 3 or 4 maximal embolic responses of 50% in lavage group vs. 91.7% in control,	"We consider that thorough lavage should be an essential part of the preparation	Thorough lavage appears important.

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		fractures	cement insertion vs. extensive washout by allocation of alternate cases to groups	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.	of the proximal femur before cement insertion."	
Acetabular Components						
Faris 2006 RCT	6.0	N = 407 Unclear diagnoses	Acetabular cups (Biomet) with cement spacers made from polyethylene vs acetabular without polyethylene spacers	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.
Röhrl 2004 RCT	6.0	N = 81 OA	Press-fit only (PF) vs. press-fit and HA coating (PF+HA) vs. press-fit and 3 screws (PF+screws) vs. press-fit and 3 pegs placed similar to screws (PF+pegs). All Reflection cups.	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.
Thanner 2000 RCT	5.5	N = 62 Hip replacement	Trilogy cup with 3 cluster holes vs. Trilogy cup without 3 cluster holes	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.
Acetabular Preparation						
Flivik 2006 RCT	6.5	N = 50 OA	Removal of at least 75% of subchondral bone plate vs. retained other than ream to slight bleeding surface. All Opticup, Palacos with gentamicin cement, Optivac	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.

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			vacuum mixing system, and cement gun.			
Cement						
Nayak 1996; Rorabeck 1994; Rorabeck 1996; Laupacis 1993 RCT	8.5	N = 250 1º or 2º OA	Femoral Mallory-Head plasma spray-coated titanium or cobalt-chromium implants vs. smooth implants for cement fixation. 28mm modular titanium cobalt-chrome heads used. Used canal lavage, restrictor and cement gun.	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.
Devane 1997 RCT	7.5	N = 250 1º or 2º OA	Same population and study as above, but only 148 available	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.
Laupacis 2002 RCT	6.5	N = 250 Hip OA	Same population and study as above	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 Crossover trial	6.5	N = 21 OA	Charnley acetabular components inserted with cement vs. porous Harris-Galante acetabular components	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	"After short to medium-term follow up, there no major difference between the two designs for skeletal fixation."	No differences, but small sample size.

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			inserted without cement, one in each hip	longitudinal axis, 0.3mm for Harris-Galante and 0.2mm for Charnley (p = 0.06) along sagittal axis.		
Kim 2002 RCT and crossover for simultaneous	6.5	N = 156 n = 50 bilateral simultaneous n = 106 unilateral	Cemented (Elite Plus, Simplex-P cement) vs. uncemented (Profile) hip arthroplasty. All cups Duraloc cementless.	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 of patients had osteonecrosis. Study in Korea with authors questioning generalizability to U.S. Crossover trial for simultaneous is a study strength.
Kim J Bone Joint Surg Am 2003 RCT	6.5	N = 98 Osteonecrosis of the femoral head; simultaneous bilateral THA and unilateral THA	Simultaneous bilateral total hip arthroplasty with cemented stem in 1 hip and cementless stem in other vs. unilateral total hip arthroplasty with cementless stem	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.
Pitto 1999 RCT	5.5	N = 60 OA	Arthroplasty without cement (Group 1) vs. conventional cementing (plus bone plug) (Group 2) vs. bone vacuum cementing (methyl-methacrylate plug) (Group 3). Palacos R cement used.	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.
Wykman 1991 RCT	5.0	N = 150 76.6%OA, 10% RA	Cemented (Charnley) vs. uncemented (Honnart Patel-Garches) total hip arthroplasty	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)	"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	No clear advantage to cementation.

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				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.	arthroplasties."	
Digas 2004 RCT	5.0	N = 90 95.6% OA	Cemex fluoride vs. palacos gentamicin cement vs. hybrid group (femoral component separately randomized to either cement). All Spectron stems. Whole polyethylene Reflection and press-fit Trilogy cups.	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- (-)/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.	"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.
Reigstad 1993 RCT	5.0	N = 120 OA	Cemented Landos Titane vs. uncemented Zweymüller/ Endler	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.
Carlsson 1993 RCT	4.0	N = 226 Hip arthro-plasties	Low vs. high viscosity cement	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

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						and not in cement and not randomized. Study flaws limit potential conclusions.
Cementation Types, Techniques, and Pressurization						
Flivik 2004 RCT	6.5	N = 14 Primary coxarthrosis	Pressurized cement with conventional pressurizer vs. sequential method including individual pressurization of each anchorage hole	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 RCT	6.5	N = 57 64.9% OA, 21.1% post-trauma, 15.8% RA	Palamed G vs. Palacos R cements; all Charnley prostheses	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.
Nelissen 2005 RCT	5.5	N = 39 THA	Simplex P cement vs. Simplex AF cement; all Exeter prostheses	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.
McCaskie 1997 RCT	5.5	N = 31 THR	Finger-packing vs. cement-gun technique femoral canal before cementing	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 RCT	5.5	N = 60 THA	Femoral component inserted with vs. without distal centralizing device (PMMA) for primary hybrid total hip arthroplasty	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	"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.

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				centralizers vs. 16% of uncentralizers showed voids. Fewer cement mantle deficiencies with vs. without centralizer (p <0.001).		
Pabinger 2004 RCT	4.5	N = 22 THR	CPS stem cemented conventionally using 3rd generation cementation technique vs TRIOS cemented using transprosthetic drainage system	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.
Wykman 1992 RCT	4.5	N = 19 Cemented THA	Continuous irrigation with Ringer solution during cement curing vs. no irrigation	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 RCT	4.5	N = 30 THA	Fixation of the prosthesis, using Boneloc vs. Palacos with gentamicin	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.
Nivbrant 2001 RCT	4.0	N = 44 Primary arthrosis of the hip undergoing THR	Fixation with Cemex Rx vs. Palacos R cement of both components	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	"The stems migrated similarly inside the cement mantle regardless of the type of cement used."	Suggests low proportion monomer is not superior.

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				operation showed no significant differences."		
Comparisons between Different Cement Restrictors						
Schauss 2006 RCT	6.5	N = 130 THA due to hip OA	Degradable cement restrictor (Biostop G) vs. non-degradable cement restrictor (Allopro)	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 RCT	6.5	N = 70 Primary cemented hip replacement	Polyethylene vs. Shuttle Stop (degradable)	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.
Thomsen 1992 RCT	4.5	N = 77 THA	Comparison of 3 plugs in THA: 1) bone plug made from femoral head; 2) Richards polyethylene plug ; 3) Thackray polyethylene plug was 38mm	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.
Visser 2002 RCT	4.0	N = 93 THA	Biosem II plug vs. Cemlock plug vs. Thackray plug; all Stanmore prostheses	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	"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	Polyethylene plug superior to 2 different biodegradable plugs.

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				below plug varied between 0.5 and 4cm.	clinic."	
Wembridge 2006 RCT	4.0	N = 32 THA	Ultra-high-molecular-weight polyethylene (Hardinge) vs. biodegradable (Amberflex Summit Medical) femoral cement restrictor	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 RCT	4.0	N = 103 Total hip surgery	Three intramedullary resorbable cement plugs in vitro and in vivo. (1) SEM II plus, (2) C-plug, (3) REX plug.	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 1.71±0.46 vs. REX 2.74±0.47.	"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.
Metal-on-Metal Hip Resurfacing						
Girard 2006 RCT	6.0	N = 104 Unilateral or mild bilateral OA, also had 16 patients with dysplasia or Perthe's disease	Total hip arthroplasty (CLS Spotorno, Metasul, Allofit, Zimmer) vs. hip resurfacing (Durom, Zimmer)	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.
Howie 2005 RCT	4.5	N = 24 Not well described, but appear to be OA and AVN	Resurfacing (McMinn, Corin) vs. total hip arthroplasty (Exeter)	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.

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Medications						
Karnezis 1994 RCT	10.0	N = 92 THR and TKR patients, 88% OA	Desmopressin group vs. placebo	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.
Garneti 2004 RCT	5.5	N = 50 OA	Bolus 10mg/kg of intravenous tranexamic acid vs normal saline at anesthesia	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.
Miscellaneous						
Motobe 2004 RCT	6.0	N = 35 OA, RA and femoral neck fracture, all <55 years	Femoral component inserted with vs. without cement. Endogenous cannabinoids inserted using a conventional cementing technique vs. insertion without cement	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.
Digas 2004 RCT	5.0	N = 90 95.6% OA	Cemex fluoride vs. Palacos Gentamicin cement vs. hybrid group (femoral component separately randomized to either cement.) All Spectron stems. Whole polyethylene Reflection and press-fit	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 = 0.05. Proximal (+)/(-) p-value = 0.79. Anterior (+)/(-) p = 0.72. Cup rotations anterior (+)--posterior (-) tilt p-value = 0.56. Ante- (-)/ retroversion (+) p-value 0.66.	"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."	Suggests fluoride added to cement not helpful.

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			Trilogy cups.	Increase (+)/decrease (-) of inclination mean value: Cemex-F -0.09; Uncemented 0.23; Palacos -0.21, p = 0.14.		
Digas 2005 RCT	5.0	N = 90 95.6% OA	Same as above	At 6 month follow-up, almost no mean subsidence recorded in 2 groups, which increased to -0.07 and -0.12mm at 2 years (p = 0.25). Distal migration of stems at 2 years -0.15 and -0.09 mm, respectively (p = 0.6). In 29 of 32 patients with rheumatoid arthritis or continuous treatment with cortisone in whom subsidence could be evaluated at 2 years, mean values in C-F and Palacos groups -0.16 and -0.13mm.	"[T]here is no obvious advantage of addition of fluoride to acrylic bone cement when used to fixate the femoral component in total hip arthroplasty."	Cement not significantly different.
Digas 2006 RCT	5.0	N = 90 95.6% OA	Same as above	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 (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).	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 found suggests that stress shielding may initiate development of this complication.	Addition of fluoride to the cement of no added benefit.
Brodner 2003 RCT	5.0	N = 100 OA or osteonecrosis	Hip arthroplasty Alloclassic without cement treated with a metal-on-metal articulation vs. ceramic-on-polyethylene bearing	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 remained in a constant range. Serum cobalt concentrations did not reflect a so-called run-in wear period of metal-on-metal	Clinical significance uncertain as there is no clinical correlate.

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					articulations."	
Acupuncture for Arthroplasty Patients						
Usichenko 2005 RCT	8.0	N = 61 Hip arthro-plasty	Auricular acupuncture (hip joint, shenmen, lung, thalamus) vs. sham acupuncture (4 helix points) for up to 3 post-op days	Auricular acupuncture received 32% less piritramide vs. control in 1st 36 post-op hours (37 vs. 54mg, p = 0.004). Total dose 36% lower (0.54 vs. 0.84mg/ 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 RCT	7.5	N = 64 THA	Auricular acupuncture (lung, shenmen, forehead, hip) vs. sham (4 helix points)	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.

Bisphosphonates and Calcitonin

Bisphosphonates have been used to attempt to reduce periprosthetic bone resorption in the immediate peri-operative period.(1155) Calcitonin has been used to attempt to develop better healing after hip fracture fixation.(305)

1. *Recommendation: Routine Use of Bisphosphonates*
   There is no recommendation for or against the routine peri-operative use of bisphosphonates.
   Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

2. *Recommendation: Routine Use of Calcitonin*
   There is no recommendation for or against the routine post-operative use of calcitonin.
   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations

Multiple studies have shown less bone loss with cemented prostheses(976, 1156-1158) and a greater effect on the knee.(1155) A high-quality trial of intranasal calcitonin also found better healing after internal fixation of hip fractures compared to placebo.(305) These studies are of short-term duration and there is no long-term follow-up. Thus, the utility of these medications for this purpose is unclear. Among those patients with osteoporosis however, these medications would appear to be indicated.

Evidence for the Use of Bisphosphonates and Calcitonin

There is 1 high- and 2 moderate-quality RCTs incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Bisphosphonates						
Venesmaa 2001 RCT	5.0	N = 13 HA-coated uncemente	Alendronate 10mg plus calcium	Periprosthetic bone mass in all Gruen zones (post-op/3 months/6 months): calcium	"[A]lendronate seems to be a potent drug to inhibit the periprosthetic bone loss that occurs after primary	Small sample sizes. Data suggest alendronate

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		d THA	carbonate 500mg vs. calcium 500mg only for 6 months	(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±0.25), NS. Between group differences p <0.05.	uncemented THA…the follow-up time was too short and the study population too small to make firm conclusions…"	may be effective, but study underpowered.
Wilkinson 2001 RCT	5.0	N = 47 THA	Single-dose infusion pamidronate 90mg vs. placebo	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.
Calcitonin						
Huusko 2002 RCT	8.5	N = 260 Acute hip fracture	Intranasal salmon calcitonin 200 IU daily vs. placebo nasal spray for 3 months	At 3-months, median pain intensity 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)."	"Intranasal 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.

Antibiotics

Antibiotics have been utilized systemically and added to cement for many years.(1040, 1159-1171)

Recommendation: One Day Use of Systemic Antibiotics for Hip Surgery

One-day use of systemic antibiotics is moderately recommended for patients undergoing surgical hip procedures.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation

There is evidence from a non-randomized registry data of 10,905 hip prostheses that the risk of revision due to infection was reduced 75 to 78% with a systemic antibiotic combined with an antibiotic-impregnated cement compared with either systemic antibiotic administration or antibiotic-impregnated cement alone. The risk, if there was only antibiotic in the cement, was 6.3-fold higher, and, if the antibiotic was only systemic risk, was 4.3-fold greater.(1172) There is a belief that some cases of aseptic loosening are undiagnosed infections(1040) as there were lower rates of aseptic loosening among those with both routes of antibiotic administration compared with either alone(1172) and those with gentamicin cement appear to have lower rates of aseptic loosening compare with systemic antibiotics.(1173, 1174) In the largest comparative trial of more than 1,600 hip arthroplasties, cement with gentamicin was found to produce fewer deep infections, but more superficial infections compared with an uncontrolled arm of systemic antibiotics alone.(1159, 1173, 1174) There is one low-quality study suggesting no difference in

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infection rates between cement-antibiotic and systemic antibiotic arms.(1175) Thus, there is quality evidence that a combination of systemic and antibiotic-impregnated cement is important to prevent infections. There was no prosthesis survival benefit if systemic antibiotics were administered for greater than one day.(1176) Numerous antibiotics have been utilized, including gentamicin, cloxacillin, dicloxacillin, probenecid, cephalexin, and phenoxymethylpenicillin,(1159) but there are no large-scale, head-to-head comparative trials available.

Evidence for the Use of Antibiotics

There are 2 high-(1177, 1178) and 5 moderate-quality RCTs(1159, 1171, 1173, 1174, 1179) incorporated in this analysis. There are 2 low-quality RCTs(862, 1175) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Antibiotics (Systemic and/or within Cement)						
Bodoky 1993 RCT	10.0	N = 239 Internal fixation with dynamic hip screw for hip fractures	Cefotiam 2gm at anesthesia induction and 12 hours later vs. placebo	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 RCT	8.0	N = 284 Any metal device inserted to be eligible (plates, screws, wires). No open fracture; no hip surgery; no joint replacements	Cefamandole 2gm IV 30 minutes before, 2gm 2 hours after start of operation, 1gm IV or IM 8, 14, and 20 hours later vs. placebo	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 RCT	7.0	N = 30 67% OA, 10% fracture	Hip replacement using antibiotic-loaded acrylic cement containing 0.5g vs. 1.0g gentamicin base/ 40g polymer powder. No systemic antibiotics.	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.

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McQueen 1987 RCT	4.5	N = 295 Hip or knee arthro-plasties	Cefuroxime in bone cement (1.5g mixed in 40gm CMW cement powder) vs. cefuroxime 1.5gm IV at induction and 750mg Q6 hour x 2	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 Ten-Year Survey RCT	4.0	N = 1688 85% OA, 6.8% fracture, 4.1% RA	Prophylaxis with systematic antibiotics (not standardized) vs. gentamicin bone cement	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 Five-Year Survey RCT	4.0	N = 1,688 85% OA, 6.8% fracture, 4.1% RA	Prophylaxis with systematic antibiotics (not standardized) vs. gentamicin bone cement	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 RCT	4.0	N = 1,685 85% OA, 6.8% fracture, 4.1% RA	Prophylaxis with systematic antibiotics (not standardized) vs. gentamicin bone cement	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.

Infected Prostheses

An infected prosthesis is an occasionally serious outcome as it usually requires surgical debridement and drainage followed by gram stain, culture, and sensitivity to determine the causative organism. Treatment frequently necessitates prolonged IV antibiotics, and multiple surgical procedures. Some patients will

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require removal of the implanted hardware. These events can occur years after surgery and require referral back to the treating surgeon.

Dislocations
Dislocations are among the most common post-operative complications.(1044, 1180) A quality trial on earlier removal of activity restrictions did not increase the rate of dislocation (see post-operative rehabilitation below).(1181) There currently is insufficient evidence to conclude how best to reduce incidence of dislocations, although there are recommendations on how to approach recurrent dislocations.(1080-1085, 1180, 1182) Dislocations usually require referral back to the treating surgeon.

Prosthetic Failure
Prosthetic failures are associated with increased morbidity and decreased satisfaction.(1183) There are two major types of prosthetic failure – the most important is loosening; the other is prosthetic articular surface wear. The risks for these types of failure appear dissimilar.

The vast majority of RCTs reporting findings of loosening of prosthesis do not report activity levels. Thus, a potentially important confounder appears ignored in the bulk of the available higher quality literature. Additionally, there are no quality RCTs of exercise and long-term risks for loosening, thus there is a primary reliance on observational studies for inference on risks of prosthetic failures related to activity levels.

There have been suggestions that arthroplasty wear and loosening is related to functional use(1184-1189) and obesity(1172, 1187) rather than time.(1184-1187, 1190) Types of wear have been categorized as Mode-1 between the two surfaces as intended, Mode-2 with wear against an unintended secondary surface such as penetration through the acetabular shell, Mode-3 with wear accelerated by the presence of third bodies (e.g., bone cement) in the articulation, and Mode-4 involves two non-primary surfaces rubbing together, although most wear is believed to be Mode-1.(1184) Purported risk factors for wear are thought to include younger age,(1172) male gender,(1185, 1191) height, weight,(1172, 1185) and hip center of rotation.(1185) Additional potential risks are listed in Table 9. One non-randomized study reported higher wear for Hylamer®; however, the results appear confounded by the strong propensity for the selection of that product for their younger more active patients(1185) and thus that conclusion may not be valid (see post-operative rehabilitation).

Table 9. Purported Risks for Hip Revision

Purported Risks for Hip Revision*
Younger age
Male gender
Heavy weight
History of heavy smoking**
Diabetes mellitus
Prosthesis due to femoral neck fracture
Inhaled pulmonary steroid use
Systemic steroid use
Preoperative regular exercise among males
Females performing heavy work
Inhaled pulmonary steroid use

*This list is designed to be more inclusive. The level of evidence supporting each of these factors varies from weak to moderate.
**Current smoking was not a risk.(1172) This is a footnote.

Hemiarthroplasty
Hemiarthroplasty is most commonly performed for fracture of the proximal femur(1004) and is reviewed in the section on hip fractures above.

PRE-OPERATIVE EDUCATION

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Educational interventions have been utilized for rehabilitation of patients with hip pain, particularly for pre-operative preparation.(1192-1194) These interventions may include various combinations of procedural, sensory information, cognitive coping strategies, reassurance, and relaxation and hypnosis training.(1195, 1196) Multiple modes of instruction are frequently incorporated, including oral, written, and video.

Recommendation: Pre-operative Educational Program Prior to Hip Arthroplasty
A pre-operative educational program is moderately recommended prior to hip arthroplasty. Components should include procedural and recovery information and use at least two modes of teaching (e.g., oral and written).

Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation
Most studies of educational interventions for rehabilitation of hip pain patients have demonstrated benefits (see pre-operative education evidence table). Lengths of contact have ranged widely, although most studies do not report educational contact time. Some programs encourage involvement of family members and other care givers. Better post-operative compliance with rehabilitation has been shown.(1197) A number of studies have combined exercises and other interventions with the educational interventions. However, nearly all studies reporting length of hospital stay have shown earlier discharge from a hospital after hip arthroplasty for the educational interventions,(1192-1194, 1198, 1199) while others have shown earlier performance of activities such as stair climbing.(1200) Other studies have suggested reductions in pain and anxiety.(1201)

Evidence for the Use of Pre-operative Education Prior to Hip Arthroplasty
There are 12 moderate-quality RCTs(266, 1193, 1194, 1196-1204) incorporated in this analysis. There are 5 low-quality RCTs(1192, 1205-1208) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Giraudet-Le Quintrec 2003 RCT	6.5	N = 100 THR	Group 1 attended a ½ day collective multidisciplinary information session 2 to 6 weeks before surgery vs. controls who did not attend.	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 RCT	5.5	N = 50 THR	"Conventional" rehabilitation augmented by stay at rehab center (control group, CG) vs. pre-op and post-op education program and home visits from outpatient team.	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.

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Mancuso 2008 RCT	5.5	N = 177 THR N = 143 TKR	Two RCTs for patients undergoing THA or TKA. Controls received standard class vs. intervention (standard class plus additional information focusing on expectations of recovery during 12 months after surgery).	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 RCT	5.0	N = 60 THR patients, all thrust plate prostheses	Pre-operative physiotherapy (strengthen limbs and hip ROM for 8 weeks) plus educational program vs. no intervention prior to surgery	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, but all 5 functional post-op measures favor exercise.
Wong 1985 RCT	5.0	N = 98 THR	Intervention group (pre-operative teaching that combined educational and behavioral strategies by a research assistant) vs. control group	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 RCT	5.0	N = 222 47% THR 53% TKR	Slide-tape with post-operative inpatient rehabilitation (Information) vs. Benson's Relaxation Response with bedside audiotape (Relaxation) vs. both vs. neither	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	"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	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

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				from educational interventions.	psychological testing for denial and anxiety."	negative for differences between the groups).
Vukomanovic 2008 RCT	4.5	N = 45 THR	Study group vs. control group (with and without pre-operative education and physical therapy)	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.
Butler 1996 RCT	4.5	N = 132 THR	Total hip replacement educational booklet vs. no booklet	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 exercises prior to hospitalization, and required significantly less occupational therapy and physiotherapy while in hospital."	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.
Pour 2007 RCT	4.5	N = 100 THR, uncemented, proximally coated tapered stem (Accolade) and plasma-sprayed acetabular component (Trident)	Group A standard incision (>10cm), standard pre-op/ post-op care (2-3 days PCA analgesia). Group-B small incision (≤10cm), standard pre-op/ post-op protocols. Group-C standard incision but pre-op counseling, accelerated rehab, altered pain control regimen (OxyContin 5mg Q4-6 hour. PRN plus	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 (mg): 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.

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			celecoxib 200mg a day. Group-D small incision, pre-op counseling, accelerated rehab,altered pain control regimen.			
Gammon Intl J Nurs Stud 1996 RCT	4.0	N = 82 All pre-surgery THA patients	Educational program (procedural, sensory and coping information) vs. usual education (usual advice by ward, medical and nursing staff)	Length of hospitalization 14 vs. 17 days (p <0.001). Intramuscular analgesia doses favored intervention (2 vs. 4, p <0.001). Mobilization, breathing exercise frequency, exercise frequencies all favored intervention (p <0.05). No differences in post-op complications or oral analgesic doses. Patient assessments of ability to cope favored intervention (6.6 vs. 4.1, p <0.001).	"[P]reparatory information, given pre-operatively, post-operatively and pre-discharge had positive effects on the physical recovery and coping outcomes measured."	Quasi-randomized every other patient. Suggested benefits of more focused information on arthroplasty and recovery processes.
Gammon J Adv Nurs 1996 RCT	4.0	N = 82 All pre-surgery THA patients	Educational program (procedural, sensory and coping information) vs. usual education (usual advice by ward, medical and nursing staff)	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 RCT	4.0	N = 105 Hip or knee OA	Group receiving program, "Living with osteoarthritis of the hip or knee" consisted of 6 weekly sessions of 2 hours, including health education by a peer and physical exercise taught by physical therapist vs. group without intervention.	Significant MANOVA group x time effects (p < 0.05, 1-sided) found for pain, quality of life, strength of left M. quadriceps, knowledge, self-efficacy, BMI, physically active lifestyle, and visits to physical therapist. Most effects negative; those positive were moderate at post-test assessment and smaller at followup. No effects for ROM and functional tasks.	"[T]his self-management program was reasonably effective in terms of the educational and exercise components. However, future interventions should pay more attention to proactive follow up interventions such as telephone follow up."	Stratification by hip or knee OA not performed. Most results negative and those positive were mild.

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Venous thromboembolic disease (VTED) is a high-risk complication among post-operative hip or knee arthroplasty patients resulting in morbidity and mortality. Reported risk factors in these post-operative patients include age, general anesthesia, and obesity. There has been some review of risk of VTED from cement; however, the evidence conflicts.(1209, 1210) Treatments have included early ambulation (discussed elsewhere), compression boots, and medications. There are currently four classes of medications used to prevent VTED: warfarin/coumadin, low molecular weight heparin, Factor Xa inhibitors, and direct thrombin inhibitors.(1211) Of these options, all are currently available in the U.S. with the exception of no oral direct thrombin inhibitor. While initially believed to be a complication of hospitalization, post-hospital discharge surveillance data suggest high risk of thromboembolism continues well after discharge(1212) with many studies treating patients for 30 days for longer.

1. *Recommendation: Prevention of Venous Thromboembolic Disease*
   Prevention of venous thromboembolic disease is strongly recommended for post-operative hip patients, particularly arthroplasty patients or other post-operative patients with prolonged reductions in activity. Early ambulation is recommended.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

2. *Recommendation: Compressions Stockings for Prevention of Venous Thromboembolic Disease*
   The use of post-operative graded compression stockings is moderately recommended for the prevention of venous thromboembolic disease.(1213, 1214)

   Indications – All 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).

   Duration – Duration of treatment is unclear and longer use does not add expense. As risk of VTED is high, particularly for these major procedures, threshold for use of 2 weeks or longer should be generally low.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

3. *Recommendation: Lower Extremity Pumps for Prevention of Venous Thromboembolic Disease*
   The use of lower extremity pump devices is moderately recommended for the prevention of venous thromboembolic disease.(1215-1217)

   Indications – All 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).

   Devices – Devices include foot pumps, foot plus calf pumps, entire lower extremity intermittent compression devices and various other combinations. As there are no quality comparative trials, there is no recommendation for a particular device.

   Duration – Duration of treatment is unclear. Most have utilized devices for the duration of hospitalization. As risk of VTED is high particularly for these major procedures, threshold for use of 2 weeks or longer should be generally low including while at home.

   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. Some patients are also unable to tolerate devices.(1218)

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

4. *Recommendation: Low-molecular Weight Heparin for Prevention of Venous Thromboembolic Disease*
   Low-molecular weight heparin is strongly 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.(1213, 1219-1230) There is some evidence LMWH is generally preferable to warfarin for VTED prophylaxis. Patients with prior reactions to LMWH should generally receive other treatments first.

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Dose/Frequency – Subcutaneous injections of enoxaparin (Lovenox) 4,000 IU or 40mg SC QD(1213, 1219, 1220, 1222, 1227, 1231-1236) for variable durations ranging from 5 to 9 postoperative days(1234-1236) to 8 to 14 days(1233) to 10 to 14 days,(1231) 21 days,(1219, 1220) 30 days,(1227) to 12 weeks.(1222) There is no consensus on duration of treatment, and individualization based on activity level appears indicated.

Duration – Duration unclear. Available quality studies utilized treatment courses ranging from 4 days(1226) to 12 weeks.(1222) A plurality of the studies utilized a course of 30 to 35 days.(1224, 1225, 1227, 1228) There is quality evidence that treatment is generally required beyond hospitalization; there is evidence of deep venous thromboses many months later (reviewed above). One quality trial suggested no benefits from extending 4 to 10 days treatment out to 12 weeks.(1223) In the absence of substantive quality data comparing various durations of treatment, it is suggested that approximately 30 days of treatment after surgery may be required for average patients (a single trial suggested 30 to 42 days after arthroplasty).(1212) Patients with prior histories of venous thrombi, prolonged inactivity, delayed recovery or recurrences of thromboses, or family histories of venous thrombi likely require longer courses. Those with major risk of bleeding may warrant individualized shorter courses. Patients who regain activity rapidly may be appropriate candidates for shorter courses of treatment.

Indications for Discontinuation – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

Strength of Evidence – **Strongly Recommended, Evidence (A)**

5. *Recommendation: Factor Xa Inhibitors for Prevention of Venous Thromboembolic Disease*
   Factor Xa inhibitors are strongly 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.(1210, 1237-1239) 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.

   Dose/Frequency – Subcutaneous injections of Fondaparinux (Arixtra) 2.5mg SC QD. Currently Rivaroxaban (Xarelto) is investigational in the U.S.

   Duration – The recommended duration of a course of treatment is unclear. The literature suggests duration be individualized based largely on factors such as prolonged inactivity, delayed recovery or thrombotic recurrences, prior history and risks of bleeding.

   Indications for Discontinuation – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

6. *Recommendation: Warfarin and Heparin for Prevention of Venous Thromboembolic Disease*
   Warfarin and heparin are moderately recommended for prevention of venous thromboembolic disease.

   Indications – Post-operative arthroplasty patients, hip fracture patients and other major hip surgery patients.(1240, 1241) Patients with adverse reactions to warfarin may be maintained on heparin throughout the treatment course. Patients with reactions to heparin, but at increased risk of thrombosis may be begun on the other agents and switched to warfarin.

   Dose/Frequency – Subcutaneous injections of Heparin, which can be titrated to the activated partial thromboplastin time (aPTT). Warfarin dose titrated to International Normalized Ratio (INR). Magnitude of anticoagulation is recommended to be individualized, and include risks of thrombi versus risks of bleeding and it is notable that the quality studies utilized a range of INRs.

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Duration – The recommended duration of a course of treatment is unclear. The literature suggests duration be individualized based largely on factors such as prolonged inactivity, delayed recovery or thrombotic recurrences, prior history and risks of bleeding.

Indications for Discontinuation – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

7. *Recommendation: Prevention of Venous Thromboembolic Disease*
   Aspirin is moderately recommended for the prevention of deep venous thrombosis.
   Indications – Post-operative arthroplasty patients, hip fracture patients and other major hip surgery patients, particularly after cessation of other treatments such as LMWH, heparin, or other anticoagulants.(1242)

   Dose/Frequency – Aspirin 160mg per day was used in the PEP trial. Other studies have found 85mg/day sufficient for heart attack prevention.

   Duration – Duration of a course of treatment is unclear. One month is suggested, however due to other risk factors, prolonged or indefinite treatment may be recommended.

   Indications for Discontinuation – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendations

There are many quality studies of various means to reduce risk of venous thromboembolic disease (see venous thromboembolic disease evidence table), although various methodological issues in the available trials have been raised.(1212, 1243-1248) Graded compression stockings have been compared with no compression stockings and found to reduce risk in one moderate quality study.(1214) They also have been included in quality studies as adjunctive therapy in a trial comparing enoxaparin plus stockings vs. enoxaparin alone and found to reduce risk.(1213) Stockings are not invasive, have few adverse effects and are low cost, thus, they are moderately recommended.

Pumps have been evaluated in quality trials that have included comparisons with no pump devices, as well as in therapeutic combinations.(1215-1217) One quality study suggested superiority of pump devices to a low molecular weight heparin,(1218) while another found superiority to unfractionated heparin.(1249) Devices include foot pumps, foot plus calf pumps, entire lower extremity intermittent compression devices and various other combinations. As there are no quality comparative trials, there is no recommendation for a particular device. Pump devices are not invasive, have few adverse effects and are low cost, thus, they are moderately recommended.

Generally, major bleeding is the most significant adverse effect of most of the medications used to prevent VTED. The high or moderate quality trials are mostly underpowered to detect these events. The general trend across the medications and studies is for more bleeding in the more effective agents. This suggests individualization is needed, and among patients with a greater risk for bleeding, consideration of the agents with apparently lower risk (e.g., enoxaparin or warfarin) is suggested.

There are many quality studies of low-molecular weight heparin with the quality studies comparing treatment with placebo all suggesting benefits.(1219-1221, 1223-1230) These have shown approximately 1/3 reductions in deep venous thrombosis compared with warfarin(1250) and result in lower incidence of heparin-associated thrombocytopenia.(1251-1253) While mildly invasive and with some adverse effects, these medications are effective in reducing risk of VTED and thus are strongly recommended.

There are a few studies of Factor Xa inhibitors, with quality studies having shown Fondaparinux superiority to placebo.(1238) Additionally, these agents have been shown to be superior to enoxaparin in two quality studies,(1210, 1237) although equivalent in another.(1239) Major bleeding appears more

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common with Fondparinux than enoxaparin.(1247) While mildly invasive and with some adverse effects, these medications are effective in reducing risk of VTED and thus are strongly recommended.

The oral thrombin inhibitor, Dabigatran etexilate is investigational in the US. It appears to have a superior profile to enoxaparin for deep venous thrombosis prevention.(1235) A prior medication in this category was withdrawn due to hepatotoxicity. There is no recommendation at this point for this medication.

There is quality evidence that heparin is effective compared with placebo.(1240) However, a moderate quality study found dextran superior to subcutaneous heparin administration.(1254) Heparin may still be an option in select patients who have contraindications for using other more effective medications for VTED prevention. While mildly invasive and with some adverse effects, these medications are effective in reducing risk of VTED and thus are strongly recommended.

There also is quality evidence from the large scale PEP trial that aspirin reduces risk.(1242) However, other agents reviewed above are likely superior for DVT prevention and ASA may be best used for treatment after cessation of other anti-thrombotic therapy(ies).

Duration of prophylaxis is one of the areas of controversy.(1255) One quality study suggested a reduction if the treatment period after arthroplasty is extended to 30 to 42 days with an OR = 0.38 and NNT = 50.(1212) Another study suggested no benefits from extending treatment from 4 to 10 days out to 12 weeks.(1223) Individualization of treatment likely is required to include factors such as activity level, other joint involvement, cancer status, prior venous thromboembolism history, and bleeding risks. Onset of treatment is another area of controversy, as European surgeons initiate prophylaxis preoperatively and North American surgeons initiate prophylaxis post-operatively.(1243)

Evidence for the Prevention of Venous Thromboembolic Disease
There are 30 high-(1210, 1219-1229, 1231-1236, 1238-1241, 1256-1264) (one with 2 reports) and 57 moderate-quality(154, 1213-1218, 1230, 1237, 1242, 1249, 1254, 1265-1309) RCTs incorporated in this analysis. There are 5 low-quality studies(1310-1314) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Compression Stockings vs. No Stockings						
Hui 1996 RCT	4.0 (5.0 for TKA patients)	N = 177 Total hip or knee arthroplasties	Above vs. below-knee graded compression stocking vs. controls	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.
Compression Devices vs. None						
Hull 1990 RCT	6.5	N = 310 THR	Sequential intermittent calf and thigh compression vs placebo for 14 days. 3-month follow up. Total hip arthroplasties	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 measured	Data suggest efficacy.

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					impedance plethysmography."	
Bradley 1993 RCT	6.0	N = 74 THA	Compression foot pump vs. no foot pump post-operatively until discharge. All thigh-length compression stockings, heparin 5000 IU SC BID, hydroxychloroquine sulphate 40mg BID.	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 RCT	6.0	N = 98 THR	Intermittent foot/calf compression 1 week vs. untreated. Compression continuous day/night other than walk, PT, etc.	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.
Compression Devices vs. Other Treatment						
Robinson 1997 RCT	9.0	N = 1,024 Total hip or knee replacement	Bilateral screening compression ultrasonography vs. sham ultrasonography	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 RCT	7.0	N = 93 THR	Enoxaparin 4000 anti Xa IU SC QD vs. enoxaparin 4000 anti Xa IU SC QD plus graduated compression stockings vs. placebo	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

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						alone as well as placebo.
Bailey 1991 RCT	6.5	N = 95 THR	Low-dose warfarin (LDW) vs. sequential compression devices (SCD) after total hip arthroplasty	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 RCT	6.5	N = 200 THR	A-V impulse system foot pump vs. low molecular weight heparin (Fraxiparin). All treated with stockings.	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.
Woolson J Bone Joint Surg Am 1991;73:507-12 RCT	5.0	N = 239 THA	Thigh-high stocking with graduated elasticity, thigh-high 6 chambered boot for sequential intermittent compression vs. elastic stockings, intermittent pneumatic-compression boots, 650mg aspirin orally BID beginning evening before operation vs. elastic stockings, compression boots, 7.5 or 10mg warfarin orally evening before operation	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 treatment. Study suggests addition of ASA or warfarin not significant.
Kaempffe 1991 RCT	5.0	N = 149 Total hip or knee arthroplasty	Coumadin 10mg night before surgery, 5mg night after, then dose keeping PT = 15s vs. thigh-length intermittent pneumatic compression (IPC). Treatment duration unclear, appears to be	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	Relatively small numbers of subjects. Different clotting risk in revision THA. Data suggest equivalency.

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			during hospitalization.		thrombi in this group of patients."	
Santori 1994 RCT	5.0	N = 132 THR	Calcium heparin 5000 IU TID vs. intermittent plantar pump for 10 days. Pump used except when walking or PT.	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 .
Low Molecular Weight Heparin vs. Placebo						
Heit 2000 RCT	11.0	N = 1195 Total hip or knee arthroplasty	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 vs placebo for total hip or knee replacement from hospital discharge to 6 weeks after surgery.	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.
Planes 1996 (2 reports) RCT	10.5	N = 179 THR	Enoxaparin 40mg SC QD vs. placebo 12 hrs preop, 12 hours post-op then QD for 21±2 days	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 RCT	10.0	N = 873 Total hip or knee	Enoxaparin 40mg QD vs. placebo for 12 weeks	Prevalence of venous thromboembolism in enoxaparin 8% (18/224) vs. 23.2% (49/211) for	"[T]he recommended seven to ten-day postoperative thromboprophylactic	Suggests efficacy. Includes younger

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		replacement		placebo (p <0.001). OR = 3.62 (95% CI 2.00- 6.55), Relative risk reduction 65.5%.	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)"	patients. Stratified analyses suggest no effect in males with knee replacement. Suggests treatment for 4 weeks.
Lassen 1998 RCT	9.5	N = 281 THR	Dalteparin 40mg vs. placebo QD for 35 days	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.
Turpie 1986 RCT	9.0	N = 100 Elective hip surgery	PK10169 low-molecular-weight heparin vs placebo for 14 days	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.
Arnesen 2003 RCT	9.0	N = 265 THR	Dalteparin 5000IU vs. placebo for 35 days	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	9.0	N = 82	Low molecular weight heparin	Fourteen (14) excluded. DVTs in 30% Fragmin vs.	"Fragmin given once daily offers an	Short term study of 6

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RCT		Hip fracture surgery	(Fragmin) 2,500 IU for first 2 injections then 5000 IU antifactor Xa SC vs. placebo for 6 days	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.	effective and safe thromboprophylaxis in hip fracture surgery."	days. Unknown if co-interventions . Suggests efficacy.
Bergqvist 1996 RCT	8.5	N = 262 THR	All treated actively in hospital with enoxaparin for 7-11 days, then Enoxaparin 40mg vs placebo QD for 30 days	66/233 (28%) with DVT or PE. 39% of placebo group and 18% of enoxaparin had thromboembolism. Rehospitalization because of DVT judged necessary for 32 in placebo vs. 11 in enoxaparin group.	"[P]atients receiving prophylaxis with enoxaparin for a full month after surgery had significantly less venous thromboembolic disease (most of which was asymptomatic), including proximal deep-vein thrombosis, than patients receiving enoxaparin prophylaxis only during their hospitalizations."	Data suggest efficacy. Medications after hospital
Dahl 1997 RCT	8.5	N = 308 THR	Dalteparin 5000 IU vs. placebo QD for 4 weeks	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 replace-ment 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 RCT	8.5	N = 218 Hip arthroplasti es	Org 10172 (Lomoparan) anti-factor Xa 750U vs. placebo SC BID for 10 days	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.
RD Heparin Arthroplasty Group 1994 RCT	7.5	N = 1173 Total hip or knee arthroplasty	Anti-factor-X_a 50U of RD 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	VT disease among 8% (14 patients). RD bid heparin 3% (n = 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 patients who had a total hip arthroplasty, a fixed dose of anti-factor-Xa units of RD heparin per kilogram of body weight, administered unmonitored twice daily, beginning postoperatively, and	Accounted for medications & physical exams. Suggests comparable efficacy, although trend

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			PTT 1.2-1.5 for total hip replacement	for QD vs. warfarin.	low-dose warfarin were equally effective and safe."	towards BID heparin dosing.
Low Molecular Weight Heparin vs. Other LMWH Doses or Other Treatments						
Bara 1999 RCT	10.5	N = 440 THR	4,500IU anti-Xa tinzaparin vs. 4000IU anti-Xa (40mg) enoxaparin for 8-14 days	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 activity was significantly higher with tinzaparin. No clear relationship between these two activities and the clinical outcomes was observed."	Actual study of DVT published (Planes, et al 1999). Used much of same scoring. Most details are left out of this report.
Kakkar 2000 RCT	10.5	N = 298 Hip arthro-plasties	Bemiparin 3,500 IU SC once daily plus placebo injection (saline) vs. 5,000 IU Unfractionated heparin 5,000 IU BID 2 hours before surgery continued for at least 8 days post surgery	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.
Eriksson Circulation 2006 RCT	10.5	N = 873 THR	Phase 2 study. Oral rivaroxaban 5, 10, 20, 30, or 40mg once daily vs subcutaneous enoxaparin 40mg once daily for 5-9 days after totally hip replacement.	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.
Eriksson J Thromb Haemost 2006 RCT	10.5	N = 722 THR	Oral BAY 59-7939 2.5, 5, 10, 20, or 30mg BID vs. enoxaparin 40mg QD for 5-9 days after	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	"[I]n patients at high risk for developing thrombosis and bleeding, direct FXa inhibition with BAY-59-7939 was effective	Data suggest comparable efficacy.

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			surgery	bleeding not different (NS).	across the dose range studied, and compared favorably with enoxaparin; safety was similar between BAY 59-7939 2.5-10mg twice daily and enoxaparin."	
Adolf 1999 RCT	9.5	N = 172 THR	Certoparin 3,000 IU aXa vs. 5,000 IU aXa low molecular weight heparin daily 12-14 days	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.
Levine 1991 RCT	9.5	N = 669 Hip replacement	Low molecular weight heparin 30mg vs. standard calcium heparin 7,500U SC BID. First dose 12-24 hours after surgery continued for 14 days or until 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 RCT	9.5	N = 136 THR	Low molecular weight heparin 5000 IU SC QD vs. unfractionated heparin 5000U TID for 10 days	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 patients who received low-molecular-weight heparin."	Medications not mentioned. Data suggest LMWH superior.
Planes 1998 RCT	8.5	N = 498 THA	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.	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.

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Spiro 1994 RCT	8.5	N = 572 Hip replacements	10mg enoxaparin QD vs. 40mg enoxaparin QD vs. 30mg enoxaparin every 12 hours, all subcutaneous injections with 1st dose within 24 hours before surgery and continued up to 7 days	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.
Hull 1993 RCT	8.5	N = 795 Hip surgery patients N = 641 Knee arthroplasty patients	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.	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 RCT	8.0	N = 641 THA	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	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.

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			surgery.			
Leyvraz 1991 RCT	7.0	N = 409 THR	Unfractionated heparin subcutaneous injections at intervals of 8 hours, 1st dose "4.0 IU" then injections adjusted based on patient's activated thromboplastin time (increased or decreased by 500 IU) vs. low molecular weight heparin one injection of 41 IU/kg for first 3 days then increased to 62 IU/kg from days 4-9, 10, or 11.	12.6% of low molecular weight heparin group vs. 16% unfractionated heparin group developed DVT, p = 0.45. Proximal thrombi in 2.9% LMWH vs. 13.1% heparin (p <0.001).More injection site hematomas in unfractionated heparin group, p = 0.001.	"[T]he low molecular weight heparin Fraxiparine, with the dose adjusted for body weight and given subcutaneously once a day, is at least as efficacious and safe in the prevention of total deep vein thrombosis after elective hip replacement as individually adjusted unfractionated heparin give thrice daily. In addition, the low molecular weight heparin was significantly more efficacious in preventing deep vein thrombosis of proximal veins and is simpler to use than unfractionated heparin."	Data suggest LMWH superior to unfractionate d for reduced proximal DVT.
Samama 2002 RCT	7.0	N = 1,279 THR	Fixed-dose subcutaneous low-molecular-weight heparin or adjusted-dose oral anticoagulant (acenocoumarol) for 6 weeks	Failure rate reviparin (4.2%) lower than acenocoumarol (10.3%). Low-molecular-weight heparin with fewer bleeding complications (p = 0.0001).	"[T]he extended use of low-molecular-weight heparin given in a single subcutaneous injection per day is superior to acenocoumarol prophylaxis in patients undergoing elective hip surgery and that it avoids the need to monitor the level of anticoagulation."	Clinically significant events – more "real world." Sufficient power to find differences. Suggests LMWH superior.
Kalodiki 1996 RCT	7.0	N = 93 THR	Enoxaparin 4,000 anti Xa IU SC QD vs. enoxaparin 4000 anti Xa IU SC QD plus graduated compression stockings vs. placebo	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. Data suggest enoxaparin plus stockings superior to medication alone, as

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						well as placebo.
Dechavanne 1989 RCT	6.5	N = 124 Elective hip surgery	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	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.
Yoo 1997 RCT	5.5	N = 100 THR	Low molecular weight heparin, nadroparin calcium 41 IU/kg initial dose through 3rd day then 65 IU/kg vs. no prophylaxis pre-operatively, 10 days post-op	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.
Avikainen 1995 RCT	5.0	N = 167 THR	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	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 2006 RCT	5.0	N = 100 THA	Enoxaparin 40mg SC QD 12 hours pre-op vs. 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	DVT in 2 enoxaparin vs. 0 heparin (NS), 0 late DVT in enoxaparin vs. 2 heparin (NS). No differences in complications and blood loss.	"[L]ow molecular weight heparin (Enoxaparin) was found to be as safe and as effective as standard heparin in the prophylaxis of DVT in patients undergoing elective hip arthroplasty."	Some details sparse. Blinding unknown. Compliance and dropouts unclear. Underpowered.
Borris 1991 RCT	5.0	N = 246 THR	Enoxaparin 40mg SC QD for 8 days starting 12 hours after surgery vs. dextran 70 (60mg) IV starting during anesthetic induction, 2nd	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	"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	Lack of power in enoxaparin - no decision on usefulness of D-dimer. Article mainly on association

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			dose 6 hours later, and 3rd and 4th on Days 1 and 3 post-op	DVTs in favor of enoxaparin (p <0.01).	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."	between blood tests and DVT for mechanism hypothesis generation.
Colwell 1999 RCT	5.0	N = 3,011 THR	Enoxaparin 30mg SC vs. warfarin dose adjusted to INR 2.0-3.0 for 14 days after surgery; 3-month follow-up	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 patients (10%). DVT was found in 0.1% of enoxaparin group and 1% of the warfarin group.	"[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 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."	Warfarin allowed. Blinding unknown. Some differences at baseline. Variable dosing intervals results in questions regarding conclusions of relative efficacy.
Menzin 1994 RCT	4.0	N = 607 THR	Enoxaparin 30mg q12 hour vs. enoxaparin 40mg QD vs. unfractionated heparin 5,000 U q8hour for 7 post-operative 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.
Heparin vs. Placebo						
Beisaw 1988	11.0	N = 148 THA	Dihydro-ergotamine 0.5mg and	128 patients completed the study; 52.3% placebo vs. 25.4%	"[T]he combination agent dihydroergotamine	Heparin appears more

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RCT			heparin sodium 5,000 units vs. placebo of lidocaine hydrochloride for 7-9 days	dihydroergotamine mesylate/heparin sodium developed DVT, p = 0.0021. No PEs.	mesylate/heparin sodium was effective and safe prophylaxis against deep-vein thrombosis for the patients who underwent total hip replacement in this study."	effective for reducing proximal thrombi; thought more clinically useful. Intent to treat done on efficacy study, not safety.
Westrich 2005 RCT	9.0	N = 165 THA	Unfractionated heparin 1 IV dose intra-operative before femoral preparation vs. IV saline. Both treated with elastic stockings and 325mg aspirin BID 1 month.	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.
Bergqvist 1979 RCT	5.0	N = 80 Hip fracture N = 220 Hip surgery including 213 THA	Heparin 5,000 IU SC 1 hour before surgery and 5,000 IU SC Q12 hour 5 days vs. dextran 70 500ml during operation, 500ml right after operation; 500ml on 1st and 3rd post-op days vs. no treatment controls	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.
Heparin vs. Other Treatments						
Kakkar 1979 RCT	5.0	N = 300 Major abdominal surgery, 100 THR	Abdominal surgery trial: dihydroergot-amine mesylate vs. heparin 5000 IU SC. Second trial: 5,000 IU heparin calcium vs. 5,000 IU heparin calcium plus 0.5mg dihydroergotamin e mesylate 2 hours before surgery and Q8 hours 7 post-op days or longer if confined to bed.	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 dihydroergot amine in abdominal surgery and combination better than heparin alone for THR.
Factor Xa Inhibitors vs. Placebo						

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Eriksson Arch Intern Med 2003 RCT	10.0	N = 656 Hip fracture surgery	Fondaparinux sodium 2.5mg SC vs. placebo for 19-23 days after total hip replacement	Venous thromboembolic incidence of 35% (77/220) on placebo vs. 1.4% (3/208) with fondaparinux. Relative 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).	"[E]xtended prophylaxis with fondaparinux for 3 weeks after hip fracture surgery reduced the risk of VTE by 96% and was well tolerated."	Suggests efficacy. Few exclusions except for drug safety. Physical exam not allowed. Appears to include ITT, but not labeled such in report.
Factor Xa Inhibitor vs. Other Treatments						
Agnelli 2007 RCT	10.5	N = 511 Total hip or knee replacements	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.	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 RCT	10.0	N = 2079 THR	Desirudin 15mg SC BID, first injection 30 minutes before surgery vs. enoxaparin 40mg QD, first injection evening before surgery. Both 8-12 days treatment.	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.

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Eriksson 2001 RCT	7.0	N = 1711 Hip fracture surgery	Fondaparinux 2.5mg QD vs. enoxaparin 40mg QD for at least 5 days after surgery	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
Warfarin vs. Aspirin vs. Placebo						
Powers 1989 RCT	8.5	N = 194 Hip fracture	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	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.
Dermatan Sulphate vs. Placebo						
Agnelli 1992 RCT	9.5	Phase 1: N = 80 Phase 2: N = 126 Hip fracture	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	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 701 group, 63.9% of placebo group developed DVT (p = 0.01). 3 patients died, 2 in hospital, 1 during follow-up.	"[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 resulting in side effects. Our study also provides evidence of the biological role of HC II."	Some co-interventions . Phase 1 and 2 studies. Trend towards more DVT in active treatment group in one study and towards placebo in other.
Aprotinin vs. Placebo						
Eriksson J Thromb Haemost 2003 RCT	9.0	N = 2,835 Total hip or knee replacemen t	Melagatran/ ximelagatran 2mg SC immediately before surgery and 3mg melagatran evening after surgery followed by 24mg ximelagatran orally vs. enoxaparin 40mg	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	"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/xi melagatran superior.

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			SC QD 12 hours before surgery. Both treatments 8-11 days.	(66.8% vs. 61.7%) and somewhat higher blood loss (geometric mean 1,014mL vs. 913mL) with ximelagatran.		
Hayes 1996 RCT	7.0	N = 40 THR	Aprotinin 2M KIU vs. placebo over 20 minutes. All received enoxaparin and stockings.	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.
Varying Heparin Doses						
Colwell 1994 RCT	6.0	N = 610 THR	Enoxaparin 30mg Q 12 hours. vs 40mg QD vs. unfractionated heparin 5,000U Q 8 hours after surgery	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.
Leyvraz 1983 RCT	5.5	N = 96 THR	Heparin 3,500 IU SC Q 8 hour vs. adjusted dose by PTT for 8 days	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.
Huo 1992 RCT	5.0	N = 286 THA	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	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.

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			plus 500U before femoral canal prep) during surgery. All ASA 325mg BID post-op.			
Durations and Doses of Warfarin						
Schulman 1995 RCT	7.5	N = 897 First episode of venous thrombo-embolism	Warfarin 6 weeks vs. 6 months oral anticoagulant targeting INR 2.0-2.85	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.
Hull 1979 RCT	7.0	N = 68 THR	Adjusted-dose warfarin sodium 10mg (1.5-2x) vs. low-dose subcutaneous heparin 5,000IU (PTT to 1.5-2 times) after surgery for 14 days with 12 week follow up	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 RCT	7.0	N = 290 Idiopathic DVT patients	Warfarin 3 months vs. 1 year. INR 2.0-3.0.	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.

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Bern 2002 RCT	7.0	N = 98 Unilateral hip replace-ment or degenerativ e joint disease	Warfarin 1mg QD vs. variable dose warfarin 7 days pre-operatively continued until discharge	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.
Pinede 2001 RCT	6.5	N = 736 DVT or PE	Warfarin 6 weeks for isolated calf deep vein thrombosis (C-DVT) vs. 3 to 6 month warfarin for proximal DVT (P-DVT) or for pulmonary embolism (PE), INR 2.0-3.0	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 recurrence, other trials are necessary to assess prolonged therapy beyond 6 months."	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.
Vives 2001 RCT	5.5	N = 245 Total hip or knee arthroplasti es	Fixed minidose warfarin 2mg a day vs. adjusted higher dose warfarin with target PT range of 14 to 16 seconds (INR 1.4 - 1.8); both taken for 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	Study thrust to reduce warfarin to oviate need for testing. Conclude that need to monitor on low dose as well.

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					to outpatient thromboembolic prophylaxis after total joint arthroplasty. The efficacy of the fixed minidose regimen appears similar to that of adjusted-dose warfarin."	
Campbell 2007 RCT	5.0	N = 810 DVT and/or PE	Three months warfarin vs. 6 months warfarin with an INR between 2.0 and 3.5	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 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).	"For patients in the UK with deep vein thrombosis or pulmonary embolism and no known risk factors for 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."	Uneven follow-up and treating physicians. Bias not discussed. No blinding. No clear advantage of 6 vs. 3 months. May have excluded many orthopedic patients.
Miscellaneous						
Colwell 2003 RCT	7.5	N = 1,557 THR	Ximelagatran 24mg vs. enoxaparin 30mg SC BID for 7-12 days	[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.
Pulmonary Embolism Prevention (PEP) Trial 2000 RCT	7.0	N = 13,356 hip fracture surgeries plus 4,088 arthroplasty patients	ASA 160mg QD vs. placebo for 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 venous and arterial events.
Defibrinating Enzyme vs. Placebo						
Belch 1982 RCT	7.5	N = 73 THR	Daily subcutaneous injections of ancrod 280 U vs. saline injections immediately post-op, then 70U QD for 8 days	Calf DVT in Ancrod (24/62) vs. placebo (21/72) (NS). Major femoral DVT in 5/62 vs. 18/72 (p<0.01). DVT length lower with Ancrod. 3 in Ancrod with PTE vs. 1 in saline.	"[A]ncrod has been shown to protect patients undergoing hip replacement from major femoral DVT."	Small study for DVT risks. Concealment / compliance unclear. Suggests some efficacy, though not for total

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						DVTs.
Perhoniemi 1996 RCT	7.0	N = 165 Hip or knee replacement or remural fractures	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 operation.	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 RCT	7.0	N = 1,119 THR	10, 15, or 20mg CGP 39393 twice daily vs. 5,000 IU unfractionated porcine heparin TID right before surgery and for 8-11 days	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 significant. No differences in blood loss.	"[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.
Francis 1992 RCT	7.0	N = 232 THR	Warfarin 10-14 days before operation on 2-step regimen with dose adjustments for 6-8 days vs. EPC (external pneumatic compression) with 11 second inflation cycle and 60 second deflation cycle. Treatment until venography 6-8 days	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.
Sørensen 1990 RCT	6.5	N = 70 THR	LMWH Logiparin 50 anti-Xa U/kg SC QD vs. placebo for 7 days. Both groups with and without DVT.	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	"[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

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				<0.001) due to high levels Days 3, 5, 7 vs. Days -1 and 1.		to assess baseline comparability.
Manganelli 1998 RCT	6.5	N = 61 THR	Short-term prophylaxis (subcutaneous UH 15,000 IU/24 hours for 15 days vs. 30days	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.
Gerhart 1991 RCT	6.5	N = 289 Hip fracture surgery	Org 10172 (Lomoparan) 750 U SC pre-op and Q12 hour until 9th post-op day plus warfarin on 7th post-op day until discharge vs. warfarin orally until hospital discharge	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.
Cohen 1994 RCT	6.5	N = 195 THA	Dermatin sulphate 200mg QD vs. BID vs. 300mg BID for 10 days	DVT in 53% vs. 51% vs. 34%, p = 0.06. Incidence of major DVT was 21%, 19% and 8.5%, p = 0.095. Proximal major DVT in 11%, 8.5% and 2.1%, p = 0.11.	"In preventing thromboembolism, a dose response was seen. The highest dose, 300 mg twice daily, was most effective and the two lower doses seem to be subtherapeutic in terms of overall thrombosis rate."	Physical not addressed. No placebo. Suggests higher dose more effective.
Hamulyak 1995 RCT	6.5	N = 672 Total hip or knee replacement	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 vs. low molecular weight heparin (LMWH, nadroparine) SC Q24 hour (about 60 IU of antifactor Xa (AXa)/kg), 0.3ml for patients	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.

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			weighing <60kg, 0.4ml for those 60-80kg, 0.6ml for patients weighing >80kg, for 10 days			
Schmidt 2003 RCT	6.0	N = 346 1º or 2º THR and TKR	Prolonged prophylaxis nadroparine 2500-4,000 IU between Day 11 and Day 35 vs. sonographic screening for DVT before Day 10	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.
Comp 1998 RCT	6.0	N = 488 THR	Danaparoid 750 anti-Xa units SC vs. Warfarin 10mg until hospital discharge	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.
Planes 1991 RCT	6.0	N = 188 THR	(I) Spinal anesthesia and no injection of enoxaparin vs (I) spinal anesthesia and enoxaparin 20mg vs. (III) general anesthesia and enoxaparin 40mg	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 RCT	6.0	N = 102 THR	Heparin sodium as 3 SC injections Q24 hour except day of admission given 4,000 IU at 2pm and 10pm. Doses adjusted after each APT	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.

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			determination vs. 2 SC doses Q 24 hour combination heparin plus DHE (5,000 IU heparin sodium plus 0.5mg dihydroergotamine mesylate plus 7mg lidocaine hydrochloride) with first dose 6pm day of admission.			
Flicoteaux 1977 RCT	6.0	N = 40 THR	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	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.
Fredin 1985 RCT	6.0	N = 70 Hip fracture surgery	Dihydro-ergotamine 0.5mg SC soon as hip fracture diagnosed and BID until Day 5 vs. no dihydroergotamine. All received Dextran 70 500mL (first infusion soon as hip fracture diagnosed; if necessary 500ml QOD until surgical day. During operation, 500ml Dextran 70, post-operatively within 12 hours. Post-operative days 1, 3, and 5).	DVTs in 5/27 (19%) controls vs. 10/28 (36%) dextran plus dihydroergotamine (NS). Higher number of patients with PE in combination group. 2 patients died.	"[T]he incidence of thromboembolic complications is high among patients with hip fracture and should be combated by prophylactic treatment. Peroral anticoagulants, dextran 70 and low dose heparin have been found effective in this respect. Use of a combination of dextran 70 and dihydroergotamine, which was evaluated in the present study, did not give results superior to those from dextran 70 alone."	Small numbers, underpowered. Trend is towards dihydroergo-tamine increasing DVT risk.
Francis 1997 RCT	6.0	N = 580 THA	Dalteparin sodium 1st dose 2,500 IU SC 2 hours before operation then 5,000 IU QD 1st post-op day until	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	Some baseline differences. Co-interventions unknown. Suggests

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			venography (about 7th post-op day) vs. warfarin sodium 1st dose orally evening before operation, patients weighing ≤57kg received 5mg, patients weighing >57kgs 7.5mg, daily doses adjusted to maintain INR 2.5.		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."	pre- and early post-operative dalteparin superior to warfarin.
Eriksson 1988 RCT	5.5	N = 113 THR	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 vs. dextran 70, 500ml during operation, 500ml within 6 hours post-operatively, then 500ml 1st and 3rd post-op days	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.
Kim 1998 RCT	5.0	N = 150 THR; some trauma	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	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.
Hogevold 1991 RCT	4.0	N = 50 Total hip protheses	Methyl-prednisolone 30mg/kg 1.5 hours pre-op and 4 hours and 12 hours post-operatively vs. no steroids	No clinical signs of DVT or PE during first 3 postoperative weeks. 2 with normal venograms on 2nd day after surgery developed clinically and venographically evident DVT 21 and 38 days post-operatively.	"[A]fter total hip replacement there is a high incidence of asymptomatic DVT before the 2nd postoperative day despite dextran prophylaxis. However, all thrombi were localized distally in the leg. Treatment with high dose corticosteroids did not influence the incidence or localisation of the thrombi."	Sparse methods, including compliance, dropouts. Data suggest glucocortico-steroids ineffective.
Zanasi	4.0	N = 63	Defibrotide vs.	"Although the size of the	"[T]he effectiveness of	Sparse

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1988 RCT		Most hip surgery; some trauma	calcium heparin and ASA for 8 days	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."	defibrotide in preventing DVT in patients recovering for orthopedic surgery is approximately equal to that of established treatments such as calcium heparin and ASA."	methods and details. Heterogeneous patients. Little baseline data. Underpowered.
Barber 1977 RCT	4.0	N = 128 THR	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, 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.	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.

PRE- AND POST-OPERATIVE REHABILITATION, INCLUDING HIP ARTHROPLASTY AND HIP FRACTURES

Numerous studies have evaluated post-operative rehabilitation and activity levels that appear important for recovery from hip procedures, especially for arthroplasty and hip fracture patients(1315, 1316) (see post-operative rehabilitation evidence table). Considerations have included pre-operative exercise programs, post-operative activity limitations, post-operative rehabilitation programs and late rehabilitation programs several months after surgery.(1317) 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.

PRE-OPERATIVE EXERCISE PROGRAMS

Pre-operative exercise programs have been prescribed to attempt to improve arthroplasty results and reduce complications.(230, 1200, 1203, 1318-1323)

Recommendation: Pre-operative Exercise Program

A pre-operative exercise program particularly emphasizing cardiovascular fitness and strengthening is moderately recommended, especially for patients who exhibit evidence of weakness or unsteady gait. Flexibility components may be reasonable in those without fixed deficits.(1200, 1320, 1322)

Indications – Pre-operative arthroplasty patients, particularly those with weakness or unsteady gait.

Frequency/Duration – Most program elements require an initial appointment to teach exercises followed by a home exercise program prescription. Two or three follow-up appointments for adherence and additional exercise instruction may be needed. Patients with severe deficits may require 2 to 3

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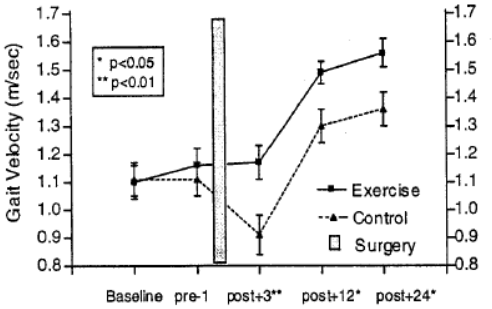
appointments a week for 4 to 6 weeks in advance of arthroplasty.(1322) Those with minimal deficits may benefit from a single appointment to teach programmatic elements for a self-directed program.

Indications for Discontinuation – Achievement of program goals, resolution of strength or gait deficits, intolerance or other adverse effects.

Strength of Evidence **- Moderately Recommended, Evidence (B)**

Rationale for Recommendation
A moderate-quality study demonstrated there were benefits from a 6-week pre-operative exercise program that consisted of several elements broadly including cardiovascular, strengthening and flexibility exercises with 30-60-minute sessions three times a week.(1322) The benefits included reduced post-operative complications, earlier discharge and higher probability to be discharged directly to the patient's home. A second moderate-quality study also demonstrated benefits of a perioperative exercise program and also demonstrated benefits lasting 6 months after surgery (see Figure 24).(1320) Another moderate-quality study was reported as negative using the author's main outcome of changes in Harris Hip Scores. However, all 5 post-operative milestones (e.g., walking, chair transfer, stair climbing) statistically favored the exercise group.(1200)

Figure 24. Before and After Surgery Graph (mean ± standard error) for Gait Velocity (m/sec) in 28 Subjects



Wang AW, Gilbey HJ, Ackland TR. Perioperative exercise programs improve early return of ambulatory function after total hip arthroplasty: a randomized, controlled trial. *Am J Phys Med Rehabil*. 2002;81(11):801-6. Reprinted with permission from Wolters Kluwer Health.

Evidence for the Use of a Pre-operative Exercise Program
There are 4 moderate-quality RCTs incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Rooks 2006 RCT	5.0	N = 108 Patients scheduled to undergo hip (n = 63) or knee (n = 45) arthroplasty	Six-week pre-op program of exercise (water and land-based exercise, cardiovascular, strength and flexibility, 30-60 minute sessions, 3 times a week) vs. education controls	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). 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%.	"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 the odds of inpatient rehabilitation."	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 exercise effective for improving functional status and preventing inpatient rehabilitation.

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Wang 2002 RCT	5.0	N = 28 Patients scheduled to undergo hip arthro-plasty	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) vs. controls with usual peri-op care. All given post-op exercises during Weeks 3-12, with some to Week 24.	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.
Gocen 2004 RCT	5.0	N = 60 THR, all thrust plate prostheses	Pre-op physiotherapy (strengthen limbs and hip ROM for 8 weeks) plus educational program vs. no intervention prior to surgery	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 RCT	4.5	N = 45 THR	Study group vs. control group (with and without pre-operative education and physical therapy)	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.

POST-OPERATIVE ACTIVITY LIMITATIONS AND REHABILITATION PROGRAMS: HIP ARTHROPLASTY

Historically, post-operative rehabilitation has been empirically derived and emphasized a graded return to normal function.(1317, 1324) Early weight bearing was previously discouraged due to the belief that it would increase the risk for early loosening and incomplete bone growth.(1317, 1324-1330) Recent rehabilitation protocols have usually prohibited early weight bearing for a typical period of 6 weeks.(1315, 1324, 1327-1331) Yet, delayed weight bearing and advancement of activities may similarly delay, and possibly reduce, functional recovery.(1315) A comparative clinical trial also suggests patients with

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delayed weight bearing are at increased risk for late development of deep venous thromboses discovered after hospital discharge.(1327) Additionally, reductions in hospital stays have not been shown to increase morbidity related to prostheses.(1332) Trials of exercises with a patient with an experimental pressure-instrumented implanted prosthesis found a lack of correlation between peak pressures and exercise or rehabilitation progression after total hip arthroplasty.(1326)

Post-operative exercises have been widely used for arthroplasty patients,(1315, 1324, 1333) although a minority of motivated patients do not undertake formal rehabilitation programs. Most rehabilitation benefits appear to be realized by 3 to 6 months after surgery;(1190, 1317, 1330, 1334, 1335) however, there is evidence of persisting, measureable impairments (see late postoperative exercises).(1330, 1333, 1336-1338)

Typical post-operative exercise regimens emphasize non-weight-bearing exercises that target isolated muscle groups.(1339-1341) Other exercise regimens include treadmill training,(1342) high-intensity quadriceps strengthening,(1343) and progressive resistance and functional training.(1344) Many programs mix these elements in an exercise regimen.(1340, 1345) No quality studies have compared these exercise regimens either between specific exercises, among exercise regimens, or with other interventions. Considering that a patient's activities of daily living require weight bearing and strength capabilities, it is recommended that those be the primary exercises emphasized. Patients with significant reductions in ranges of motion may derive benefit from adjunctive flexibility exercises. There are multiple variables that affect the timing of weight-bearing exercises after hip arthroplasty and include the prosthesis utilized, bone quality, stability of the prosthesis, prosthesis type, patient compliance, and patient balance and coordination. The following recommendations assume good bone quality, good immediate surgical results, and no contraindications to initiating a program.

Recommendation: Post-operative Exercise and Rehabilitation Program for Hip Arthroplasty Surgery Patients

A post-operative exercise program and rehabilitation program is moderately recommended for hip arthroplasty surgery patients.

Indications – All hip arthroplasty patients. Programs and protocols should be closely coordinated with the treating orthopedist, particularly as patient variability is wide, although workers' compensation patients tend to be younger, in better condition, and able to advance conditioning exercises more rapidly than the elderly. Programs need to be individualized, based on factors such as preoperative condition, bone quality, surgical results, contraindications, and other medical conditions. Workers' compensation patients may benefit from immediate post-operative weight bearing,(1181, 1328, 1334) progressive walking,(1181) progressive stair climbing, and marching in place exercises, flexibility, and strengthening. Program advancement must be individualized based on progress.

Frequency/Duration – Duration based primarily on progress. Program may typically be daily in hospital settings and rehabilitation inpatient settings, 2 or 3 times weekly in outpatient settings gradually tapered as home exercises are instituted and the patient's recovery advances. Courses of up to 3 months in more severe cases may be required.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

The following are recommended for at least the first 6 weeks (or as long as needed):

1. Use walking aid.(1181)**– Recommended, Evidence (C)**
2. Add other recommendations only if needed (e.g., elevated toilet seats, prohibiting driving).(1181) – **Recommended, Evidence (C)**
3. ADL adaptive equipment as needed (e.g., long-handled reacher or shoe horn or sock aid). – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations

Quality studies have evaluated risks and benefits from immediate and early post-operative weight bearing (see below). Benefits of immediate or early post-operative weight bearing include: earlier patient

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transfer activities,(1334) greater walking ability or distances,(1328, 1334) earlier hospital discharge,(1328, 1334) and superior function muscle strength and 6-minute walk test results at 3 months(1334) attributed to an early full weight-bearing programs. No significant complications have been reported in any of the quality studies. Additionally, a radiographic comparative clinical trial found greater initial uncemented prosthesis subsidence in the immediate weight bearing group, but no differences in long-term bony in-growth or other outcomes,(1329) and a quality trial found no differences in either bone in-growth or development of radiolucent lines,(1328) from which the authors concluded early weight bearing may be acceptable.(1328, 1329)

Earlier removal of activity limitations (including removing an abduction pillow, elevated toilet seats, elevated chairs, side sleeping and no automobile use as either driver or passenger) has been shown to lower costs, improve patient satisfaction and strongly promoted the ability to perform activities of daily living without increasing the risk of dislocation.(1181, 1346) Those in the quality trial's restricted group returned to work on average 3 weeks later (46%, 9.5 versus 6.5 weeks, p <0.001).(1181) There is no quality study reported that evaluated removal of all limitations (A low-quality, uncontrolled study reported results from a hospital where removal of all restrictions resulted in no increased complications.)(1346) Results from the quality trial(1181) suggest routine use of all of the following are potentially unnecessary: transfer in the OR with an abduction pillow, use of abduction pillows in bed, use of elevated toilet seats, use of elevated chairs, prevented from sleeping on the side, prohibited from driving and are being a passenger in a car. However, selected use may remain indicated, for example, an elevated toilet seat for someone who otherwise could not use their home toilet.

Evidence for the Use of Post-Operative Activity Limitations and Rehabilitation Programs for Hip Arthroplasty

There are 8 moderate-quality RCTs(1181, 1199, 1328, 1334, 1347-1350) incorporated in this analysis. There is 1 low-quality RCT(1345) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Peak 2005 RCT	6.0	N = 265 All cementless femoral (Accolade) and cups (Trident PSL). All anterolateral approach.	No post-operative restrictions other than limit to <90º flexion, 45º external and internal rotation, avoid adduction for first 6 weeks post-op 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	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	"[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.

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				sooner (p < 0.001), ride in autos more often (p < 0.026), and drive autos more often (p < 0.001).		
Unver 2004 RCT	5.5	N = 51 All thrust plate prostheses	Rehab programs with early partial weight bearing (Group 1) vs. early full weight bearing (Group 2). Programmatic differences include weight bearing at 6-8 weeks post-op Day 2; active isotonic exercises at 3-4 vs. 2-3 weeks; endurance training at 8-10 vs. 6-8 weeks.	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 RCT	5.0	N = 114 RA or OA hospitalized for joint flares or arthro-plasty	Intensive treatment (3 weeks at a resort; BID to QID exercise sessions) vs. usual care (e.g., physical therapy, temporary nursing home placement)	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.
Kishida 2001 RCT	4.5	N = 33 All cementless arthroplasties	Full weight-bearing vs. delayed 6 weeks post-operatively	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 RCT	4.5	N = 94 THR, uncemented, proximally coated tapered stem	Group A standard incision (>10cm) and standard pre-/post-op care (2-3 days PCA analgesia). Group-B small	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 =	"This study highlights the importance of factors such as family education, patient preconditioning, preemptive	Due to multiple interventions, the effects of any single intervention are unclear. Suggests combination of

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		(Accolade) and plasma-sprayed acetabular component (Trident)	incision (≤10 cm) and standard pre-/post-op protocols. Group-C standard incision 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.	0.009. Walking distance at discharge: 24.3m (range 3.5-91.5) vs. 35m (range 7-91.5), p = 0.008. Equianalgesic requirement (mg): 26.8(2.4-113.7) vs. 41.2 (2.4-120); p = 0.01. No benefits of short incision shown.	analgesia, and accelerated preoperative and postoperative rehabilitation in influencing the outcome of total hip arthroplasty."	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.
Galea 2008 RCT	4.5	N = 23 Unilateral THR	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.	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 RCT	4.0	N = 14 All post-THR	Training group for 6 weeks vs. controls. Training 1 week after surgery, 3-30 minute sessions a week. Only training group had ergometer exercises. Both groups had exercises (walking, aquatics, ROM) 2 hours a day.	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.
Bulthuis	4.0	N = 85	Intensive	Twenty-five percent of	"(Intensive	Sub-sub group

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2008 RCT		Patients with rheumatic diseases	treatment (3 weeks at resort; BID to QID exercise sessions) vs. usual care (e.g., physical therapy, temporary nursing home placement)	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.	exercise training) results in better quality of life at lower costs after 1 year. Thus, IET is the dominant strategy compared with (usual care)."	analysis of data from Balthuis 2007 and same weaknesses, except dropout rate greater. Unclear of extent costs apply outside Netherlands.

POST-OPERATIVE ACTIVITY LIMITATIONS AND REHABILITATION PROGRAMS: HIP FRACTURE

The above considerations among arthroplasty patients are likely important in hip fracture patients, and vice versa, particularly as the bodies of evidence appear to support similar conclusions (see post-operative rehabilitation evidence table). There are many quality trials and other studies that involve largely or solely hip fracture patients(1341, 1351-1356) and many of these patients are often debilitated, potentially producing a few unique indications. Others have reviewed this literature and drawn disparate conclusions. A Cochrane review concluded that the available trials were insufficient to draw conclusions.(1351) Another Cochrane review concluded there was no evidence of reductions in mortality among those treated in an interdisciplinary setting versus an orthopedic unit.(1354) A third review recommended physical therapy, occupational therapy and assessments of the home environment particularly to prevent falls in the elderly.(1318) Cost effectiveness of accelerated rehabilitation has been suggested.(1357)

Variability between patients is large; the general literature does not generally discuss more complex patients. It is advised that the rehabilitation components be coordinated with the treating orthopedist who will be better able to address critical questions of bone strength, quality and immediate post-operative results.

There are no quality studies directly evaluating immediate weight-bearing among hip fracture patients. Accelerated rehabilitation has been shown to reduce hospital stays(1357-1359) while remote trials found no adverse effects from earlier weight bearing.(1360, 1361) There is a belief that similar to arthroplasty patients, lack of weight bearing is harmful. Thus, early weight bearing is recommended for those patients with good immediate surgical results and without contraindications to early weight bearing.

There are multiple studies that have attempted to identify whether treatment in a geriatric unit is superior to an orthopedic ward;(1362-1366) however, the studies do not agree. There also are two quality studies reported of interdisciplinary rehabilitation, one inpatient and one outpatient, which both failed to find superiority to usual care.(1353, 1367) It appears that the location of the care, as well as the field of study of the attending is immaterial. Instead, the quality and components of the care required for a given patient are believed to be important. There is no recommendation for or against treatment in a geriatric unit or given as an interdisciplinary intervention for most patients. There is quality evidence that those patients with multiple health care issues, particularly including moderate dementia, benefit from treatment in a geriatric unit.(1368)

Throughout the exercise literature, a pattern exists that active, functional exercises (e.g., walking, stairs) are more effective and patients are more compliant with those prescriptions. This pattern appears to continue in the quality studies of rehabilitation of hip pain patients.

There is relatively little quality evidence that directly addresses the importance of a walking program (see post-operative rehabilitation evidence table). However, ambulation and walking programs are components of nearly all rehabilitation programs, particularly including accelerated or intensive rehabilitation programs. Those programs are nearly all reportedly beneficial in the quality studies.(1340, 1357-1359, 1369) Quality studies that appear to have particularly included an ambulatory program as an important component also document benefits.(1370-1372) One quality study found aerobic exercises to

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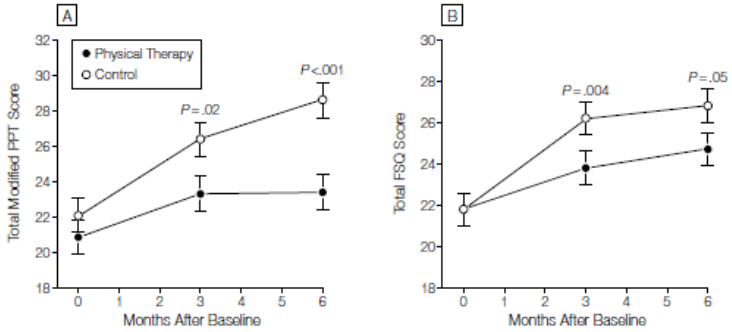
be comparable to a resistance training program,(1371) which as noted below suggests efficacy. Available evidence suggests the primary exercise program elements should entail activities patients require for daily living, especially focusing on walking.(1333, 1338) Thus, a progressive walking program is recommended.

Perhaps the most studied exercise program among hip fracture patients is strengthening or resistance exercise (see post-operative rehabilitation evidence table). These exercises may include steps, stairs, and weight machines. Strengthening exercises have been evaluated in many quality trials(1343, 1344, 1370, 1371, 1373-1377) with all but one of those trials(1377) documenting benefits of the strengthening or resistance exercises. Thus, strengthening and resistance exercises are recommended. Exercises included sit to stand, unilateral heel raises, partial knee bends, 1-legged standing balance, knee raises with alternating arms, marching, side and back leg raises in standing, and unilateral pelvic raising and lowering in standing. These data suggest an evaluation at 4 months post-op and consideration of additional strengthening program components and postural stability through controlled weight bearing is recommended.(1378)

Flexibility exercises have traditionally been emphasized in rehabilitation programs; however, there are few quality trials. One quality trial that emphasized flexibility in one treatment arm was negative(1373, 1374) (see Figure 25). Thus some caution is warranted regarding how much, or whether to include flexibility exercises. These are recommended for those patients with significant reductions in functional range of motion, but not generally recommended for other patients.

Figure 25. Changes in Total Modified PPT and Total FSQ Scores from Baseline to End of Study



PPT indicates Physical Performance Score; FSQ, Functional Status Questionnaire. Data are least square means (SEs). *P* values are for comparisons between physical therapy group vs control group and indicate significantly different values from baseline.

Binder EF, Brown M, Sinacore DR, et al. Effects of extended outpatient rehabilitation after hip fracture: a randomized controlled trial. *JAMA*. 2004;292(7):837-46. Reprinted with permission from the American Medical Association.

Evidence is not consistent on whether the program should be home-based or supervised, although home-based programs are generally preferable for reasons of better approximation of long-term environmental factors for purposes of sustenance and cost. The number of appointments and intensity has varied widely in the quality trials (see post-operative rehabilitation evidence table). This suggests individualization is often required, particularly utilizing factors including immediate surgical results, bone quality, patient motivation, caregiver support, degree of deficits, confounding medical conditions, mental health (especially dementia and depression), and mismatches between current functional status and occupational or avocational functional status to be factored into the decision on numbers of appointments and intensity of treatments. An initial instructional appointment is recommended for all patients. Variability is large. Some patients require daily inpatients appointments while others may require thrice weekly appointments and others may require weekly appointments.

The following program components are recommended and are similar to post-arthroplasty components though individualization is similarly required that incorporates the surgical results and patient characteristics as noted above. The following are specific components of a progressive physical or occupational therapy program that are recommended based on the quality treatment literature. They

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assume good surgical results, good bone quality, and reasonable pre-injury medical and physical condition.

1. *Recommendation: Post-operative Exercise and Rehabilitation Program for Hip Fracture Patients*
   A post-operative exercise program and rehabilitation program are moderately recommended for hip fracture patients.(1357-1361, 1369)

   Indications – All hip fracture patients. Programs and protocols should be closely coordinated with the treating orthopedist, particularly as patient variability is wide, although workers' compensation patients tend to be younger, in better condition, and able to advance conditioning exercises more rapidly than the elderly. Programs need to be individualized, based on factors such as preoperative condition, bone quality, immediate surgical results, contraindications, and other medical conditions. Workers' compensation patients may benefit from immediate post-operative weight bearing,(1357-1361, 1369) progressive walking,(1370, 1371) progressive stair climbing,(1376) and marching in place exercises, flexibility,(1373, 1374) and strengthening.(1343, 1370, 1371, 1373-1376) Program advancement must be individualized based on progress.

   Frequency/Duration – Duration based primarily on progress. Program may typically be daily in hospital settings and rehabilitation inpatient settings, 2 or 3 times weekly in outpatient settings gradually tapered as home exercises are instituted and the patient's recovery advances. Courses of up to 3 months in more severe cases may be required.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

2. *Recommendation: Geriatric Unit Treatment*
   There is no recommendation for or against the use of treatment in a geriatric unit(1362-1366) **or the use of interdisciplinary rehabilitation.**(1353, 1367)

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

3. *Recommendation: Geriatric Unit Treatment for Select Patients*
   Geriatric unit treatment is recommended for patients with multiple health care issues, particularly for those with moderate dementia.(1363)

   Strength of Evidence – **Recommended, Evidence (C)**

Rationale for Recommendations
There are multiple quality studies of post-operative rehabilitation programs for hip fracture patients (see post-operative rehabilitation evidence table). Most of these patients appear to require formal physical or occupational therapy, usually in the form of a progressive treatment program. The available evidence suggests functional exercises are helpful, and these include activities patients must successfully perform upon return to home, such as walking, stair climbing and other activities required to perform activities of daily living. These programs are not invasive, have few adverse effects, but help the patient return to normal or improved functional abilities. These programs generally require many visits for success in these patients, thus they are costly. They are recommended.

Evidence for the Use of Post-Operative Activity Limitations and Rehabilitation Programs for Hip Fractures
There is 1 high- and 20 moderate-quality RCTs (one with two reports) incorporated in this analysis. There are 10 low-quality RCTs(1342, 1360, 1361, 1366, 1369, 1379-1383) in Appendix 2.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Lamb 2002 RCT	9.5	N = 26 Females over 75 years with hip fractures	Patterned neuromuscular stimulation (PNMS) vs. placebo of quadriceps muscle	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	"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

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				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.		generally shown, but sample size small.
Hauer 2003 RCT	7.0	N = 57 Geriatric females with history of severe falls	Ambulatory training of strength, functional performance, and balance 3 times a week for 3 months vs. placebo	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 improve-ments less strong, likely due to fewer differences in physical activity.
Hauer 2001 RCT	7.0	N = 57 Geriatric females with history of severe falls	Ambulatory training of strength, functional performance, and balance 3 times a week for 3 months vs. placebo	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.
Huusko 2002 Acta Orthop Scand RCT	6.5	N = 243 Community dwelling hip fracture patients over 64 years	Geriatric ward for team rehabilitation for 2 weeks (early ambulation, self-motivation and function) then 10 home PT visits over 2 months vs. local ward for standard care	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 geriatric stay superior to

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						usual ward care.
Huusko 2000 RCT	6.5	N = 243 Community dwelling hip fracture patients over 64 years (same as Huusko 2002; this report on mild dementia)	Geriatric ward for team rehabilitation for 2 weeks (early ambulation, self-motivation and function) then 10 home PT visits over 2 months vs. local ward for standard care	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."	Suggests geriatric care is helpful for those with mild, but especially those with moderate dementia.
Binder 2004, 2005 RCT	6.5	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	Supervised physical therapy (3 times a week, 36 sessions), exercise training vs. home exercise (emphasizing flexibility) for 6 months. Supervised PT at indoor exercise facility, 2x3-month phases. Initial phase with small group including flexibility, balance, coordination, movement speed and some strengthening. Second phase progressive strengthening.	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.
Ruchlin 2001 RCT	6.0	N = 114 Hip fracture	Routine post-op care vs. patient education and high intensity strengthening	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 RCT	6.0	N = 33 Elderly who completed physical therapy following hip fracture	Resistance vs. aerobic training vs. controls; 20 visits, twice a week 2 months, then once a week 1 month. Resistance training (hip extensor/	Six-minute walk distances: Resistance (197.1±104.2/ 278.9±114.6m) vs. Aerobic (232.4±122/321.1±101.7 m) vs. controls (180.6±104.3/ 266.2±82.4m), NS. MVC Resistance (48.5±12.6/	"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

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			abductors/knee extensors, plantar flexors with latex band machine). Aerobic 20-minutes walking at 65-75% HR max. Education controls.	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		beneficial.
Naglie 2002 RCT	6.0	N = 279 Surgical hip fracture	Interdisciplinary post-op care (geriatrician, PT, OT, social worker, clinical nurse specialist with 2 times a week interdisciplinary rounds) vs. usual care	Total hours PT time favored ID rehabilitation (14.2±11.7 vs. 5.7±4.0 hours). OT time averaged 10.8±7.6 vs. 3.3±2.2 hours. Social work, dietitian, speech-language pathologist time did not differ. Initial hospitalization longer for interdisciplinary care (29.2±22.6 vs. 20.9±18.8 days, p <0.001), total institutionalization over 6 months not different (p = 0.84). At 6 months, 17 (12.1%) ID care vs. 21 (15.2%) usual care patients died (NS). No differences in decline in ambulation, transfers of changes of residence.	"Postoperative inpatient interdisciplinary care did not result in significantly better 3- or 6-month outcomes in elderly patients with hip fracture."	Suggests location of care in an interdisciplinary unit is not important.
Kennie 1988 RCT	5.5	N = 106 All females with proximal femoral fractures	Rehabilitation ward (general practitioner care, geriatric consultant with 2 ward rounds and 1 weekly multidisciplinary team conference vs. orthopaedic ward care. Both groups received PT, OT, and orthotics.	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.
Reid 1989 RCT	5.5	N = 106 All females with proximal femoral fractures	Same study as Kennie, except 1-year follow-up	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 RCT	5.5	N = 80 All had hip fracture from a fall and in inpatient rehabilitatio n	Two week programs of daily weight-bearing exercise program vs. non-weight-bearing (exercises same as Sherrington 2004 above). All	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	"Weight-bearing and non-weight-bearing exercise programs produce similar effects on strength, balance, gait and functional performance among inpatients soon after	Trial length of only 2 weeks and co-interventions of exercises with both weight-bearing appear likely to have reduced

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			received practice with walking and advancement with walking aids.	measures not different between groups. Ability to walk with either 1 stick or no aid 20% vs. 5%, p <0.05.	hip fracture."	possible differences. Walking ability favored weight bearing exercise group.
Mitchell 2001 RCT	5.0	N = 80 Patients rehabili-tating after proximal femoral fracture	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.	Quadriceps training group: baseline; week 6; week 16. Leg extensor power fractured leg (W): 10.1 (0.8); 25.7 (2.1) p ≤ 0.01; 33.0 (3.9) p ≤0.001. Leg extensor power non-fractured leg (W): 20.5 (1.6); 34.9 (3.0) p ≤ 0.01; 40.1 (4.3) p ≤0.05. Elderly Mobility scale (median IQR): 10 (7, 12); 17.5 (16, 20) p ≤0.001; 18 (16, 20) p ≤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.
Lamb 1998 RCT	5.0	N = 24 Females over 75 years with hip fractures	Patterned neuromuscular stimulation (PNMS) of the quadriceps muscle vs. placebo stimulation	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
Tinetti 1999 RCT	4.5	N = 304 27 home care agencies All had had surgical repair of hip fracture	Home-based multicomponent rehabilitation program vs. usual care; multi-component program included identification of deficits and tailoring PT program plus functional therapy; usual care included home PT	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 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	"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 rehabilitation program not superior to usual care.

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				program (p = 0.08).		
Galvard 1995 RCT	4.5	N = 371 Community dwelling hip fracture patients	Orthopedic vs. geriatric rehabilitation (scant descriptions of program components)	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.
Cameron 1993 RCT	4.0	N = 252 All uncompli-cated proximal femoral fractures with surgery within 7 days	Accelerated rehabilitation (early mobilization after surgery, comprehensive rehabilitation program, liaison with a care-giver, early hospital discharge, community-based rehabilitation) vs. conventional care (variously interdisciplinary program, discharge home, and transfer to nursing home	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 RCT	4.0	N = 252 All uncompli-cated proximal femoral fractures with surgery within 7 days	Same study as Cameron 1993	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.
Quine 1994 RCT	4.0	N = 252 All uncompli-cated proximal femoral	Same study as Cameron 1993	Thirty-eigth percent of carers assessed by social worker as having burden caring for fracture patient; 55% mild, 40% moderate, 5% severe. Initial assessment of	"Accelerated rehabilitation does not impact greatly on carer burden, but already severely burdened carers may benefit from	Suggests disruption results in care-giver burden.

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		fractures with surgery within 7 days		burden highly correlated with initial disruption (r = 0.9, p <0.001).	additional counseling/ information."	
Sherrington 1997 RCT	4.0	N = 42 All hip fracture mean 7 months earlier	Home exercise program (step exercises) vs. no exercise controls; 1 follow-up visit at 1 week	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.
Karumo 1977 RCT	4.0	N = 87 All femoral neck fractures. Thompson prostheses (n = 39) and 48 with internal fixation.	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, stair training on 2nd post-op day.	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.

LATE POST-OPERATIVE EXERCISES

While pain is typically resolved after hip arthroplasty,(1082, 1384, 1385) there is some evidence of reductions in strength and postural stability persisting months to at least 1 or 2 years after surgery.(1330, 1333, 1336-1338, 1345, 1378, 1385-1387) Total strength deficits have been estimated at approximately 10-20% compared with the unaffected side.(1330, 1338) Whether these deficits are clinically meaningful is unclear particularly in the more functionally recovered patients.(1337) There are some low quality data suggesting muscle weakness is associated with prosthetic loosening.(1336)

Some have used results from case series to recommend that strengthening exercises be continued after hip arthroplasty for at least 1 year(1330) (see post-operative rehabilitation evidence table), with either a supervised or home program,(1388) but with a supervised program continued for those who lack self-discipline.(1336) Components of a late phase physical or occupational therapy regimen have been thought to best emphasize weight bearing, resistance and postural stability.(1338, 1378, 1388) A non-randomized trial comparing a home exercise program including range of motion and isometric strengthening exercises versus a second home exercise program that also included eccentric muscle contractile exercises of hip abductors in a standing position versus controls with no exercise program found the home programs comparably effective.(1386)

There are three quality studies that have evaluated late post-operative exercise programs for treatment of post-fracture patients.(1344, 1371, 1389) These studies have found comparable results to those for arthroplasty patients. A weight-bearing home exercise program,(1389) resistance, functional and balance training program(1344) were found to be effective. The third quality trial found aerobic exercises to have equivalent efficacy to a resistance training program.(1371) The parallel findings between the hip arthroplasty and hip fracture patients strengthen these conclusions.

Recommendation: Late Post-operative Exercise Program for Arthroplasty or Hip Fracture

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A late post-operative exercise program after arthroplasty or hip fracture emphasizing cardiovascular fitness and strengthening or resistance is recommended for patients who exhibit significant evidence of weakness or unsteady gait. A home exercise program among motivated patients may be sufficient.(1345)

Strength of Evidence – **Recommended, Evidence (C)**

There is no recommendation for or against the use of a late post-operative program for patients with mild reductions of questionable significance in the late post-operative period.

Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

Evidence for the Use of Late Post-operative Exercises
There are 5 moderate-quality RCTs incorporated in this analysis.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Trudelle-Jackson 2004 RCT	7.5	N = 34 4 to 12 months post-operative THA patients	Strength and postural stability exercises vs. isometric and active range of motion exercises	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 RCT	6.5	N = 120 All had had hip fracture from a fall average 6 months earlier	Weight-bearing home exercise (sit to stand, lateral step-up, forward step-up-and-over, forward foot taps, stepping grid) vs. non-weight-bearing home exercise (hip abduction, flexion, hip and knee flexion and extension, range of knee extension, ankle dorsiflexion and plantarflexion) vs. control groups. Follow-ups at 1 week, 1 and 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 weight-bearing group (p <0.05).	"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.
Mangione 2005 RCT	6.0	N = 41 7-50 weeks after hip fracture, with ORIF, partial or total	Aerobic (target 65-75% heart rate max. for 20 minutes) vs. resistance training (hip extensors, abductors, knee	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	"High-intensity exercise performed in the home is feasible for people with hip fracture. Larger sample sizes may be	Small sample size. High dropout rate for resistance training group.

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		arthroplasty.	extensors, plantar flexors, 3 sets of 8 repetitions) vs. wait-list controls. Exercise sessions 30-40 minutes, 2 "overload" sessions a week first 2 months, then 1 a week for 1 more month.	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).	necessary to determine whether the exercise regimen is effective in reducing impairments and improving function."	
Hauer 2002 RCT	5.0	N = 28 Admitted for injurious falls or hip fracture or arthroplasty, 6-8 weeks after rehabili-tation	Twelve-week trial of progressive lower extremity resistance training, progressive functional and balance training vs. "placebo motor activity" (calisthenics, games, memory tasks). Intensity at 70-90% maximum workload, 3 times a week, 12 weeks.	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.
Unlu 2007 RCT	4.0	N = 26 1-2 years after hip arthroplasty	Group 1 (home exercise program) vs. group 2 (PT supervised hospital based program) vs. group 3 (control)	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.

POST-OPERATIVE ACTIVITIES AND SPORTS

There are three primary methods to assess appropriate sports or activities for hip arthroplasty and hip fracture patients: epidemiological studies, biomechanical models, and experimental studies.(1390) The available studies from these different methods produce substantial conflicts that are not readily resolved. Since the evidence conflicts and the epidemiological studies are the gold standard for the development of quality guidance,(1391-1393) this review emphasizes epidemiological studies.

Exercise recommendations are developed largely without epidemiological data. The following activities have been recommended: bicycling, ballroom dancing, croquet, golf, horseshoes, shooting, shuffleboard, swimming, doubles tennis, and walking.(1390, 1394) Activities recommended with appropriate experience included low-impact aerobics, road bicycling, bowling, canoeing, hiking, horseback riding and cross-country skiing. Activities recommended against included baseball, basketball, football, jogging, singles tennis, and volleyball. There was no conclusion regarding square dancing, fencing, ice skating,

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speed walking, downhill skiing, or weight lifting.(1390, 1394) However, these recommendations do not necessarily conform with epidemiological evidence.

It has been argued that high-impact loading activities should be prohibited in hip arthroplasty patients;(1336) however, increased risk of loosening has been reported among patients who were *not* skiing compared with skiers.(1055) The same researchers also reported a longer term trend of accelerated wear in the more physically active group.(1055) Another study found an approximately 9-fold greater risk for loosening among patients engaged in no sporting activity compared with those engaged in sports (e.g., hiking, climbing, skiing, swimming, running, cycling, and tennis).(1395) Uncemented prostheses have been reported to have less radiographic loosening in active golfers.(1056) Another study found no apparent deteriorating effect of intensive recreational activities.(1054) Higher rates of aseptic loosening are reported among men in registry studies and case series;(1047, 1396) however, whether that is related to force is unknown. Currently, the balance of the epidemiological literature does not support the argument that activity results in loosening.

Studies on prosthetic wear rates have been used to imply appropriate work limitations for the post-arthroplasty patient; however, no quality studies have been reported that address the appropriateness of work limitations. Additionally, the avocational studies reviewed above do not provide quality evidence in support of activity limitations. Thus, although reduced return-to-work status has been reported among patients with more physically demanding work(1397) there is not a strong rationale for work restrictions in the post-surgical hip population.

Recommendation: Post-Operative Vocational or Avocational Activities
There is no recommendation for or against specific vocational or avocational pursuits post-operatively.

Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
Quality evidence does not sufficiently support evidence-based guidance and therefore there is no recommendation for or against specific vocational or avocational activities.

Evidence for the Use of Vocational or Avocational Activities
There are no quality studies evaluating the use of vocational or avocational activities.

PSYCHOLOGICAL SERVICES

Psychological issues appear to be substantially less prevalent among patients with osteoarthrosis compared with spine disorders for unclear reasons. Thus, psychological services are rarely needed for hip pain patients (see Chronic Pain chapter for further discussion of psychological evaluation).

1. *Recommendation: Psychological Evaluation for Chronic Hip Pain*
   A psychological evaluation is recommended as part of the evaluation and management of patients with chronic hip pain with any of the below indications in order to assess whether psychological factors will need to be considered and treated as part of the overall treatment plan.

   Indications – 1) Hip pain or dysfunction that persists longer than typical for the condition; 2) disability or impairments thought to be disproportionate to usual or expected findings; 3) demonstration or suspicion of significant psychosocial dysfunction; 4) medication issues and/or drug problems;(1398-1401) 5) current or premorbid major psychiatric symptoms or disorder thought to be impacting disorder; 6) non-compliance with the prescribed treatment regimen; or 7) experiencing delayed functional recovery.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

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2. *Recommendation: Cognitive Behavioral Therapy (CBT) for Patients with Subacute or Chronic Hip Pain*

   Cognitive-behavioral therapy is recommended as an adjunct to an interdisciplinary program for treatment of subacute or chronic hip pain.

   Indications – Specific indications for CBT in chronic pain conditions are:

   1. Management of clinically significant behavioral aberrations and/or anxiety during opiate weaning or detoxification;
   2. A component therapy integrated into an interdisciplinary or other functional restoration program;
   3. Clinically significant problems of noncompliance or non-adherence to prescribed medical or physical regimens;
   4. Vocational counseling for resolution of psychosocial barriers in return to work (requires a current or imminent medical release to return to work);
   5. Resolution of interpersonal, behavioral, or occupational self-management problems in the workplace, during/after return to work, where such problems are risk factors for loss of work or are impeding resumption of full duty or work consistent with permanent restrictions.

   Frequency/Duration – Therapy provided for the above indications should be limited to 6 sessions or less. When therapy is provided as a component of an interdisciplinary or functional restoration program, the number of sessions is based on the needs of the program to provide relevant treatment objectives.

   Indications for Discontinuation – Noncompliance, failure to obtain functional or behavioral improvement, or resolution of problems.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
There are no quality studies specifically addressing hip pain as nearly all studies evaluated low back pain patients (see Chronic Pain and Low Back Disorders chapters). Psychological assessments are routinely accomplished for the purposes given above, including treatments for which various levels of evidence are provided herein, e.g., functional rehabilitation or interdisciplinary pain programs, candidacy for certain procedures, or chronic use of opioid medications. Evaluations are moderate cost and, when done appropriately, present little risk of harm.

Evidence for the Use of Psychological Evaluations/Cognitive-Behavioral Therapy
There are no quality studies evaluating the use of psychological evaluations for patients with chronic hip pain. However, there are quality studies evaluating spine patients (see Low Back Disorders and Chronic Pain chapters).

REHABILITATION FOR DELAYED RECOVERY

BIOFEEDBACK

Biofeedback is a behavioral medicine method providing automated information and training to improve control of certain physiologic processes which are normally inaccessible to a subject's perception. Biofeedback most commonly involves surface EMG input to a monitor with audible or visual feedback of the degree to which there is muscle activity.(1402) Through this feedback, the patient may learn to control the degree of muscle contraction.

Recommendation: Biofeedback for Chronic Hip Pain
There is no recommendation for or against the use of biofeedback for chronic hip pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
Biofeedback is not invasive, has no complications, and is moderately costly. However, there are other efficacious treatment strategies.

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Evidence for the Use of Biofeedback
There are no quality studies for use of biofeedback for treatment of hip pain patients.

FUNCTIONAL RESTORATION

Functional restoration is both a type of interdisciplinary pain management and rehabilitation program and a general approach to medical care. Fundamental elements of a functional restoration approach include assessment of the patient's dynamic physical and functional status including traditional tests for strength, sensation, and range of motion. Psychosocial strengths and stressors must also be assessed including the patient's support system; evidence of mood disorders; assessment of education and skills; medication use; presence of litigation; and work capacity. Following this evaluation, the emphasis is on expectation management, directed conditioning and exercise, cognitive behavioral therapy, setting functional goals and decreased medication use. An ongoing assessment of patient participation and compliance (with documentation of complicating problems and progress toward specific goals, including reduction in disability and medical utilization) is needed.

In functional restoration, the treatment team members are educators. Passive therapies and invasive interventions are de-emphasized while home exercise/self-management efforts are stressed. There should be a shift of health, function, and well-being responsibility (locus of control) from physicians and therapists to the patient. A functional restoration approach may include the limited/adjunctive use of medications and interventional measures (where specifically indicated) however, these should not be viewed as ongoing solutions. It may also involve institution of preventive measures, education for relapse prevention, proper activity and work pacing, ergonomic accommodation, and when appropriate, transitional return to employment.

Functional restoration's goals are returning to a productive life despite having a chronic pain problem and mitigation of a patient's suffering. If an individual fails to recover within the appropriate biological healing time frame, the acute care paradigms of specific diagnosis and treatment change to biopsychosocial approaches that address pain, function, work, and psychological factors impeding progress. Treatment programs focus on restoration of work-related function. These programs include work conditioning and work hardening, interdisciplinary pain rehabilitation programs and functional rehabilitation. Because functional restoration is an approach, not just a specific program, the approaches taken both overlap on a continuum.

WORK CONDITIONING, WORK HARDENING, AND EARLY INTERVENTION PROGRAMS

Work conditioning and work hardening programs are often recommended for patients who are not able to return to work because of persistent symptoms and functional limitations following acute care and rehabilitation. Early intervention functional restoration programs are sometimes recommended during the first 3 to 6 months if the injured worker is noted to have increased risk factors and evidence of delayed recovery. These risks and delays suggest that a more coordinated functional restoration approach with a psychosocial emphasis is needed beyond conditioning or hardening alone.

Work Conditioning and Work Hardening Programs

Differentiating work conditioning from work hardening is problematic as the terms are sometimes used interchangeably. The American Physical Therapy Association (APTA) defines work conditioning as "an intensive, work-related, goal-oriented conditioning program designed specifically to restore systemic neuromusculoskeletal functions (e.g., joint integrity and mobility, muscle performance (including strength, power, and endurance), motor function (motor control and motor learning), range of motion (including muscle length), and cardiovascular/pulmonary functions (e.g., aerobic capacity/endurance, circulation, and ventilation and respiration/gas exchange)."(1403) APTA classifies work conditioning as a single-discipline program and work hardening program as interdisciplinary. The Commission on Accreditation of Rehabilitation Facilities (CARF) defines occupational rehabilitation as work conditioning, and comprehensive occupational rehabilitation as work hardening. Although not universally accepted, some physicians consider work conditioning as a generalized endurance and strengthening program that includes work simulation activities, whereas work hardening is a program where a specific job has been

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identified and stresses involvement in sets of occupationally-related tasks and functional activities that are directly related to a patient's work. Work conditioning and work hardening programs in the U.S. are heterogeneous and are often provided by a single-therapy discipline, either physical or occupational therapy.(1404-1406)

Work conditioning and work hardening programs generally involve structured programs of gradually increased levels of exertion to bridge a significant gap between the patient's current physical or perceived capabilities and the requirements needed to return to everyday activities and work. Regardless of the terminology used, the most successful programs involve a detailed appreciation of the worker's capabilities, a detailed knowledge of the job physical requirements (if possible, obtained from on-site analysis or familiarity), and individualization of the program to address specific deficits that are barriers to return to work. These programs can be somewhat heterogeneous with varying components and there is some overlap with multidisciplinary programs.

Work conditioning and work hardening programs focus on increasing physical efforts, using fear avoidance belief training if necessary. These programs may also use a cognitive-behavioral model and overlap with early intervention programs. In the majority of return-to-work situations, work conditioning or work hardening programs are not required as the gap between worker abilities and capabilities are not sufficiently large to justify either the time or expense. These programs are generally utilized for workers involved in significant materials handling tasks that commonly involve high-force expenditures or highly repetitious activities. Not infrequently, work conditioning or work hardening programs are the next step after conventional physical or occupational therapy is exhausted and a gap remains to return the patient back to work, particularly in the subacute pain setting. These programs are also utilized for patients who have tried to return to work but failed due to either the gap between abilities and capacities or the lack of modified duty in physically demanding occupations. These programs are not invasive and have low adverse effects, but are moderate to high cost depending on program length.

Patients who may benefit from work conditioning or hardening include those who: 1) remain completely off work or are on modified duty for 6 to 12 weeks; 2) have not responded to less costly interventions including a 4 to 6 week physical or occupational therapy program or a graded therapy program of at least 6 to 8 weeks that includes aerobic and strengthening exercise components; 3) have a stated strong interest and expectation to return to work; 4) involve cooperation of the employer; 5) are supervised by a qualified physical or occupational therapist; 6) have had a careful assessment of their occupational demands; 7) have a FCE that indicated appropriate performance effort and consistency at a level of work lower than that to which they need or wish to return; and 8) are in a program that includes a cognitive-behavioral approach with a focus on function rather than pain, a conditioning or aerobic exercise component and simulated graded work tasks, and is tailored to their needs and identifies gaps between current capabilities and job demands.

Early Intervention (Functional Restoration) Programs

Early identification and appropriate management of patients exhibiting signs of delayed recovery is believed to decrease the likelihood that they will go on to develop chronic pain.(1407) These patients may benefit from a limited but intense program of physical restoration with a strong emphasis on education that identifies barriers to recovery and return to work. They may require an abbreviated early intervention interdisciplinary rehabilitation program (IPRP), preferably using functional restoration principles, rather than a longer program utilized for more complex cases. Early intervention programs are an alternative to work conditioning and work hardening programs for subacute or patients with early chronic pain who have evidence for delayed recovery with an increased need for education and psychological assessment and intervention. These programs are usually appropriate in cases of work incapacity lasting 3 to 6 months. The interdisciplinary functional restoration program used for early intervention contains the features of a functional restoration IPRP, but involves lower intensity and duration of services than a program for patients with greater chronicity of disability. The type, intensity, and duration of services is dictated by the patient's unique rehabilitation needs and may be used for those who fail work conditioning and work hardening programs, usually within 6 months of onset of

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disability post-injury. The time frame of 3 to 6 months post-injury is vital for intervening with the most effective treatment possible in order to avoid the negative sequelae that come with increasing duration of disability. During this time, normal musculoskeletal healing generally occurs, eliminating any remaining physical barriers to intensive rehabilitation. Such programs are appropriate for prevention, before the patient is entrenched in a chronic pain syndrome or before severe pain and illness behavior evolves.

Recommendation: Work Conditioning, Work Hardening, or Early Intervention Programs for Chronic Hip Pain Syndromes

Work conditioning, work hardening, and early intervention programs are recommended for treatment of chronic hip pain syndromes.

Frequency/Duration – Three (3) to 5 times a week for work conditioning and early intervention programs; daily for work hardening. Weekly evaluations demonstrating sufficient levels of physical effort and consistency, compliance with the plan of care, and functionally significant progress toward the return-to-work goal must be documented to justify continuation. Program length and intensity is dictated by each patient's unique rehabilitation needs.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

There are no quality studies of hip pain patients and limited evidence that work conditioning, work hardening, or early intervention programs are effective for chronic spinal pain, nevertheless there is a longstanding belief and experience that they are highly effective. While there is potential for overlap, work conditioning, work hardening, and early intervention are distinct programs and are not intended for sequential use, although this might be appropriate in certain situations depending on program components. In acute cases, where delayed recovery is not an issue, these programs are inappropriate. In more chronic cases, particularly with pain and illness behavior and a high level of reported dysfunction, a more intense IPRP should be considered. Although less costly, work conditioning, work-hardening, and early intervention programs do not need to be attempted before moving to an IPRP as long as a quality interdisciplinary program with proven outcomes is accessible to the patient. Program choice depends on availability and matching patient needs to the services offered to provide the most cost-effective and beneficial outcome. Hence, these programs might provide the greatest potential impact when used to manage patients during the subacute phases of injury, although they might also be appropriate for use in those with chronic pain who do not, after evaluation, have significant psychosocial factors contributing to their clinical presentation.

Evidence for the Use of Work Conditioning, Work Hardening, and Early Intervention Programs

There are no quality studies evaluating the use of work conditioning, work hardening, and early intervention programs for chronic hip pain.

INTERDISCIPLINARY PAIN REHABILITATION PROGRAMS

An interdisciplinary pain rehabilitation program (IPRP) is a type of chronic pain management program that uses a biopsychosocial paradigm (preferably employing a functional restoration approach), that can enhance function, reduce pain and illness behavior, and mitigate chronic pain associated disability. These programs are intended to manage psychological, social, physical and occupational factors and are discussed in detail in the Chronic Pain chapter. All IPRP programs involve an integrated team of professionals who provide intensive, coordinated care. This team may include physical and occupational therapists, psychologists, vocational counselors, nurses, and case managers. Quality programs emphasize functional recovery and active, progressive physical activity and generally involve intensive 5-days-a-week treatment regimens that should be individualized. **All medical and therapy services must be supervised by a physician who is directly involved with the program and regularly interviews and examines the patient for relevant parameters.** For reasons that are unclear, there appear to be few hip pain patients who require these programs. Nevertheless, a minority of patients may derive benefits (see Chronic Pain chapter for on program components, criteria for admission, treatment objectives, inpatient care, and follow-up).

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Recommendation: IPRPs for Chronic Hip Pain

A multidisciplinary or interdisciplinary program (IPRP) with a focus on behavioral or cognitive-behavioral approaches combined with conditioning exercise is recommended for patients who due to chronic hip pain, demonstrate partial/total work incapacity.

Indications – Chronic hip pain in patients who are not working, or unable to return to full duty, and have significant, pain-related limitations in activities of daily living. Patients should have failed other standard approaches (e.g., physical therapy, occupational therapy, interventions, medication) and have reasonable probability of recovery.

Frequency/Duration – Median 20 days, with trial of the first 10 days to assess patient compliance, attendance, and progress. Program duration is variable due to the patient's needs, the rehabilitation strategies used, and the demonstrated program outcomes. IPRP treatment is generally provided 5 full days per week, though slightly fewer hours and longer calendar durations are utilized in some programs. Complicating problems involving activities of daily living (such as coordinating part-time employment, transportation, or child care needs) or limitations imposed by co-morbid medical conditions which preclude the patient from participating in the program full-time (thus preventing them an assessment at 10 days) are considerations that might necessitate program modification.

Indications for Discontinuation – Failure to improve, noncompliance, resolution of symptoms and disability, exhaustion of reasonable program duration for a specific condition.

Strength of Evidence **– Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

Participation in an IPRP to treat chronic hip pain patients has not been evaluated in quality studies. These programs may be helpful if there is medical need to wean the patient from opioids or other medications and/or if the patient has shown demonstrable clinical progress with less intense rehabilitation but “pain limitation” has impeded adequate recovery. Development of entrenched psychosocial barriers to recovery and a chronic pain syndrome as sequelae of the original physical components of the injury may be associated with this group of patients. Functional restoration might be appropriate, as well as vocational re-entry in positions not requiring the same job physical characteristics when all previous treatments have failed. With the possible exception of workplace-based interventions, most successful multidisciplinary programs appear to utilize either a cognitive-behavioral approach or involve psychologists.(1408-1411) While exercise is a major focus in many of these successful programs,(1408-1412) the one trial that compared a graded exercise approach with a participatory ergonomics approach found exercise inferior.(1413) This suggests that of the options available, the participatory ergonomics approach may be superior to other approaches.(1414) These heterogeneous studies also suggest that multidisciplinary programs that focus on functional improvements are superior.

IPRPs of the types described in the literature are not invasive, have few adverse effects, but are high cost. Some U.S.-based programs involve significant interventions, but there is no documentation of superior outcomes from such programs which can cost $20,000 to $50,000. IPRPs are indicated for select, more severely affected patients, including those who have failed appropriate conservative management (e.g., appropriate medications, specific exercises, etc.). Generally, these referrals are most indicated in the early chronic pain management timeframe (3 to 6 months). However, there are times when earlier referral in the mid- to late-subacute interval is indicated. (Physicians should be aware that there is a belief that earlier referral results in higher probability of successful treatment, but that supposition has not been rigorously tested and is prone to a strong spectrum bias whereby all patients tend to do worse the longer they have a acute, subacute, or chronic pain condition.) Referrals beyond 6 months might also be indicated if there has been failure to progress with numerous interventions and there is reasonable expectation for potential benefits. Referrals during the subacute phase best occur when there is a quality program with proven outcome efficacy is available, the patient has documented delayed recovery, yet there is interdisciplinary assessment that the patient is likely to benefit from the program.

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APPENDIX 1. ANESTHETIC ISSUES FOR HIP SURGERY PATIENTS

ANESTHESIA/ANALGESIA TECHNIQUES

Major hip/knee surgery is most commonly performed under anesthesia delivery through one or more techniques, including general anesthesia, intrathecal (spinal) block or epidural block. Selection of the best anesthesia technique is usually individualized based on underlying patient medical history and practitioner preferences.

Post-operative pain control is achieved through a wide number of techniques, including parenteral opioid administration through patient controlled anesthesia delivery systems (PCA), single dose or continuous infusion of local anesthetic and/or opioids through intrathecal or epidural indwelling catheters, adjuvant regional blocks such as caudal block, femoral 3-in-1 block, psoas compartment block, facia iliaca compartment block, lumbar plexus block, local infusion at the surgical site, and finally through administration of oral medications such as opioids, non-steroidal anti-inflammatories and acetaminophen (see anesthesia evidence table for RCTs reviewed related to major hip/knee surgery and anesthetic/analgesic technique for post-operative pain control).

Post-operative analgesia that attenuates pain and improves patient satisfaction in the immediate recovery period is the most common outcome measure found in quality literature. Poor pain control is thought to restrict rehabilitation and functional recovery. Two moderate-quality studies have shown a reduced hospital stay with adequate pain control versus comparison groups.(1415, 1416) However, these studies were conducted in other health care systems and may not be applicable in the United States. In contrast, another quality study examining analgesia quality and functional improvement showed no difference in recovery of physical independence despite improved pain relief.(1417) The significance of pain control and long-term rehabilitation and functional outcomes measures appears somewhat uncertain, requiring further research.

Regional Blocks

1. *Recommendation: Regional Blocks – Caudal Block with Buprenorphine*
   A caudal block with buprenorphine is moderately recommended.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation
A high-quality study comparing the addition of buprenorphine to bupivacaine caudal block provided increased duration of analgesia on average 8 hours (2 versus 10 hours).(1418)

2. *Recommendation: Fascia Iliaca Compartment Block (FICB) for Emergency Room Management of Hip Fractures*
   Fascia iliaca compartment block (FICB) is moderately recommended for emergency room management of hip fractures.

   Strength of Evidence **– Moderately Recommended, Evidence (B)**

Rationale for Recommendation
A high-quality study demonstrated that a fascia iliaca compartment block with bupivacaine provided superior pain relief compared with IM morphine injection in the emergency room for patients with suspected hip fracture.(1419)

3. *Recommendation: Posterior Lumbar Plexus Block*
   Posterior lumbar plexus block is moderately recommended.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation
A high-quality study demonstrated lumbar plexus block improving pain control and reducing PCA morphine requirements up to 4 hours after surgery over sham block. Long-term reduction of morphine (24 hours) and reduced hospital stay trended positive, but the study lacked statistical power to reach significance.(1420) A moderate-quality study comparing posterior lumbar plexus block in general

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anesthesia patients demonstrated reduced postoperative analgesic requirements and reduced blood loss in both postoperative (170ml versus 310ml) and intraoperatively (420ml versus 538ml).(1421) Another moderate-quality study demonstrated improved patient satisfaction and analgesia with a continuous lumbar plexus block compared with PCA morphine alone.(1422) Therefore, there is evidence that lumbar plexus block is effective for short-term pain control and may have the added benefit of reducing blood loss, although of limited clinical significance in most patients. Continuous lumbar plexus block may be an effective alternative to epidural or spinal analgesia.

4. *Recommendation: Psoas Compartment Block (PCB) with or without IV Clonidine*
   There is no recommendation for or against the use of Psoas compartment block (PCB) with or without IV clonidine.

   Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
A moderate-quality study comparing psoas block to PCA morphine demonstrated no added benefit for psoas block except in the immediate 4 hours post-operative.(1423) Another moderate-quality study demonstrated clonidine administered IV prolonged the duration of analgesia compared to perineural block and placebo.(1424) However, despite improvement in duration, there were no differences in analgesic requirements or pain scores, making the result of uncertain clinical significance.

5. *Recommendation: Surgical Wound Infiltration with Local Anesthetic*
   Surgical wound infiltration with local anesthetic is recommended.

   Strength of Evidence – **Recommended, Evidence (C)**

Rationale for Recommendation
A moderate-quality study investigated if wound infiltration of ropivacaine prolongs the analgesia provided by bupivacaine/fentanyl spinal block compared with PCA morphine and ketorolac analgesia.(1416) The study demonstrated significant reduction of pain, reduced rescue medication usage, and a nearly 2.5 day reduction in hospital stay.

6. *Recommendation: Femoral Nerve Block*
   Femoral nerve block is not recommended.

   Strength of Evidence – **Not Recommended, Evidence (C)**

Rationale for Recommendation
A moderate-quality study comparing 3-in-1 femoral nerve block with a sham block in patients that underwent general anesthesia found no difference in pain scores or analgesic requirements.(1425) Another moderate-quality study compared femoral nerve block with PCA anesthesia,(1423) demonstrating no added benefit and recommended against this intervention. A high-quality study showed adequate analgesia after psoas compartment block, with no added benefit of tramadol IV or perineurally.(1426) The results however are obscured by co-interventions, including lumbar plexus block. Therefore, there is limited evidence that femoral nerve block is inadequate for long-term pain relief of hip arthroplasty.

Opioids (Oral, Parenteral, Iontophoresis)
Iontophoresis is a method of transdermal administration of ionized drugs in which electrically charged molecules are propelled through the skin by an external electrical field.

1. *Recommendation: Pre-operative Oral Morphine*
   Pre-operative use of oral morphine is recommended.

   Strength of Evidence – **Recommended, Evidence (C)**

Rationale for Recommendation
A high-quality study demonstrated that pre-operative oral administration of morphine sulfate did not reduce pain scores post-operatively, but did reduce post-operative consumption of opioids.(1427)

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Prophylaxis with buprenorphine administered orally and IM, as well as IM morphine, did not provide any benefit over placebo.(1428) Oral opioids are inexpensive, have few adverse effects in pretreatment doses, and may provide added benefit despite their short half-life. Therefore, limited evidence supports pre-operative prophylaxis with oral morphine.

2. *Recommendation: Oral Opioids for Post-operative Pain Control*
   Scheduled oral morphine (20mg every 4 hours) is recommended for post-operative pain control.

   Strength of Evidence – **Recommended, Evidence (C)**

3. *Recommendation: Oral Opioids for Post-operative Pain Control*
   Oral opioids are moderately recommended for post-operative pain control.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendations
A high-quality study demonstrated oral morphine (20mg) administered every 4 hours provided statistically significant reduction in PCA morphine use versus lower dose oral morphine (10mg) and placebo.(1429) However, patients in all groups were similarly satisfied with pain control quality of treatment, suggesting limited clinical significance. A moderate-quality study presented equivocal results of meperidine versus tramadol in post-operative pain relief, as both provided only partial analgesia.(1430) Oral Tramadol provided no benefit over paracetamol and codeine in another study.(1431) Moderate-quality studies of oxymorphone(1432) and oral transmural fentanyl citrate(1433) and a low quality of controlled release oxycodone(1415) demonstrated these synthetic opioids provided analgesic relief over placebo. However, many of the patients in the intervention group withdrew from the treatment arm, or had better but not excellent pain control. A moderate-quality study compared oral morphine (20mg) to IM morphine (10mg), and found no difference in quality of pain control.(1434) Therefore, the available evidence supports the use of oral opioids for treating post-operative pain in patients who undergo general anesthesia. The quality of analgesia from oral opioids is inferior to epidural and spinal analgesics as detailed in recommendation summaries for epidural and spinal anesthesia.

4. *Recommendation: Patient-controlled Analgesia (PCA) Opioids*
   The use of patient-controlled opioids is strongly recommended.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale for Recommendation
Patient-controlled analgesia (PCA) is commonly used to deliver parenteral opioid medications. Many of the reviewed interventional studies for anesthesia/analgesia techniques utilize PCA delivery of opioids as an objective measure (gold standard) for effectiveness. There are no quality studies of PCA opioid versus placebo, as parenteral opioid is the gold standard for analgesic relief. However, in a majority of studies reviewed, PCA morphine or other opioid is used as the rescue medication. As an example, comparison of epidural diamorphine to PCA morphine demonstrated both were effective, with no advantage to either technique.(1435) Thus, each study using PCA confirms the effectiveness of intervention. Evidence for the use of one opioid over another via PCA is limited.

Few quality studies compared opioids used in PCA. A moderate-quality study comparing PCA morphine with PCA meptazinol showed no differences in pain control or adverse effects, thereby providing no advantage over morphine.(1436) There were also no differences found between morphine and diamorphine.(1437) A moderate-quality study comparing variable-dose PCA versus a fixed-dose PCA of morphine, did not find any advantage of one over the other.(1438) Tramadol used in a PCA also provides adequate anesthesia but with higher incidence of nausea and vomiting and lower quality analgesia scores than PCA morphine, and thus should be considered a second-line alternative to morphine or other opioids.(1439)

5. *Recommendation: Opioid Iontophoresis*

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There is no recommendation for or against the use of opioid iontophoresis.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation
There are two moderate-quality studies of iontophoresis for systemic opioid delivery. Iontophoresis of morphine demonstrated sufficient systemic delivery of morphine to provide early postoperative analgesia.(1440) Iontophoresis of fentanyl was also shown to be effective in postoperative analgesia, comparable to PCA morphine.(1441) Both studies have limitations, as there were significant differences in baseline comparability in the first, and the co intervention of rofecoxib in the latter, making the results of uncertain application. Thus, although this technique may provide an alternative to parenteral or oral opioid delivery, there is insufficient evidence to recommend it as a 1st-line therapy.

NSAIDS for Pain Management

1. *Recommendation: Prolonged Pre-operative Prophylaxis with NSAIDs*
   Prolonged pre-operative prophylaxis with NSAIDs is not recommended.

   Strength of Evidence – **Not Recommended, Evidence (C)**

Rationale for Recommendation
A high-quality study(1442) compared ibuprofen 600mg TID versus placebo for 2 weeks pre-operatively in patients undergoing hip replacement. The ibuprofen group had statistically significant differences in blood loss in the intraoperative (700mL versus 416mL) and post-operative periods (461mL versus 380mL), with total blood loss 1,161mL versus 796mL ($p < 0.01$). There were no differences in post-operative pain scores or morphine consumption. A moderate-quality study(1443) tested ibuprofen 800mg plain and with 60mg codeine versus placebo in a single prophylactic dose, demonstrating both had a small effect reducing opioid consumption in the first 5 hours. Blood loss was not mentioned in the study. Therefore, pretreatment with ibuprofen, and inferred to other NSAIDS, is not recommended, as it has an adverse effect on hemostasis, and any postoperative effect on pain can likely be gained through other techniques.

2. *Recommendation: IV Acetaminophen and Propacetamol*
   IV acetaminophen and propacetamol are moderately recommended.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation
A high-quality study demonstrated that IV acetaminophen (1gm) or propacetamol (2gm, equivalent to 1gm acetaminophen) administered over a 24-hour period provided more effective relief of pain than placebo measured by reduced morphine usage (38.3±35.1 versus 40.8±30.2 versus 57.4±52.3) and longer duration to rescue medication (3 hours versus 0.8 hours).(1444)

3. *Recommendation: Ketorolac During Post-operative Period*
   Ketorolac is strongly recommended during the post-operative period.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale for Recommendation
There are 5 high-quality studies demonstrating ketorolac as an effective analgesic in the post-operative period. Ketorolac 30mg IV provided faster onset of relief (10 minutes), lower percentage of patients requiring rescue medications (48% versus 73% placebo), and using significantly lower doses of rescue medication.(1445) Ketorolac 30mg IV with 5mg an hour infusion had less severe pain ratings at 4 hours and 35% less requirement for morphine.(1446) Ketorolac 60mg IV compared to diclofenac and placebo showed both NSAIDS having significantly lower pain scores and morphine usage over 24 hours.(1447) Ketorolac 30mg IM at the start of the operation, and 4 scheduled doses every 6 hours, also demonstrated powerful analgesia over 24 hours.(1448) A single oral dose of 10mg was shown to be as effective as two fenazon (Doleron) tablets.(1449) Ketorolac injection into the wound (inguinal hernia repair) was also shown to be of similar efficacy as IV ketorolac 60 mg in post-operative pain relief,

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although of uncertain benefit in post-hip arthroplasty patients.(1450) Therefore, there is strong evidence to recommend ketorolac (IV, IM, and oral preparations) for post-operative pain control. Caution however is warranted particularly in elderly and other patients with reduced glomerular filtration rates in whom the kidneys may be dependent on prostacylcin for renal blood flow.

4. *Recommendation: COX-2 Selective NSAIDs During Post-operative Period*
   COX-2 selective NSAIDs are strongly recommended during the post-operative period but only when bone healing is not required.

   Indications **–** COX-2 selective NSAIDs have evidence of efficacy, however, there are also concerns that they might inhibit bone healing and therefore, should be used with caution, or avoided altogether, in the acute post-operative period in situations where bone healing is required, such as in fracture repair or in hip replacements where cementless acetabular and/or femoral components are utilized.(316)

   Indications for Discontinuation – Patients taking anti-coagulation regimens as concomitant use with non-selective COX inhibitors may increase the risk of hemorrhaging.

   Strength of Evidence – **Strongly Recommended, Evidence (A)**

Rationale of Recommendation

There are 3 high- and one moderate-quality studies supporting the efficacy of cyclooxygenase 2 (COX-2) inhibitors for post-operative analgesia. Lumiracoxib 400mg once daily was demonstrated to be more effective than placebo, with similar efficacy as naproxen 500mg BID.(1451) Valdecoxib (Bextra®) was found effective in both 20mg and 40mg doses,(1452) reducing the amount of morphine required by 34% over placebo. Parecoxib (Prexige®), the prodrug of valdecoxib, was most effective in the 40mg dose.(1453) Rofecoxib (Vioxx®) reduced pain scores over placebo. The study also measured inflammatory markers from the wound drain site. The authors suggest "that upregulation of prostaglandin E_2 and interleukin 6 at central sites is an important component of surgery induced inflammatory response in patients and may influence clinical outcome."(1454) Of this class of NSAIDS, one drug, celecoxib (Celebrex®) is currently on the U.S. market. By inference, it will likely show similar effects of providing postoperative analgesia. It should be noted that concomitant use of non-selective COX inhibitors and anti-coagulation regimens may increase the risk of hemorrhage. **There is also concern that COX inhibitors, particularly COX-2 inhibitors, may inhibit bone healing.** Therefore, these agents should be used with caution or avoided altogether in acute post-operative period where bone healing is required, such as in fracture repair or in hip replacements where cementless acetabular and/or femoral components are utilized.(316)

5. *Recommendation: Non-selective and Less-selective COX-inhibiting NSAIDs During Post-operative Period*
   Non-selective and less-selective COX-inhibiting NSAIDs are moderately recommended during the post-operative period.

   Strength of Evidence – **Moderately Recommended, Evidence (B)**

Rationale for Recommendation

There are multiple studies evaluate the post-operative analgesic use of NSAIDs that have included ketoprofen, piroxicam, and diclofenac. One moderate- and one low-quality study support the use of ketoprofen for post-operative analgesia. Intravenous ketoprofen was demonstrated to be as efficacious as epidural morphine with fewer adverse effects (pruritus, urinary retention, respiratory depression) in a 13-hour follow-up.(1455) Ketoprofen administered IM was demonstrated to be as efficacious as 6mg morphine IM in a weak study with low sample size.(1456) Two moderate-quality studies demonstrated piroxicam reduced post-operative morphine consumption by 50%(1457) and buprenorphine by 42%(1458) – both studies showed reduced pain scores over placebo without significant adverse effects. Another moderate-study of piroxicam with epidural opioids vs. systemic morphine was conducted, but because of multiple interventions conclusions regarding piroxicam are weak.(1459) Two moderate-quality studies from the same author demonstrated indomethacin delivered via suppository provided improved analgesia over placebo by reduction of morphine requirements and improving pain scores,

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without significant adverse effects.(1460, 1461) Thus, there is evidence that indomethacin is effective in post-operative analgesia. One high-quality study demonstrated excellent analgesia from IV diclofenac equivalent to ketorolac without significant adverse effects.(1447) Two moderate-quality studies demonstrated diclofenac delivered IM provided improved analgesia over papaveretum (opioid) by reduction of morphine requirements and improving pain scores, without significant adverse effects.(1462) Thus, there is evidence that from multiple trials of multiple NSAIDs that these medications are effective in post-operative analgesia.

6. *Recommendation: Tricyclic Antidepressants (TCAs) During Post-operative Period*
   Tricyclic antidepressants are moderately not recommended during the post-operative period.

   Strength of Evidence – **Moderately Not Recommended, Evidence (B)**

Rationale for Recommendation
A high-quality study demonstrated post-operative treatment with amitriptyline 50mg QHS for 3 nights provided no statistically significant benefit in any of the outcomes measures.(1463) Although TCAs have been found helpful in chronic pain, there is no evidence of benefit in the studied population.

7. *Recommendation: Nefopam During Post-operative Period*
   Nefopam is recommended during the post-operative period.

   Strength of Evidence – **Recommended, Evidence (C)**

Rationale for Recommendation
Nefopam is a centrally acting nonopioid analgesic agent with anti-shivering effects that is structurally related to antihistamines and anti-Parkinsonian drugs. In combination with PCA morphine, oral nefopam demonstrated significant morphine-sparing with lower immediate post-operative pain scores without major adverse-effects. The analgesic effect seemed to be particularly notable for patients with intense preoperative pain. Based on limited evidence, nefopam is recommended for post-operative analgesia.

Epidural Anesthesia/Analgesia

1. *Recommendation: Epidural – Single Injection-Extended Release Epidural Morphine*
   There is quality evidence that single epidural injection of extended release morphine is more effective than parenteral or oral opioid medications for post-operative analgesia in this group of patients. However, epidural catheters and injections in the presence of DVT prophylaxis are associated with potentially severe adverse effects. Therefore, it is recommended for highly select use in patients who are without contraindications and who are closely monitored. Extended release morphine provides longer term analgesia than morphine.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
There is one high-quality study which shows significant pain relief over placebo for 48 hours with a single epidural injection of extended release epidural morphine.(1464) This technique has a primary advantage of eliminating the indwelling epidural catheter. There is no quality data comparing extended release epidural morphine to other opioid or opioid-local combination continuous infusions. There was a statistically significant increase in vomiting and pruritus versus placebo. There were an increased number of patients with respiratory depression, although not statistically significant. Another moderate-quality study(1465) demonstrated a single epidural bolus of 2mg morphine (non-extended release) was superior to a single IM morphine 10mg injection. Another moderate-quality study also suggests an additional benefit of pre-operative epidural opioid (morphine 75µg/kg) injection in reducing physiological stress to surgery reflected by lower serum cortisol levels.(1466) However, either injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects.

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2. *Recommendation: Continuous Epidural Opioids*
   There is quality evidence that opioid epidural analgesia is more effective than parenteral or oral opioid medications for post-operative analgesia in this group of patients. However, epidural catheters and injections in the presence of DVT prophylaxis are associated with potentially severe adverse effects. Therefore, it is recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
Three moderate-quality RCTs support the use of epidural opioid analgesia over parenteral or oral opioid analgesia. A moderate-quality RCT showed continuous epidural of both morphine or fentanyl was effective in pain control with minimal adverse effects.(1467) Another moderate-quality RCT showed epidural pethidine (meperidine) to be superior to IM pethidine.(1468) However, either injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects.

3. *Recommendation: Epidural Local Anesthetics with Opioids*
   There is quality evidence that continuous epidural infusions of local anesthetics (bupivacaine, levobupivacaine) in combination with opioids are effective in providing post-operative analgesia. However, epidural catheters and injections in the presence of DVT prophylaxis are associated with potentially severe adverse effects. Therefore, it is recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
A high-quality study of bupivacaine and morphine continuous infusion(1469) versus placebo demonstrated superior analgesia without any significant differences in rehabilitation and functional recovery compared to placebo. A moderate-quality study demonstrated excellent analgesic relief of bupivacaine in combination with fentanyl or morphine, with no difference in analgesic effect between the two. Patients receiving morphine demonstrated a statistically significant decrease in SpO_2 which was clinically insignificant in the population.(1470) Another moderate-quality study of the efficacy of bupivacaine with 5 different opioids (fentanyl, morphine, methadone, diamorphine, and meperidine) demonstrated that all combinations provided adequate pain relief with no differences in analgesic quality between opioids. The adverse effect profiles showed significant differences, each with specific characteristics, with no conclusion on which opioid is superior.(1471) There is one moderate-quality study comparing the efficacy of epidural morphine versus bupivacaine, which demonstrated longer analgesia (28 versus 4.3 hours) in the morphine group.(1472) A study of epidural tramadol added to lidocaine anesthesia did not provide any clinical benefit for post-operative analgesia.(1473) However, either injections or catheters utilized when there is DVT prophylaxis have been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks; highly select use is recommended with careful monitoring of adverse effects.

4. *Recommendation: Continuous Epidural Local Anesthetics Only*
   There is quality evidence that continuous epidural infusion of local anesthetics in the absence of opioids provides effective post-operative analgesia, and theoretically may provide an alternative to opioid analgesia for patients who have contraindications. However, epidural catheters and injections in the presence of DVT prophylaxis are associated with potentially severe adverse effects and a high adverse effect profile for hypotension has been reported.(1417) **Therefore, there is no recommendation for or against use of continuous epidural local anesthesia.**

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

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Rationale for Recommendation
A high-quality study demonstrated adequate post operative pain relief without detectable motor blockade using a high concentration of levobupivacaine (0.25%).(1417) A moderate-quality study showed continuous infusion of bupivacaine provided significantly better analgesia than PCA morphine, and allowed patients to be discharged sooner from the post-anesthesia care unit.(1474) Another moderate-quality study demonstrated epidural ropivacaine at multiple rates of infusion was superior to PCA morphine in all doses, and suggested an optimal dose of 10 ml/hr of 0.2% to limit adverse effects of urinary retention and hypotension.(1475) There are no quality studies comparing local anesthetic infusions to combination local-opioid infusions, or to other local anesthetic agents (i.e., bupivacaine versus levobupivacaine). Therefore, there is no recommendation for the use of one agent or technique over another. However, injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects. As the adverse effects of this intervention have included hypotension, there is no recommendation for or against use of anesthetics alone delivered by continuous epidural.

5. *Recommendation: Epidural Local with Clonidine*
   As epidural catheters and injections in the presence of DVT prophylaxis are associated with potentially severe adverse effects, an epidural local with clonidine it is recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
Clonidine is an α adrenoceptor agonist and is believed to have antinociceptive properties.(1476) A moderate-quality study comparing extradural clonidine alone and in combination with morphine versus morphine alone demonstrated less PCA morphine requirement and longer time to first use in the clonidine (50µg) group and in the morphine/clonidine combination group, but with no difference between these two.(1477) Epidural clonidine provided improved analgesia and anesthesia in a combination intrathecal/epidural clonidine study.(1478) These studies suggest that clonidine is effective in immediate postoperative pain in epidural analgesia, both alone and in combination with opioids. However, either injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects.

Intrathecal Anesthesia/Analgesia
Spinal administration of local anesthetic and other medications is another technique for delivery of operative anesthesia and postoperative analgesia. Controlled trials of intrathecal (IT) administration of local anesthetics, opioids, and combinations of the two are available. Intrathecal analgesia, while effective, has a high incidence of manageable adverse effects, primarily pruritus, nausea, vomiting, urinary retention and respiratory depression. **However, epidural catheters and injections in the presence of DVT prophylaxis are associated with potentially severe adverse effects. Therefore, it is recommended for highly select use in patients who are without contraindications and who are closely monitored for adverse effects.**

1. *Recommendation: Spinal/Local Anesthetic Only*
   Spinal/local anesthetic is recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation

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There are no quality studies of local anesthetic vs. saline placebo. However, many of the studies reviewed include intrathecal local anesthesia as a control arm. Intrathecal anesthesia generally with bupivacaine or ropivacaine provides post-operative analgesia for approximately 6 hours. Intrathecal anesthesia in most cases is enhanced by the use of opioid adjuvants. Therefore, intrathecal anesthesia with bupivacaine is effective in postoperative pain relief, but another technique is usually added to enhance duration and quality after the immediate post-operative period.

2. *Recommendation: Spinal Continuous/Local Anesthetic*
   Spinal continuous/local anesthetic is recommended for select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

3. *Recommendation: Spinal/Continuous Opioid Infusion*
   Spinal/continuous opioid infusion is recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendations
There is high-quality evidence that intrathecal opioids provide superior analgesia of postoperative lower extremity surgery compared to parenteral opioids. The primary opioids studied are morphine, sufentanil, fentanyl and meperidine. There is insufficient evidence to recommend one opioid over another as they each have different adverse effect profiles. Careful selection by the practitioner is warranted. A high-quality study of intrathecal sufentanil compared with parenteral sufentanil(1479) showed the continuous spinal route of administration with more rapid, better quality, and longer duration analgesia compared with the intravenous route. A moderate-quality study comparing continuous spinal anesthesia vs. single shot showed continuous anesthesia to have the advantage of providing better postoperative analgesia over PCA morphine, with better hemodynamic stability during general anesthesia induction.(1480) There are no quality studies comparing continuous infusion to placebo. There is one moderate-quality study comparing continuous intrathecal morphine versus epidural bupivacaine, which reported a high level of technical complications with catheters, recommending against indwelling intrathecal catheters.(1481) Two high-quality studies and one moderate-quality study compare the efficacies between opioids. No difference between intrathecal morphine-6-glucuronide and morphine sulfate as measured by objective measures (PCA pain relief) were found.(1482) A moderate-quality study described excellent results in pain relief with no recommendation between intrathecal sufentanil or fentanyl (40µg).(1483) Another moderate-quality study comparing intrathecal fentanyl infusion (120µg/24 hours) versus intrathecal morphine (bolus or infusion) found the fentanyl infusion to be inadequate, but the morphine bolus or infusion to be equally effective in the first 18 hours.(1484) However, either injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects.

4. *Recommendation: Spinal – Combination Local/Opioid Anesthetic*
   Spinals with combination local/opioid anesthetic are recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Rationale for Recommendation
There is one moderate-quality study of local spinal anesthesia without opioids compared to spinal anesthesia with opioids. However, many of the studies reviewed for other adjuvant therapies include intrathecal local anesthesia with and without opioid as control arms, which have demonstrated enhancement of the spinal block by the use of opioids. A high-quality study comparing IT bupivacaine alone with IT bupivacaine with morphine did not address pain relief, but demonstrated a delay in gastric emptying in the morphine group.(1485) Intrathecal bupivacaine was less effective as the control arm

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versus IT bupivacaine with opioid(1486) in a moderate-quality study. Another moderate-quality study demonstrated a significant improvement in duration of analgesia with the addition of diamorphine to bupivacaine.(1487) There are two other moderate-quality studies comparing single IT injections of morphine to another opioid. In the first study,(1488) morphine 1.0mg was more effective than diamorphine 0.75mg in reducing PCA rescue analgesia. In a second study,(1489) nalbuphine was more effective at reducing PCA use with faster onset of pain relief than morphine (.160mg). Caution must be taken in making inferences regarding opioid preference because of the wide difference in morphine dosages. However, either injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects.Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects.

5. *Recommendation: Spinal – Clonidine in Combination with Local Anesthetics*
   Spinals with clonidine are recommended for highly select use in patients who are without contraindications and who are closely monitored.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**

6. *Recommendation: Spinal – Clonidine Alone or in Combination with Opioids*
   Spinals with clonidine are moderately not recommended.

   Strength of Evidence – **Moderately Not Recommended, Evidence (B)**

Rationale for Recommendation
Clonidine, an alpha-adrenoreceptor agonist, has been used as an adjuvant or opioid substitute in intrathecal anesthesia. There is conflicting quality evidence for support of clonidine, with the balance opposing routine use of clonidine. Clonidine provides no additional benefit to concomitant use of intrathecal opioids in the dosages studied. However, clonidine with opioid may be considered an effective substitute when bupivacaine is contraindicated. A high-quality study comparing administration of 75µg clonidine with IT morphine (0.5mg) versus intrathecal morphine (0.5mg) alone versus placebo showed no added benefit, as both were profoundly better than placebo. Further, the incidence of emesis was similar to the morphine group and patients receiving clonidine had a significantly lower mean arterial blood pressure.(1490) A similar moderate-quality study comparing 75µg clonidine to 1.0mg morphine demonstrated weak effect for clonidine and strong effect for morphine.(1491) A moderate-quality study comparing a clonidine (75µg)/meperidine combination versus morphine (0.5mg) as an adjuvant to IT bupivacaine provided no added benefit and again resulted in hypotension.(1486) Intrathecal clonidine was shown to cause less bladder distension compared with morphine in a moderate-quality study.(1492) In another moderate-quality study, IT clonidine dose-response was evaluated, showing significant analgesia improvement over placebo. The authors recommend clonidine 150µg, which was double that used in other described trials.(1493) Clonidine was shown to be an effective adjunct with bupivacaine in a combination intrathecal/epidural local anesthetic with clonidine study.(1478) Based on available evidence, clonidine does not appear to be effective alone as an intrathecal agent or in combination with opioids. There is limited evidence suggesting clonidine can act as an adjunct with intrathecal bupivacaine. However, either injections or catheters utilized when there is DVT prophylaxis have also been associated with major adverse effects. Thus, use of injections and catheters when patients are treated for DVT prophylaxis should be carefully considered and balanced with the adverse risks and highly select use is recommended with careful monitoring of adverse effects.

7. *Recommendation: Spinal Infusion – Ziconotide*
   Spinal infusion with ziconotide is moderately not recommended.

   Strength of Evidence – **Moderately Not Recommended, Evidence (B)**

Rationale for Recommendation
Continuous intrathecal infusion of ziconotide, an N-type calcium channel blocker, versus placebo was studied in a high-quality RCT in two different doses (7µg/h versus 0.7µg/h).(1494) The high dose was demonstrated to be significantly more effective than placebo in analgesia. However, there was a high

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adverse effect profile that resulted in discontinuation of the higher dose. The lower dose was not statistically different than placebo. Therefore, ziconotide spinal infusion is not recommended at either of the doses in this study. Future studies may determine if there is an effective dose that balances adverse effects.

Prevention of Adverse Effects

1. *Recommendation: Tropisetron for Control of Adverse Effects of Spinal Opioid Anesthesia*
   Tropisetron is not recommended for patients receiving spinal anesthesia with local anesthetic and morphine.

   Strength of Evidence – **Not Recommended, Evidence (C)**

Rationale for Recommendation
Tropisetron is a selective 5-HT3 receptor antagonist used for control of nausea and emesis. A moderate-quality study of tropisetron given to patients receiving spinal infusion of bupivacaine/morphine was compared with saline placebo.(1495) The addition of tropisetron showed no significant difference in post-anesthesia rates of nausea, emesis, or pain control. Therefore, there is moderate evidence against the use of tropisetron to control adverse effects related spinal anesthesia in this patient population.

2. *Recommendation: Spinal – Naloxone for Control of Respiratory Depression*
   The addition of intravenous naloxone infusion in combination with local/opioid intrathecal infusion is not recommended.

   Strength of Evidence – **Not Recommended, Evidence (C)**

Rationale for Recommendation
A moderate-quality study compared the ventilation in patients given intrathecal bupivacaine and morphine with and without IV naloxone. At 8 and 24 hours postoperatively, there were no significant differences between the comparison groups in ventilation.(1496)

3. *Recommendation: Propofol Infusion for Control of Nausea and Emesis*
   Propofol infusion is not recommended for control of nausea and emesis.

   Strength of Evidence – **Not Recommended, Evidence (C)**

4. *Recommendation: Phenothiazines for Control of Nausea and Emesis*
   There is no recommendation for or against the use of phenothiazines.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendations
A high-quality study demonstrated propofol infusion (30mg/hour) compared to inert lipid emulsion did not provide significant relief of post-operative nausea, emesis, or pruritus.(1497) Therefore, propofol in low dose is not recommended for this use. A low-quality study compared symptomatic relief of cyclizine, perphenazine, prochlorperazine, droperidol, and metoclopramide and domperidone for antiemetic effects. The phenothiazines (perphenazine, prochlorperazine) demonstrated a significant improvement in patient report of nausea.(1498) However, study details were sparse and design unclear, making application of the results difficult.

5. *Recommendation: Nicardipine to Induce Hypotension*
   Nicardipine to induce hypotension is not recommended.

   Strength of Evidence – **Not Recommended, Evidence (C)**

Rationale for Recommendation
A moderate-quality study demonstrated nicardipine to have no advantage over nitroprusside inducing deliberate hypotension during hip surgery to reduce blood loss.(1499) Nicardipine had cumulative and persistent effects after discontinuation. Therefore, nicardipine to induce hypotension is not recommended.

Evidence for the Use of Anesthesia/Analgesia

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There are 25 high-quality and 47 moderate-quality RCTs incorporated in this analysis. There are 2 low-quality RCTs(1456, 1498) included in the treatment of adverse anesthesia effects section below for completeness but they were not relied upon to develop guidance.

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Epidural Anesthesia and Analgesia for Hip/Knee Arthroplasty						
Viscusi 2005 RCT	9.5	N = 200	Extended release epidural morphine (EREM) 15mg, 20mg, or 25mg vs. epidural saline placebo	Mean post-op fentanyl consumption significantly lower in all groups receiving EREM vs. placebo (p <0.0001). Median time to first post-op use of PCA fentanyl, 3.6 hours in placebo group vs. 21.3 hours for all patients receiving EREM (p <0.0001). Patients receiving EREM showed a significant increase in vomiting and pruritus vs. placebo. Numerically, more EREM patients with respiratory depression, although not statistically significant.	"EREM provided significant postoperative pain relief over a 48-h period after hip surgery, without the need for indwelling epidural catheters."	May be particularly beneficial in post-op rehabilitation as no indwelling epidural catheter is required in this often anti-coagulated cohort.
Murdoch 2002 RCT	9.5	N = 105	Continuous epidural infusion of levobupivacaine at three different concentrations for post-op pain relief in patients undergoing knee or hip arthroplasty.	Epidural infusion of levobupivacaine administered at 0.0625% vs. 0.125% vs. 0.25% at 6 ml/hour 24 hours. Total normalized dose of morphine, number of patient-controlled analgesia requests, overall post-op VAS pain scores significantly lower for 0.25% group vs. other two. No difference between groups in maximal motor blockade. Safety data equivalent among 3 groups. Rescue analgesia: no morphine: (3%) vs. (11%) vs. (47%) Average time to rescue (hour): 8.1 vs. 9.5 vs. 16.7. Rescue morphine dose (mg/h): 1.5 vs. 1.0 vs. 0.2.	"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%).
Foss 2005 RCT	8.0	N = 60	Post-operative pain relief by continuous epidural 4 ml/hour infusion of bupivacaine 0.125% and morphine (50µg) vs. saline placebo	"Epidural analgesia provided superior dynamic analgesia during all basic physical functions, and patients were significantly less restricted by pain, which was the dominating restricting factor in the placebo group. Motor blockade was not a restricting factor during epidural analgesia. Despite improved pain relief, scores for recovery of physical independence were not different between groups."	"Postoperative epidural analgesia after hip fracture surgery provides superior analgesia attenuating pain as a restricting factor during rehabilitation without motor dysfunction. However,	Study examines post-operative analgesia and functional recovery outcomes. Absence of improved recovery with pain control is an important finding in light of the numerous studies determining which post-operative pain control method is most effective.

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					superior analgesia did not translate into enhanced rehabilitation. Future studies with multimodal rehabilitation are required to establish whether superior analgesia can be translated into enhanced rehabilitation and reduced morbidity in hip fracture patients."	
Berti 1998 RCT	7.5	N = 30	Post-operative anesthesia by continuous epidural infusion of bupivacaine 0.125% at 4ml/hour) in combination with either fentanyl (0.005mg/ml) vs. morphine (0.05mg/ml)	"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 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).	"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.
Gedney 1998 RCT	7.0	N = 160	Study groups received epidural infusions of bupivacaine (6-8ml an hour) in combination with morphine (0.05 mg/ml) vs. fentanyl (2.0 µg/ml) vs. methadone (0.1 mg/ml) vs. diamorphine (0.05 mg/ml) vs. pethidine (1.0 mg/ml).	"The incidence of nausea and vomiting was significantly greater with morphine than fentanyl (p = 0.0097) and pethidine (p = 0.0021). The incidence of pruritus was significantly greater with morphine and diamorphine than with methadone (P=0.12) and pethidine (P=0.027). Morphine was also associated with a significantly greater incidence of urinary retention than pethidine (P=0.012) and methadone (P=0.025)."	"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 the lowest overall incidence of	Pethidine is also known as meperidine (Demerol). There is no clear conclusion by these authors as to which opioid is superior.

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					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 RCT	7.0	N = 68	Bolus followed by continuous epidural infusion of morphine vs. fentanyl. (dosages were variable)	Pain relief similar in both groups. In morphine group, PaCO2 elevation and nausea occurred over 12 hours (p <0.05). In fentanyl group, there was no PaCO2 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 RCT	6.0	N = 100	Extradural clonidine (25µg/ mL/hour) vs. extradural clonidine (50µg/ mL/hour) vs. extradural morphine (0.1mg/ mL/hour) vs. clonidine plus morphine (50µg/ mL/hour and 0.1mg/mL/hr).	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 use: 144/286/109/283 minutes respectively.	The requirements for systemic analgesia were least in the combination and larger dose clonidine group.	
Wulf 1999 RCT	5.5	N = 90	Ropivacaine epidural anesthesia and analgesia vs., general anesthesia and PCA morphine	"On the day of operation, 9% of patients in the epidural anesthesia and analgesia (EDA) group received morphine. In the GA/PCA group, 67% of patients received morphine in addition to PCA morphine. Patients with wound pain at rest EDA vs. GA/PCA n(%): 2h after arrival in the PACU: 1(2.3) vs. 27(60.0) 10h after arrival in the PACU:	"Compared with general anesthesia and postoperative IV patient-controlled analgesia with morphine, epidural anesthesia and analgesia with the new local anesthetic	No blinding of patient, providers, or assessors.

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				9(20.9%) vs. 17(37.8) 48h after arrival in the PACU: 4(9.3) vs. 7(15.6)."	ropivacaine enables patients to be discharged sooner from a postanesthesia care unit and provides superior pain relief during the first 24 h after hip replacement."	
Gustafsson 1986 RCT	5.5	N = 21	1 mg/kg of pethidine IM vs.20mg of pethidine IM vs. 60mg of extradural pethidine	"At 0.25-1.5 h after administration VAS scores were lower in patients treated with extradural doses of pethidine than in those given the drug imp."	"The present study shows that extradural pethidine produces short-lived analgesia, in contrast to the long-lasting effect of morphine found in other studies."	Blinding unclear, small sample size.
Reiz 1981 RCT	5.5	N = 33	Single epidural morphine (2mg) injection vs. morphine (10mg) IM injection after hip replacement surgery using epidural anesthesia	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, compared to 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.
Turner 1996 RCT	5.0	N = 151	PCA morphine vs. epidural ropivacaine (0.2%) infusion at rates of 6, 8, 10, 12, or 14ml/hour post-operative for knee/hip surgery.	"Median total morphine consumption during the study was 36mg in the control group, 13mg in the 6-ml h-1 group. 11mg in the 12ml h-1 group and 3mg in the 14-lm h-1 group. Median VAS scores in the control group were 18-30 for the first 10 h whereas VAS scores for the ropivacaine groups did not exceed 8 during the same period."	"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 RCT	5.0	N = 32	Epidural morphine vs. 0.5% bupivacaine with epinephrine	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	

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					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."	
Kilickan 2000 RCT	4.0	N = 60	Pre-dermal incision intravenous morphine (0.15mg/kg) vs. pre-emptive epidural (75 µg/kg) morphine vs. IV saline in hip and knee arthroplasty	"The pre-i.v. group used significantly less morphine than the pre-epi group ($p < 0.0003$). In all groups, plasma cortisol levels increased as compared to pre-op values, but plasma cortisol increased more significantly in the pre-i.v. and control groups within 4 hrs of surgery and was still significantly elevated at 7 am of the first postoperative morning compared to the pre-epi group ($p <0.001$) and the increase persisted to the next morning in patients pre-i.v. and control groups. In pre-epi group, VAS pain scores at rest and on movement at 3, 6, 12, 24, and 48hours were significantly less than in the pre-i.v. groups and control groups ($p <0.001$)"	"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.
Intrathecal Anesthesia and Analgesia for Hip/Knee Arthroplasty						
Atanassoff 2000 RCT	8.5	N = 30	Continuous intrathecal infusion post-operatively of placebo vs. ziconotide (an N-type calcium	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	"The high dose group required significantly less narcotic and non-steroidal medication than placebo as	This was a phase II trial with discontinuation of the higher dose infusion, and no difference in placebo vs. low

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			channel blocker) 7µg/hour vs. 0.7µg/hour	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.	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."	dose therapy group.
Grace 1995 RCT	8.5	N = 75	Intrathecal co-administration of clonidine hydrochloride (75µg) and morphine sulfate (0.5mg) vs. intrathecal morphine (0.5mg) vs. saline placebo in spinal anesthesia for hip replacement surgery	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 significantly lower in clonidine/morphine group than others. Incidence of emesis similar to morphine-alone group, and significantly higher than control group.	"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 0.5 mg alone, and, furthermore, it was associated with marked reductions in mean arterial pressures between 2-5 hours after IT administration."	No added benefit of IT clonidine.

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Fournier 2005 RCT	8.5	N = 40	Intrathecal (7.5 µg) vs. intravenous sufentanil (1.25 mg) for postoperative pain relief after total-hip replacement where total spinal anesthesia was used.	"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 RCT	8.5	N = 75	Intrathecal morphine-6-glucuronide (M6G) at 100µg and 125µg vs. intrathecal morphine sulfate (500µg) for post-operative hip replacement pain control	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 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.	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 group. Side effects were high in all groups but not significantly different.	Pain relief as measured by subjective pain scale was improved in treatment group, but no clinical difference was observed by objective measures of patient-controlled analgesia (PCA).
Lydon 1999 RCT	8.0	N = 24	Intrathecal bupivacaine (17.5mg) vs. combination of intrathecal morphine (0.6mg) and bupivacaine (17.5mg) in spinal anesthesia for hip arthroplasty	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 Acta	7.5	N = 40	Morphine 160µg vs. nalbuphine 400µg	VAS pain scores decreased more rapidly in nalbuphine group with time to pain	After total hip replacement, administration	Study prematurely terminated due to slow onset of action

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Anaesthesiol Scand RCT				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).	of intrathecal nalbuphine resulted in a significantly faster onset of pain relief and shorter duration of analgesia than intrathecal morphine.	in morphine group. Dosage of morphine is significantly lower than other studies, making comparison difficult.
Fogarty 1993 RCT	7.5	N = 90	Intrathecal clonidine 75µg (100µg if over 76kg) vs. morphine 1mg vs. saline	Post-operative morphine consumption much lower in intrathecal morphine group and diverged within 4 hours (graphic representation). Time 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).	"Both intrathecal clonidine and intrathecal morphine prolonged the time to first analgesia compared with saline (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."	This demonstrated a weak effect of intrathecal clonidine and a strong effect of morphine.
Pitkanen 1993 RCT	7.0	N = 54	Tropisetron 5mg (5-HT3-receptor antagonist) vs. saline placebo in patients undergoing intrathecal bupivacaine (0.5%)/ morphine (0.3mg) block for	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	Negative study.

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			lower extremity surgery		bupivacaine and morphine."	
Fournier Anesth Analg 2000 RCT	7.0	N = 42	Intrathecal sufentanil (7.5µg) vs. fentanyl (40µg) in bupivacaine spinal anesthesia	There were no significant differences between the groups in pain scores, rescue analgesia, adverse effects, elapsed time for pain relief, time to lowest pain score and duration of pain relief.	"After total hip replacement, both lipid soluble opioids produce excellent analgesia with comparable onset, duration of action, and low incidence of minor adverse effects."	No recommendation of one over the other from this study. Both effective in post-operative pain management.
Niemi 1993 RCT	7.0	N = 60	Post-op intrathecal fentanyl infusion (120µg/24 hour) vs. intrathecal morphine infusion (200µg/24 hour) vs. intrathecal morphine bolus (200µg)	"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 RCT	7.0	N = 90	IT bupivacaine vs. IT bupivacaine with morphine sulfate (0.5mg) vs. IT pethidine (0.75mg/kg) and clonidine (75µg)	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.

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Gentili 1996 RCT	6.5	N = 40	Intrathecal morphine (0.2mg) vs. clonidine (75µg) in combination with bupivacaine spinal anesthesia (15mg) for hip surgery	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.
Fogarty 1995 RCT	6.0	N = 60	Intrathecal diamorphine 0.75mg vs. intrathecal morphine 1.0mg	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."	
Maurer 2003 RCT	6.0	N = 68	Continuous spinal anesthesia and post-operative analgesia vs. single-shot spinal anesthesia	"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 RCT	6.0	N = 75	Spinal anesthesia with bupivacaine (18mg) in combination with saline placebo, clonidine (37.5µg), clonidine (75µg) or clonidine (150µg) (Groups 1, 2, 3, 4 respectively)	"Time to regression of spinal anesthesia below level L1, was 228±62 min Group 1 (control), 311±101 min (+8%) in Group2, 325±69 min (+13%) in Group 3, and 337±78 min (+17%) in Group 4 (estimated parameter for dose 0.23 [95% CI, - 0.05-0.50]). Time interval between spinal anesthesia and first request for supplemental PCA morphine was significantly longer in all clonidine groups. 295±80 min in Group 1 (control), 343±75	"We conclude that small doses of intrathecal clonidine (≤150 µg) significantly prolong the anesthetic and analgesic effects of bupivacaine in a dose-dependent manner and that 150 µg of clonidine seems to be the preferred dose, in terms of	Blinding unclear.

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				min (+16%) in Group 2, 381±117 min (+29%) in Group 3, and 445±136, in (+51%) in Group 4 (estimated parameter for dose 1.02 [95% CI 0.59-145]).”	effect versus unwarranted side effects, when prolongation of spinal anesthesia is desired.”	
Johnson 1992 RCT	5.5	N =3 0	IT bupivacaine (20 mg) vs. IT bupivacaine + IT morphine (0.3 mg) vs. IT bupivacaine (20mg) + IT morphine (0.3mg) + IV naloxone infusion	“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.
Reay 1989 RCT	5.0	N = 60	Intrathecal bupivacaine + diamorphine 0.25mg or 0.5mg vs. bupivacaine anesthesia	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 intervention groups (p, 0.001), but not between diamorphine groups.	“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 and vomiting, was high in both groups receiving intrathecal diamorphine.”	Baseline differences present, method details sparse.
Niemi 1994 RCT	4.0	N = 55	Continuous intrathecal morphine (8.3µg/hour) vs. epidural catheter (200µg/hour +0.25 % bupivacaine 4ml/hour) for hip arthroplasty	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.	There were high rates of technical problems not reported in other studies.

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					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."	
Regional Block Anesthesia and Analgesia for Hip/Knee Arthroplasty						
Bogoch 2002 RCT	9.5	N = 115	Lumbar paravertebral nerve block compared with sham procedure	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, including for a shorter hospital stay.
Gao 1995 RCT	8.5	N = 30	Bupivacaine vs. bupivacaine with buprenorphine in caudal block for post-operative pain relief in hip and knee arthroplasty	The duration of analgesia was much longer (mean 606 minutes vs. 126 minutes p <0.001) in those receiving added buprenorphine; mean morphine consumption in the first 24 hours was halved (14mg vs. 28mg) and patient satisfaction greatly increased.	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.

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Foss 2007 RCT	8.0	N = 48	Patients with suspected hip fracture given fascia iliaca compartment block (FICB) with 1.0% mepivacaine on affected side, with saline injection placebo on contralateral vs. saline injected FICB placebo with 0.1mg morphine injection on contralateral side	"Maximum pain relief was superior in the FICB group both at rest (P<0.01) and on movement (P=0.02). The median total morphine consumption for rescue pain was significantly higher in the placebo group. More patients were sedated in the morphine group at 180 minutes after block as compared with the FICB group."	"Pain relief was superior at all times and at all measurements in the FICB group."	The study suggests FICB is a superior pain management technique to morphine IM injection in the emergency department for patients suspected to have a hip fracture.
Mannion Anesth Analg 2005 RCT	7.0	N = 36	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	"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."	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 RCT	6.5	N = 45	PCA morphine vs. femoral nerve block versus psoas compartment block	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 results suggest a lack of power to detect a beneficial effect of psoas compartment blocks on total post-operative opioid consumption.

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					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."	
Bianconi 2003 RCT	6.5	N = 37	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 infusion vs. saline i.v. infusion with ropivacaine irrigation and wound instillation (0.2% at 5ml/hour)	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 plasma concentration remained below toxic concentrations and no adverse effects occurred.	"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).
Fournier 1998 RCT	6.5	N = 40	General anesthesia (GA) with sham block vs. general anesthesia with a "3-in-1" femoral nerve block (FNB)	"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.
Siddiqui 2007 RCT	6.0	N = 32	Continuous lumbar plexus block combined with PCA vs. PCA only	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	Continuous perioperative lumbar plexus block provides superior analgesia, and reduces opioid requirements and opioid-related adverse	

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				follow-up in umbar plexus block (approximately VAS 5 vs. 3 at 20 hours, graphic representation). Patient satisfaction also favored blocks (p = 0.02).	effects compared with systemic opioids after hip arthroplasty.	
Stevens 2000 RCT	6.0	N = 60	General anesthesia vs. general anesthesia with posterior lumbar plexus block (bupivacaine)	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-operative (48 hour): 170±125 vs. 310±204 p = 0.003.	"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 should be anticipated in a minority of cases."	Suggestive of attractive option for postoperative pain management.
Parenteral/Oral Anesthesia for Hip/Knee Arthroplasty						
Manoir 2006 RCT	8.5	N = 63	Oral morphine 10mg, 20mg vs. placebo every 4 hours for 24 hours post total hip arthroplasty	Amount of morphine administered via patient-control analgesia over 24 hours reduced in 20mg group compared with placebo (19±2.7 vs. 33±5.5). No significant effect observed in 10mg group. No significant differences across groups in pain scores, quality of pain relief, or incidences of nausea, urinary retention and pruritus.	Despite a limited absorption of oral morphine postoperatively, high doses of oral morphine have a significant analgesic effect after total hip arthroplasty.	Unspecified clinical significance of reducing PCA analgesia (not stopping). Patients in all groups similarly satisfied with pain control quality of treatment.
Reiter 2003 RCT	8.5	N = 98	Pre-operative oral administration of placebo vs. morphine sulfate (20mg) in hip or knee replacement surgery	Group receiving morphine had significantly less cumulative piritramide (analgesic) consumption during 24 hours post-op than placebo (37.5 +/- 12.5mg vs. 46.8 +/- 22.1, t-test, p <0.05), although similar pain scores recorded (group 1: 4.8 +/- 1.8 and 3.6 +/- 1.7, group 2: 4.8 +/- 1.6 and 3.4 +/- 2.0, at 1 and 24 hours, respectively). No significant differences observed in side effects between groups.	"These data show that the preoperative oral administration of morphine sulfate, regardless of its short half-life, can reduce postoperative consumption of opioids at similar pain levels."	Pre-op oral morphine in patients undergoing hip or knee replacement may have a positive effect on pain relief. Piritramide, is a schedule I synthetic opioid narcotic in U.S.

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Tarradell 1996 RCT	6.5	N = 48	Single doses of 100mg meperidine vs. 100mg tramadol vs. saline after general anesthesia for hip/knee arthroplasty	Thirty minutes after treatment, patients who requested additional analgesia rescued with 75mg diclofenac and morphine as required. Meperidine produced a significant depression of ventilation revealed by an increase in PaCO2 and decrease in tidal volume, respiratory rate and %02 saturation lasting approximately 1 hour. Onset for meperidine analgesia 10 minutes; >30 minutes tramadol. Both opioids produced similar degree of analgesia in patients not rescued.	"In the present study, meperidine and tramadol produced comparable analgesia, with a different time course profile, but meperidine induced sedation and respiratory depression while tramadol did not."	Both treatments at the given dosage provided only partial analgesia.
Frater 1989 RCT	6.0	N = 49	Meptazinol vs. morphine through PCA post general anesthesia for total hip replacement	Episodic hypoxemia seen in both groups. In meptazinol group, 80% of patients (21/26) had Sa02 <90% at some time and 23% (6/26) had Sa02 <85%. In morphine group, corresponding figures were 95% (22/23) and 47% (11/23). Mean linear analogue scores for pain and nausea significantly greater in meptazinol group at 8 hours only (p <0.05).	"Meptazinol and morphine in equianalgesic doses had similar effects on ventilation in the postoperative period."	Results suggest meptazinol does not provide any advantage for pain control or GI adverse effects.
Robinson Anaesthesia 1991 RCT	6.0	N = 40	Morphine vs. diamorphine administered via PCA following hip replacement surgery	Mean (SD) (95% confidence interval) dose of morphine (mg) given during surgery and in recovery room; no significant differences. Morphine vs. diamorphine: Recovery: 2.6 (3.6) vs. 3.5 (3.7)	"There were no significant differences between the two groups with regard to postoperative sedation, nausea, well-being, pain relief and requirements for antiemetic drugs."	Details of methodology and results sparse.
Ashburn 1993 RCT	6.0	N = 38	Oral Transmural Fentanyl Citrate (OTFC) (7-10µg/kg) vs. placebo	OTFC group made 10±15 vs. 25±26 PCA attempts and received 6.4±6.4mg vs. 14.6±6.6mg.	"OTFC can provide analgesia to patients following major orthopedic surgery. The specific role, if any, OTFC will play in the management of acute pain has yet to be defined. One milligram of OTFC appears to be as potent	The dropout rate was 39.1%. The results were reported in the text as statistically negative and in the abstract as statistically positive.

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					as 5mg of intravenous morphine. The incidence and severity of opioid-induced side effects not increased by use of OTFC."	
Bourke 2000 RCT	5.0	N = 39	Oral morphine 20mg and a placebo IM injection vs. oral placebo with morphine sulfate 10mg IM injection on scheduled basis post bupivacaine (15mg) spinal anesthesia	Pain scores assessed by VAS and verbal scales at rest and with movement low in both groups, no statistical significance between groups. Mean patient controlled analgesia consumption significant only at 36 hour post-op, favoring IM group with less morphine used. No differences in side effects observed.	"Oral, sustained-release morphine is a suitable alternative to the IM opiates in this population undergoing total hip replacement under spinal anesthesia."	Lack of blinding, concealment of treatment allocation.
Murphy 1984 RCT	4.5	N = 30	Epidural buprenorphine 60µg vs. intramuscular morphine 0.15mg/kg	Mean pain score reductions were comparable between groups.	"Both forms of analgesia produced excellent pain relief as assessed by the linear analogue scoring system. In both quality and duration of pain relief, no significant difference was found between the two forms of analgesia, but the total dose of epidural buprenorphine requires was 5 times less than equivalent dose of intramuscular morphine. No side effects attributable to epidural buprenorphine administration found. Authors conclude that low dose epidural buprenorphine provides an excellent alternative to intramuscular opiates for pain relief after hip surgery."	Equivocal results in pain management.

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Ashburn 1992 RCT	4.5	N = 38	Iontophoretically delivered morphine HCl vs. iontophoretic lactated ringers	In 6-hour baseline period, morphine group requested PCA 23.8±36.9 times vs. 8.8±9.2 times for LR (p = 0.032). Baseline amount of meperidine received also higher in morphine group (93.6±41.8 vs. 57.7±39.8). During subsequent 6-hour iontophoretic administrations, number of PCA requests were approximately 12 for LR group vs. 5 for MS group (interpretation of graphic data, p <0.05) and meperidine administered also lower for MS group (interpretation of graphic data, approximately 82 vs. 44mg, p <0.05).	Iontophoresis can deliver morphine systemically in sufficient quantities to provide early postoperative pain relief in patients undergoing total knee replacements or total hip arthroplasties.	Significant baseline differences result in difficulties in interpreting results, and baseline PCA requests differed between text and graphic representation.
Treatment of Adverse Anesthesia Effects						
Sinatra 2005 RCT	10.5	N = 156	IV acetaminophen (1gm) vs. propacetamol (2gm, equivalent to 1gm acetaminophen) versus placebo	Total morphine use was 38.3±35.1 vs. 40.8±30.2 vs. 57.4±52.3. Mean pain relief scores were 2.0 vs. 2.0 vs. 0.9 (p <0.005). The time to rescue medication was 3 vs. 2.6 vs. 0.8 hours (p <0.001).	"Intravenous acetaminophen , 1g, administered over a 24-hour period in patients with moderate to severe pain after orthopedic surgery provided rapid and effective analgesia and was well tolerated."	Data suggests IV acetaminophen is a useful adjunct to other treatments, but may be inadequate alone given continued need for opioid rescue.
Chan 2005 RCT	9.0	N = 180	Lumiracoxib 400mg QD vs. naproxen 500mg BID vs. placebo	Patients requiring rescue medication 70% lumiracoxib patients vs. 78.3% naproxen and 90.0% placebo patients. Mean rescue doses 12.1 vs. 17.6 vs. 22.0mg. Data at 1 to 3 hours of follow-up all favored naproxen over lumiracoxib (p <0.05). Median times to rescue medication 3.8 hours vs. 3.9 hours vs. 2.0 hours.	"Lumiracoxib is an effective alternative to traditional non-selective non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of post-operative pain."	Data suggests naproxen superior to lumiracoxib for initial post-op hours. Rescue medication doses and pain intensity differences appear to favor lumiracoxib.
Malan 2003 RCT	9.0	N = 201	Parecoxib 20mg vs. 40mg vs. placebo	Total morphine consumed at 36 hours 56.5 vs. 43.1 vs. 72.5mg (p <0.01 for both parecoxib doses). Data trended towards lowest morphine use at all follow-up intervals for the parecoxib 40mg dose. Percentages of patients not requiring PCA morphine at 36 hours were 9.8 vs. 30.9 vs. 9.2%. Less fever and vomiting in 40mg group (p <0.05).	"Administration of parecoxib sodium with PCA morphine resulted in significantly improved post-operative analgesic management as defined by reduction in opioid requirement,	Study suggests parecoxib 40mg superior to 20mg.

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					lower pain score, reduced time on PCA morphine, and higher global evaluation ratings."	
Grattidge 1998 RCT	8.5	N = 82	Propofol infusion (10mg/ml at 3ml/hour) vs. inert lipid emulsion infusion in patients undergoing hip or knee arthroplasty using spinal anesthesia and IT morphine	"Postoperative nausea and vomiting in the intervention group was 40% vs. 59% in the controls (P=0.1, not significant). Pruritus occurred in 34%, with a similar rate in both groups."	"These results suggest that routine use of postoperative, sub hypnotic propofol infusion as postoperative nausea and vomiting prophylaxis is not justified in this patient population."	Study focus not pain but side effects of anesthesia, particularly morphine. Propofol infusion not effective in controlling post-op nausea and vomiting.
Zhou 2001 RCT	8.5	N = 172	Propacetamol 2g vs. ketorolac 15mg versus 30mg vs. placebo	Times to onset of analgesia: (placebo/propacetamol/ketorolac 15mg/30mg): 16 minute/8 minute/14 minute/10 minute. Patients receiving rescue medication 73%/72%/61%/ 48%. Times to remedication 1.9/3.5/4.0/6.0 hours. Rescue morphine doses 6.2±7.2/7.0± 9.0/7.5±16.1/2.7±4.0mg.	"Propacetamol (2g IV) possesses a similar analgesic efficacy to ketorolac (15 or 30 mg IV) after total hip or knee replacement surgery."	Study suggests ketorolac provides greater pain relief than propacetamol.
Etches 1995 RCT	8.5	N=174	Ketorolac (30mg IV, followed by 5mg per hour for 24 hours) vs. placebo	Combined pain intensity ratings at 4 hours post-operatively that were moderate, severe or very severe were 39% vs. 62%, p = 0.0036. Cumulative morphine was 35% less for those receiving ketorolac (37.3±3.9 vs. 57.2±4.6mg, p = 0.03).	Patients receiving ketorolac less sedated and required fewer antiemetics. No difference in blood loss. Patients receiving ketorolac reported better analgesia and used less morphine (35% hips/44% knees) than placebo.	
Alexander 2002 RCT	8.5	N = 102	Diclofenac sodium 75mg vs. ketorolac tromethamine 60mg vs. placebo	Pain scores were higher among placebo group at almost all intervals over 24 hours for both active medications (graphic representations). Morphine usage was 36.3 vs. 47.2 vs. 51.6mg respectively.	"Preoperative administration of intravenous diclofenac 75 mg or ketorolac 60 mg significantly reduces morphine requirements and associated side effects after major orthopedic	Study supports diclofenac and ketorolac IV administration.

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					surgery."	
Fogarty Acta Anaesthesiol Scand 1995 RCT	8.5	N = 30	Ketorolac vs. saline injections (30mg IM at beginning of surgery and Q6 hours for 4 doses)	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.
Buvanendran 2006 RCT	8.5	N = 30	Placebo vs. rofecoxib	Prostaglandin E2 concentrations at hip drain site lowest for 5 day rofecoxib, somewhat higher concentrations often significant for 1 day rofecoxib and highest for placebo. Pain scores over 30 hours from surgery highest for placebo (p <0.05), largely same for 2 regimens of rofecoxib except at 25 hours where single dose lower (p <0.05). Cerebrospinal fluid IL-6 results comparable.	"These results suggest that upregulation of prostaglandin E2 and interleukin 6 at central sites is an important component of surgery induced inflammatory response in patients and may influence clinical outcome."	Rofecoxib was withdrawn from the US market in 2004.
Johansson 1989 RCT	8.0	N = 115	Single dose ketorolac tromethamine 10mg vs. 2 tablets doleron (150mg dextropropoxyphene napsylate, 350mg aspirin, 150mg phenazone)	Treatment efficacy 80% vs. 82% (NS). Investigator ratings of overall efficacy for combined excellent, very good and good ratings 51% vs. 52%.	"A single oral dose of 10 mg ketorolac was shown to be as effective and safe as two Doleron tablets in the treatment of moderate to severe orthopedic post-operative pain."	Study supports oral formulation of Ketorolac.

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Bugter 2003 RCT	8.0	N = 50	Ibuprofen 600mg TID for 2 weeks pre-operatively vs. placebo	Blood loss during surgery 700mL vs. 416mL (p <0.01); blood loss after surgery 461mL vs. 380mL; total blood loss 1,161mL vs. 796mL (p <0.01). Post-op vomiting higher in ibuprofen group (41.1% vs. 21.0%), though not statistically significantly. Morphine consumption via PCA pump 22.1mg vs. 26.6mg, p = 0.52. VAS pain scores did not differ.	"Pretreatment with ibuprofen before major hip surgery does not improve the pain scores or reduce morphine requirement but significantly increases blood loss."	Study suggests pre-treatment with ibuprofen has adverse effects of blood loss and no added benefit for analgesia.
Hommeril 1994 RCT	7.5	N = 32	Ketoprofen 200mg IV then 12.5mg/hour for 13 hours vs. extradural morphine 4mg for treatment	Pain scores did not differ across 13-hour follow-up. Epigastric discomfort in 5 ketoprofen vs. 1 morphine patient. Vomiting more common in morphine (9 vs. 4) as were urinary retention (12 vs. 5, p <0.05) and pruritus (5 vs. 0).	"Ketoprofen may be an efficient alternative to extradural morphine after hip and knee arthroplasty." Three patients in morphine group experience respiratory depression.	Study details somewhat sparse.
Camu 2002 RCT	7.5	N = ????	20mg vs. 40mg valdecoxib vs. placebo BID	No difference in total morphine consumed between 20 and 40mg doses. Placebo utilized more morphine (10.9±0.9/ 10.8±1.0/ 16.3±1.0, p <0.001). Joint mobilization at 48 hours 7.5±0.6/7.5±0.6/6.6±0.6 (NS).	"Valdecoxib has significant clinical utility for acute pain management in orthopedic surgery patients."	Study methodology details sparse.
Segstro 1991 RCT	7.0	N = 50	Placebo suppositories vs. indomethacin suppositories 100mg q.8h for 5 doses post-op	"The use of rectal indomethacin substantially reduced narcotic requirements after total hip replacement without a high incidence of side effects."	"Combination of indomethacin and morphine provided superior pain relief to morphine alone, even though the patients in the control group had liberal access to morphine via the PCA pump. This syner-gistic effect would make indomethacin a useful adjunct to intra-muscular narcotics."	

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Dahl 1995 RCT	7.0	N = 123	Ibuprofen 800mg vs. ibuprofen 800mg plus codeine 60mg vs. placebo prophylactic treatment	Placebo group required 45% more ketobemidone in the 5 hours compared with other 2 groups (p <0.001), but no differences between other 2 groups (6.8±3.1/4.7±2.0/4.7± 2.5mg).	A prophylactic dose of 800 mg ibuprofen orally has an opioid sparing effect with a tendency of less pain experience during the first hours after hip arthroplasty.	Results suggest a weak effect of codeine, in addition to positive results with ibuprofen.
Serpell 1989 RCT	6.0	N = 24	Placebo vs. piroxicam	Average total opioid use was 76mg in placebo group vs. 38mg in piroxicam group (morphine IM use 9.6 vs. 3.5mg). Pain scores 2.6 vs. 2.0.	Those receiving piroxicam required 50% less morphine than control group.	
Moiniche1994 RCT	5.5	N = 42	Epidural bupivacaine/ morphine plus piroxicam vs. general anesthesia with systemic morphine/ acetaminophen	Epidural patients had lower post-operative pain scores at rest (p = 0.001), as well as with flexion and walking. Knee surgery results similar, though higher morphine consumption present in both groups.	"Postoperative epidural low-dose bupivacaine-morphine plus systemic piroxicam provided efficient, although not optimal pain relief after major orthopedic surgery, but without effects on post-operative convalescence parameters or hospital stay."	Multiple interventions impair ability to infer effects of any single component of interventions.
Buchanan1988 RCT	5.5	N = 114	Diclofenac 75mg IM intra-operatively vs. papaveretum	Surgeon assessment of pain at 24 hours combining uncomfortable but can cope with very uncomfortable was 0 vs. 8 for papaveretum, p <0.001. Surgeon assessment of wound tenderness similarly favored diclofenac at 24 and 48 hours (p <0.001).	"The use of diclofenac given as a post-operative analgesic is rewarding, particularly in patients undergoing musculoskeletal procedures. Patients will be more comfortable and will mobilize better during their whole post-operative course."	Scaling of the comparison medication based on three factors may have introduced a lack of structure in the trial.
Segstro 1990 RCT	5.0	N = 50	Indomethacin suppositories 100mg Q 8 hour for 5 doses vs. placebo for treatment	Pain scores statistically better (graphic presentation of data).	"The use of rectal indomethacin substantially reduced narcotic	Study details sparse.

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					requirements after total hip replacement without a high incidence of side effects."	
Bernard 1991 RCT	5.0	N = 24	Deliberate hypotension with nicardipine vs. nitroprusside during hip replacement surgery	Nicardipine vs. nitroprusside mean±SEM: blood loss (ml):415±70 vs. 428±120.	"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.
Boeckstyns 1992 RCT	4.5	N = 117	Piroxicam (40mg suppository immediately post-operatively, then 20mg QD) vs. placebo	Buprenorphine consumption higher in knee patients than hip patients (0.74mg vs. 0.42mg), however both favored piroxicam treatment (graphic data presentations).	Patients receiving piroxicam consumed less buprenorphine.	
Vathana 1998 RCT	3.0	N = 50	Ketoprofen 100mg vs. morphine 6mg for 12 hours and 6 hours respectively	Intramuscular ketoprofen has a similar efficacy compared to intramuscular morphine.	"Minor side effects can be encountered following ketoprofen injection. The two times per day administration of ketoprofen is easier for the patient and the medical staff than the four times per day administration of morphine."	Data are heterogeneous and details are sparse.
Barron 1984 RCT	1.5	N = 500	Cyclizine, perphenazine, prochlorperazine, droperidol, and metoclopramide vs. domperidone	The phenothiazines made patients 'feel better' more effectively than the other drugs.	"In initial study, emetic symptoms occurred in about half of untreated patients: this incidence was not significantly affected by cyclizine; there was a non-significant trend of reduction with droperidol, metoclo-pramide and domperidone. Significant	Study details sparse and study design unclear. It is suggested to be a crossover trial, but number of patients receiving each intervention are not uniform.

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					symptomatic improvement (P< 0.01) with perphenazine and prochlor-perazine were used."	
Hip: Tricyclic Analgesia						
Kerrick 1993 RCT	8.5	N = 28	Amitriptyline 50mg QHS for 3 nights vs. placebo post-operatively	Mean scores in amitriptyline group for pain NVS greater ($p < 0.05$) (higher score = greater pain) on Day 1 and greater on Day 2 for pain VAS. Mean scores for sense of well-being greater ($p < 0.05$) (higher score = better sense of well-being) for placebo group on Days 1 and 2. On Days 2 and 3, sleep scale variable mean scores worse in placebo group ($p < 0.025$). No other statistically significant differences between control and active drug groups for any outcome variables measured.	"Amitriptyline at the dose prescribed is no different than placebo in altering the majority of postoperative symptom variables studied in the sample study population but caused no significant adverse effects."	

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APPENDIX 2: LOW-QUALITY RANDOMIZED CONTROLLED TRIALS AND NON-RANDOMIZED STUDIES

The following low-quality randomized controlled studies (RCTs) and other non-randomized studies were reviewed by the Evidence-based Practice Hip Panel to be all inclusive, but were not relied upon for purpose of developing this document's guidance on treatments because they were not of high quality due to one or more errors (e.g., lack of defined methodology, incomplete database searches, selective use of the studies and inadequate or incorrect interpretation of the studies' results, etc.), which may render the conclusions invalid. ACOEM's Methodology requires that only moderate- to high-quality literature be used in making recommendations.(213)

OSTEONECROSIS: CT, MRI, AND X-RAYS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Stevens 2003 Comparative Clinical Study	N/A	N = 45 All stages I-II hip AVN	X-ray and MRI at baseline. Helical CT and MRI 2 weeks after coring surgery. X-ray, CT and MRI at 6 and 12 months.	At 6 months, 12 fractures identified on x-ray, 18 on CT and 6 on MRI. At 12 months, 17 on x-ray, 20 on CT and 11 on MRI. X-ray sensitivity 71%, specificity 97%, PPV 96% and NPV 77%. Values for MRI 38, 100, 100, 60%.	"CT reveals more subchondral fractures in osteonecrosis of the femoral head than unenhanced radiography or MR imaging. The high-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."	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.

HIP OSTEOARTHRITIS: EXERCISE

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Cochrane 2005 RCT	1.5	N = 106 Hip and/or knee OA	Water exercises vs. usual care for 1 year of treatment	53.5% complied at 1-year. Estimated effect sizes 0.44 on WOMAC pain to 0.76 on WOMAC physical function.	"Group-based exercise in water over 1 year can produce significant reduction in pain and improvement in physical function in older adults with lower limb OA, and may be useful adjunct in the management to hip and/or knee OA."	Abstract only. Compliance low, and dropped in subsequent 6 month period to 18%.

NSAIDs AND ACETAMINOPHEN

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Shephard 1981 RCT	7.0*	N = 68 OA	Tolmetin 200mg QID vs. Indomethacin 25mg QID for 4 weeks	Few data presented. Decreased rest pain with indomethacin ($p < 0.01$). However, tolmetin results not presented. Tolmetin patients improved in pain on rising from a chair ($p < 0.05$), however indomethacin results not presented.	"Tolmetin is as effective an anti-inflammatory analgesic agent as is indomethacin and produces fewer side effect."	Data sparse, does not clearly allow head-to-head comparisons, thus despite other methodological strengths is a low-quality study. Presented results suggest no clear efficacy

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						of one treatment – one better for rest and weight bearing, other better for walking, Global assessments comparable.
Williams 1989 RCT	3.5	N = 210 Knee or hip OA	Etodolac 600mg a day vs. placebo for 4 weeks	Overall patient assessments (week 1/final visit): etodolac (32/33) vs. placebo (18/17), p <0.001. Joint tenderness/ swelling, night pain, pain intensity all significantly different. GI indigestion in 9 etodolac vs. 2 placebo. Overall GI events not different (p = 0.30).	"[E]todolac was superior to placebo in several measures of pain and function."	High dropout, sparse details. Suggests etodolac effective. Suggest hip and knee OA equally responsive to treatment.
Lehn 1992 Crossover Trial	3.5	N = 98 Knee and/ or hip OA	Enteric-coated vs. non-enteric coated naproxen for 4 weeks each. Dose range: 500, 750, 1,000mg a day.	Pain and functional measures all NS except daily activity at 4 weeks which favored enteric coated (p = 0.002). Borderline results in favor of enteric coated; 1st treatment period (9 vs. 18, p = 0.10) for adverse GI events.	"The study did not show any clinical significant difference in tolerability or efficacy between enteric-coated and plain naproxen tablets."	Variability in dosing weaken results. Results suggest no consistent findings in favor of enteric coating.
Kaik 1991 RCT	3.5	N = 31 Knee and/ or hip OA	Imidazole salicylate 750mg TID vs. ibuprofen 400mg TID for 60 days	Imidazole salicylate improved in duration of morning stiffness (p <0.01) and relief in spontaneous pain (p <0.01). No differences between treatments (p >0.05).	"Both drugs were effective in relieving the severity of painful symptoms as observed by clinical improvement."	Comparison with nonprescription strength ibuprofen. Lack of study details.
Doherty 1992 RCT	3.5	N = 455 Hip or knee OA	Arthrotec (diclofenac 50mg, misoprostol 200µg) vs. diclofenac 50mg BID or TID at physicians' choice for 4 weeks	Patient global assessment n (%) improved at 4 weeks: arthrotec 52 (27%) vs. diclofenac 51 (25%), NS. Other measures (e.g., physician's global assessments, OA severity indices) did not differ between groups.	"Misoprostol does not interfere with the antiarthritic properties of diclofenac."	Dosing variable according to treating physician assessment; 25-27% of patients demonstrated improvement in outcomes measures.
Cimmino 1982 Crossover Trial	3.5	N = 30 Spine, knee, hip OA	Meclofenamate 100mg TID vs. ibuprofen 300mg TID for 3 weeks each	Rest pain did not differ statistically but trended towards efficacy. Tenderness decreased on active treatments (p <0.05), but did not differ between groups.	"[C]onfirms the therapeutic effectiveness of sodium meclofenamate and ibuprofen in OA, and compares favourably to previous reports on sodium meclofenamate efficacy in OA."	Small sample size with low power.

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Brackertz 1978 Crossover Trial	3.5	N = 20 Knee or hip OA	Clofezone 1200mg daily 1st week; 600 mg 2nd week vs. diclofenac (150mg daily 1st week; 75mg 2nd week) for 2 weeks each	Rest pain (placebo/after clofezone/after diclofenac): 1.0±0.94/0.2±0.42/0.1±0.3 Greater changes seen in group given diclofenac followed by clofezone than opposite order.	"[C]lofezone has a longer-lasting action which wears off only slowly after withdrawal and substitution by a placebo."	High dropout rate in short trial with small sample size.
Liyanage 1978 Crossover Trial	3.5	N = 20 Hip or knee OA	Salsalate 1gm TID vs. ASA 1.2gm TID for 2 weeks each	Pain at rest (baseline/1 week placebo/salsalate/ASA): 26.1 ±5.4/33.6±5.9/22.3±5.3/32 .7±6.3. No difference between salsalate and placebo in adverse effects, but ASA had increased adverse effects compared to placebo (p <0.01); 14 had no treatment preference, 5 salsalate, and 1 ASA.	"The more important outcome of the trial is the superiority of salsalate over aspirin with regard to side-effects and faecal occult blood loss."	Small sample size. Sparse details. Short duration of 2 weeks. Most patients had no preference including placebo.
Niccoli 2002 RCT	3.5	N = 90 Hand, hip or knee OA	Amtolmetin 600mg BID for 3 days then 600mg a day for 11 days vs. diclofenac 50mg TID vs. Rofecoxib 25mg QD for 2 weeks total treatment	Diclofenac reduced creatinine clearance. Rofecoxib gained body weight, systolic blood pressure, diastolic blood pressure and serum sodium with decrease in daily urine volume. No significant changes in parameters with AMG. Diclofenac more efficacious than other 2 drugs (p <0.001).	"Diclofenac mainly impaired blood renal flow and the glomerular filtration rate, while rofecoxib negatively influenced the renal sodium-water exchange. AMG demonstrated a renal sparing effect, although the exact mechanism is unclear."	Sparse study details. Two week trial. Data suggest diclofenac superior.
Ghosh 1981 RCT	3.5	N = 32 Hip and/or knee OA	Sulindac 200mg BID vs ibuprofen 400mg TID for 12 weeks; open label	Disease activity scores decreased significantly from Week 0 values in both groups (p <0.05 ibuprofen; p <0.001 sulindac), but to greater extent (p <0.001) in sulindac group. At Week 12, both showed statistically significant improvement (p <0.001) in all 3 parameters vs. Week 0. Significant difference (p <0.001) between 2 groups in favor of sulindac, to weight-bearing pain and pain on active movement. More in sulindac compared to ibuprofen (p <0.01) categorized outcome as "excellent" or "good."	"Overall assessment of response to treatment also showed a significant preference for sulindac by patients and physicians….No significant differences were found in the haematological or biochemical profiles in either group at week 12."	Study details sparse. Comparisons with OTC ibuprofen dose limits strength of conclusions in favor of sulindac. No blinding, open label.

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Davies 1999 RCT	3.5	N = 104 Knee or hip OA	Ibuprofen 800mg TID vs. placebo TID for 4 weeks	WOMAC pain scores (baseline/Day 28): ibuprofen 59.7±21.8/75.9±23.0 vs. placebo 64.6±24.4/70.3±27.8. Ibuprofen group showed improvement in all WOMAC scale scores within 1st week.	"[T]he pain, physical function, and total score from the WOMAC and the bodily pain scale from the SF-36 were able to detect response to therapy with ibuprofen and show differences between active and placebo treatment. However, the WOMAC proved to be more efficient of the two instruments."	Inclusion criteria did not require radiographic evidence of OA. This 4 week trial did not report objective clinical outcomes (adverse events, compliance etc.).
Münzenberg 1980 RCT	3.5	N = 40 20 hip or knee OA; 20 with inflamm-atory disorders	Protacine 150mg TID vs. indomethacin 50mg TID for "average" of 10 days	Pain scores for hip/knee OA (baseline/final): protacine 2.50±0.22/1.40±0.16) vs. indomethacin 2.50±0.19/1.88±0.23 (NS). More adverse effects for indomethacin than protacine; only drop-outs were 2 taking indomethacin.	"[A]lthough preliminary, indicate that protacine has an anti-inflammatory and analgesic action at least as powerful as that of indomethacin and oxyphenbutazone."	Lack of study details; small sample size. Adverse events greater in indomethacin group, but sample size small and may not represent population.
Bain 1977 Crossover trial	3.5	N = 21 Hip OA	Feprazone 200mg TID vs. ibuprofen 300mg TID for 4 weeks each	Eighteen (18) completed both treatments with 5 without treatment preference, 6 preferred feprazone and 7 preferred ibuprofen. Daytime pain (much better or better): feprazone 11/19 (57.9%) vs. ibuprofen 10/18 (55.6%), NS.	"[F]eprazone is as effective as ibuprofen in the treatment of patients with osteoarthritis of the hip, although the number of patients involved were too small and the treatment periods too short to show any statistically significant differences from baseline assessment or between treatments in the objective parameters measured."	Small sample size. Power too low to detect significant differences. Submaximal ibuprofen dose used for comparison.
Doury 1977 Crossover trial	3.5	N = 30 Hip OA and ankylosing spondylitis	Flurbiprofen 200mg BID vs. TID for 7 days	Flurbiprofen effective in 66% of 26 patients completing trial; 24 patients had no dosing preference. Tolerance also assessed as being satisfactory in 83% of all patients.	"Comparison of the two treatment periods showed that 2 daily doses of flurbiprofen produced as good results as the 3-times daily regimen."	Sparse details. Study included ankylosing spondylitis patients mixed with hip OA. Comparable efficacy for dosing regimens suggested.
Scott 2000 RCT	3.5	N = 399 Moderate or severe hip or knee OA	Two randomized group trials: 1) nabumetone 1500mg/day vs. diclofenac SR 100mg/day and 2) nabumetone (1500-2000mg/day) vs piroxicam	Nabumetone with fewer ulcer and bleeding events compared to patients treated with comparator NSAIDs [1.1% (4/348) vs. 4.2% (15/346), p = 0.01]. Diclofenac SR reduced VAS score by statistically greater amount than nabumetone (-16±29 vs. -8±27, p <0.05). Patients withdrew due to	"[N]abumetone was similar in efficacy by most criteria to diclofenac SR and piroxicam in relieving the symptoms of osteoarthritis; however, nabumetone's GI safety profile was generally superior to that of both comparator NSAIDs. In the pooled	Sparse study details including allocation methods, blinding, compliance, and control for cointervention. Data may suggest nabumetone has lower GI

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			(20-30mg/day) for 6 months	treatment-related adverse experiences less with nabumetone (17/148 = 11%) vs. piroxicam (30/147 = 20%), p <0.04.	analysis, nabumetone was associated with a significantly lower total incidence of ulcers and bleeding events, and a significantly lower incidence of complications associated with these events."	complications and also suggest diclofenac may provide better pain relief. However the quality score tempers this conclusion.
Kienapfel 1999 RCT	3.5	N = 154 THA due to OA	Radiation dose of 600-cGy vs. indomethacin 50mg BID for 42 days vs. controls	There were significant group difference (p <0.001). The 13 patients classified Brooker 3 or 4 were all controls (26% of controls).	"[B]oth radiation and indomethacin therapy are effective in the prevention of post-operative (Heterotopic ossification)."	Sparse details, lack of blinding. Data suggest indometh-acin or XRT may reduce heterotopic ossification.
McKenna 1998 RCT	3.5	N=1824 RA or OA	Combination diclofenac/misoprostol vs. diclofenac or ibuprofen for 12 weeks	"The diclofenac 75/misoprostol group showed fewer decreases in hemaoglobin levels at all time points compared with diclofenac and was associated with a significantly lower mean decrease in hemoglobin levels between baseline and final followup (-0.172 vs. -0.311 g/dl; p=0.030)."	"Diclofenac50/misoprostol and diclofenac75/ misoprostol are effective in treating the signs and symptoms of RA and OA and are well tolerated by the majority of patients. Both of these formulations achieve a significant reduction in the incidence of both gastric and duodenal ulcers compared with other NSAID."	
Zgradie 1999 RCT	3.0	N = 180 Hip, knee, lumbar spine OA	Nimesulide 200mg BID vs. diclofenac sodium 50mg TID	After 2 weeks nimesulide therapy indicated "evidently better" response and after 4 weeks indicated "significant improvement" while those on diclofenac described their condition in same interval as "a little better than before" and then "evidently better."	"This trial confirmed that both drugs were efficacious while nimesulide exerted much better tolerability profile."	Lack of blinding, randomization in details weakens the study.
Janke 1984 RCT	3.0	N = 95 Hip or knee OA	Sulindac 200mg BID vs. naproxen 250mg BID for 12 weeks	Disease activity (baseline/ Week 12): sulindac (2.32/ 1.17) vs. naproxen (1.93/ 1.00). Weight-bearing pain: sulindac (2.42/1.32) vs. naproxen (2.41/1.10). No differences between groups.	"[N]o statistically significant differences between the effects of the two drugs. Overall, both drugs proved beneficial and well tolerated."	Lack of blinding, sparse study details.
Diamond 1976 Crossover Trial	3.0	N = 34 Spine, hip, knee or shoulder OA	Fenoprofen 200mg to 600mg Q6hour vs. aspirin 325mg to 975mg Q6 hour for 6 weeks. Doses titrated	Little difference in efficacy between fenoprofen and ASA. Data presented were largely vs. placebo and not well described.	"Fenoprofen in a dose of 200-600 mg, four times daily, showed similar efficacy to 325 to 975 mg of ASA, four times daily, in the treatment of osteoarthritis of the spine and large joints. The overall incidence of side effects was similar on the two drugs."	Lack of study details. Study used placebos in 1-week washout phases to compare with active medications; but duration may not have been sufficient and unclear if blinded.

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Perpoint1994 RCT	3.0	N = 117 Hip or knee OA	Sustained-release ketoprofen 200mg QAM vs. QPM for 14 days	Adverse events were: SRK morning 27/59 (45.8%) vs. 13/58 (22.4%), p = 0.023. VAS pain scores not different (p = 0.22). Overall efficacy assessments also not different.	"[T]o increase its acceptability, evening administration of SRK seems to be preferred to morning administration in osteoarthritis. On the contrary, the chronoeffectiveness of tenoxicam appears to be associated with morning or noon dosing time."	Sparse study details, short follow-up (2 weeks). Data suggest evening dosing may be preferable regarding adverse effects.
Crook 1981 RCT	3.0	N = 47 Severe hip OA	Ibuprofen 400mg vs diclofenac 25mg QID for 8 weeks. Dose could be titrated up first 4 weeks. Double dummy.	Assessments of condition: diclofenac made condition better for 6/17 (35.3%) vs. 6/20 (30%) for ibuprofen. No differences between groups in walking pain, pain on rising from chair or change in rheumatic condition.	"[N]o difference in the efficacy or tolerability of diclofenac or ibuprofen in this group of patients with severe disease."	No washout period at start of study. Methodology details sparse. Variable dosing.
Puscas 1997 RCT	3.0	N = 18 Healthy volunteers	Ebrotidine 800mg/d p.o. vs. indometacin 4mg/kg/d p.o. in 3 divided doses vs. ebrotidine 800mg/d p.o. plus indometacin 4mg/kg/d p.o.	"[E]brotidine reduced total gastric mucosal carbonic anhydrase activity by 62%. [I]ndometacin increased carbonic anhydrase activity in gastric mucosa by 138%. [T]he combined treatment with ebrotidine plus indometacin decreased gastric mucosal carbonic anhydrase activity by 38%."	"[E]brotidine is the first antiulcer agent with a dual mechanism of action: it is a H_2-receptor antagonist and a carbonic anhydrase inhibitor. The contribution of anti-ulcer drugs possessing two mechanisms of action could open up a new era in the therapy of ulcer disease."	Small sample size. Short-term study of 10 days. Experimental study of carbonic anhydrase.
Fendrick 1998 RCT	2.5	N = 541 Patients using NSAIDs	Omeprazole 20 or 40mg daily vs. ranitidine 150mg twice daily for 4-8 weeks	The study found a treatment success for patients treated with omeprazole 20mg daily (80%), or with omeprazole 40mg daily (79%) when compared with those individuals in the ranitidine group (63%) (p ≤0.001).	"[T]he data presented provide adequate evidence that omeprazole is an effective treatment, because of its proven efficacy regarding healing and prevention of documented lesions and, maybe more importantly, its advantage in controlling symptoms."	Two RCTs; 4-6 week treatment and 6 month … Sparse data as reported support omeprazole as superior to ranitidine, misoprostol or placebo.
Admani 1983 RCT	2.0	N = 30 Hip or knee OA	Sulindac 200mg BID vs. ibuprofen 400mg TID for 12 weeks	Weight-bearing pain, pain on active movement, pain on passive movement all improved compared with baseline in sulindac but not ibuprofen (graphic data). Percentages feeling improved were: sulindac (12.0%) vs. ibuprofen (13.3%).	"Patients acceptance of sulindac regimen appeared to be better than that of ibuprofen because of the smaller tablets and the twice daily compared with 3-times daily dosage."	Small sample; lack of details; baseline differences on some outcomes measures. Submaximal ibuprofen dose. Unusually small response rates.

*Methodology contains sufficient criteria to warrant moderate quality score, but sparse results merit low-quality rating.

GLUCOSAMINE, CHONDROITIN, AND METHYLSULFONYLMETHANE

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments

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Qiu 1998 RCT	3.5	N = 178 Knee OA	Glucosamine sulfate (1500mg/day) vs. ibuprofen (1,200mg a day) for 4 weeks	GS and IBU progressively and significantly reduced knee pain (p <0.0001). In 4 weeks, GS reduced knee pain 57% and IBU 51%. GS trend of greater pain relieving efficacy, but difference vs. IBU not statistically significant. GS and IBU progressively, significantly reduced knee swelling (p <0.0001).	Study confirms GS is a selective drug for osteoarthritis, as effective on symptoms of disease as NSAIDs but significantly better tolerated. For these properties, GS seems particularly indicated in the long-term treatments needed in osteoarthritis.	No placebo group. Allocation, randomization, and baseline characteristics unclear.
D'Ambrosio 1981 RCT	3.0	N = 30 OA	Glucosamine sulfate (400mg) vs. piperazine/ chlorbutanol (400mg) daily 7 days IV or IM, then 2 following weeks oral glucosamine capsules (500mg TID) vs. placebo for non-specific OA	Overall symptom score decreased 58% during injectable glucosamine treatment, and further 13% with oral maintenance therapy. Decrease significantly larger than that measured during reference initial treatment and placebo maintenance. No definitely drug-related intolerance symptoms evident in either group.	"The results indicate that this new preparation containing pure glucosamine sulfate is an effective and well-tolerated treatment for arthrosis."	Lack of randomization, allocation details. No data on arthritis type or baseline comparability.

HERBAL AND OTHER PREPARATIONS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Warholm 2003 RCT	3.0	N = 100 Hip or knee OA	Rose-hip powder 5g a day vs. placebo for 4 months	Pain declined in active treatment group compared with placebo, p<0.035 (no data provided).	"Hyben Vital…reduces osteoarthritic pain in the hip and also reported a statistically significant improvement in energy, motivation for their daily activities and sleep during active therapy."	Conference abstract with limited data.

DIACEREIN

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Marcolongo 1988 Possible Controlled Clinical Trial	3.0	N = 46 knee OA N = 49 hip OA	Diacerein 50mg BID vs. naproxen 375mg BID for 2 months followed by 2 months of placebo washout	Data suggest comparable pain reduction, pain on movement, and tenderness during active treatment with either, but prolonged effect after cessation of diacerein.	"The results of the present trial confirm the efficacy of DAR in the treatment of osteoarthrosis; this efficacy is generally manifested later than that of naproxen, but is of longer duration. Also, the tolerability of DAR was extremely good."	Methods not well described. Unclear if randomized. Sub-maximal naproxen dose may have modestly biased study in favor of diacerein.
Fagnani 1998 RCT	3.0	N = 207 Knee and hip OA	Standard therapy vs. diacerein 50mg BID plus standard therapy (NSAIDs, physiotherapy, exercise, injections) for 6 months, followed by 3 month monitoring period.	Analgesic consumption at Day 15 and 6 months 25.5% and 41.1% lower, respectively, in diacerein plus standard therapy group than standard therapy group. Cumulative NSAID and analgesic consumption in diacerein plus standard therapy group 26.1% (p = 0.068) lower than in standard	"The costs resulting from NSAID and analgesic consumption, additional physician office visits, injections, nursing care, physiotherapy sessions, hydrotherapy and treatment of adverse events were lower in the diacerein plus standard therapy group than in the	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

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				therapy group. Difference between two groups statistically significant during 0-to-6-month period (p = 0.01) and 0-to 9 month period (p = 0.001).	standard therapy group."	same that previously failed, then study likely biased in favor of intervention.

ACUPUNCTURE

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Haslam 2001 RCT	3.0	N = 32 Hip OA awaiting THR	Acupuncture 6 sessions up to 25 minutes each; GB29, 30, 34, 43, ST44, LI4 bilaterally and 4 "ah shi" points around greater trochanter) vs. advice/exercises for 6 weeks	WOMAC scores (baseline/8 weeks): acupuncture (870/732) vs. controls (854/878), p = 0.02.	"[T]his trial supports the hypothesis that acupuncture is more effective than advice and exercises in the symptomatic treatment of OA of the hip."	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 RCT	2.5	N = 37 Hip and knee OA	Codetron (acupuncture-like TENS device) vs. placebo device	After 6 weeks of treatment, using a VAS, Codetron group 14/19 (74%) had >25% improved pain whereas placebo only 5/18(28%) had >25% improved pain (p <0.02). Pain scores using West Haven Yale (WH/Y) scale showed significant improvement of Codetron (13/19 vs 5/18, p <0.05).	This is highly suggestive of the therapy of chronic pain conditions such as osteoarthritis.	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.

MANIPULATION AND MOBILIZATION

Author/Year/ Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Cibulka 1993 RCT	2.5	N = 20 Runners with anterior and/or lateral hip pain	Mobilization of hip joint vs. Manipulation of SI Joint with all felt to have SI dysfunction	Pain improvements at "follow-up" (unknown time interval): manipulation 3.8 vs. mobilization 0.8. Negative Faber at follow-up in 9/10 (90%) of manipulation vs. 3/10 (30%) of mobilization.	"The results suggest that a manipulation technique designed to reduce sacroiliac joint dysfunction is an effective method to reduce hip pain."	Details/results sparse. Differences at baseline with older group receiving mobilization (24 vs. 16 years) suggests randomization failure. No placebo limits conclusions, already may be limited to runners. Follow-up interval appears not fixed.

TENS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Pike 1978 RCT	2.5	N = 40 THR	Pethidine 30mg IM vs. pethidine plus TENS for first 24 hours post-op in THR patients	Mean doses of pethidine TENS 1.3±1.38 vs. control 4.3±2.05, p <0.001. Patient assessment of anesthesia also favored TENS [good/excellent 17/20 (85%) vs. 9/20 (45%)].	"There was less pethidine used in the TES group…It was well accepted by both patients and staff…An ideal stimulation effect was often achieved by similar patterns of stimulating	Study does not discuss randomization process. If valid, data suggest TENS may reduce postoperative anesthetic requirements.

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					parameters."	

GLUCOCORTICOSTEROID INJECTIONS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Robinson 2007 RCT	N/A	N = 120 Hip OA	Methylprednisolone 40mg vs. 80mg	Both doses improved pain and stiffness at week 6. 80mg dose superior for stiffness at week 12 (p = 0.026) and disability at week 6 (p = 0.026) and week 12 (p = 0.004).	"[B]oth the 40 mg and 80 mg IAST doses had a beneficial effect at week 6, while the 80 mg dose maintained this improvement at week 12….Randomized controlled trials of IAST for hip OA are now required"	Suggests 80mg superior, however baseline data have differences in synovitis and study not randomized.

HIP OSTEONECROSIS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Wang 2005 RCT	3.5	N = 53 (57 hips) Stages I, II or III osteo-necrosis	Shock-wave (SWT, single treatment with 6,000 impulses of shock waves at 28kV to hip) vs. core decompression with nonvascularized fibular grafting (CDG)	At 24 months, Harris hip scores in SWT better than CDG (baseline/24 months: SWT 78.7±13.5/97.5±2.9 vs. CDG 74.6±4.7/76.8±5.6, p < 0.001). In SWT 79% hips improved, 10% unchanged, 10% worse vs. CDG 29%, 36%, and 36% worse. SWT had 5/13 (38.5%) regressed in stage I or II. Two each of stage-II and III progressed. CDG 4 regressed and 15/19 (78.9%) of stage I or II progressed and 9 unchanged.	"Extracorporeal shock-wave treatment appeared to be more effective than core decompression and nonvascularized fibular grafting in patients with early-stage osteonecrosis of the femoral head. Long-term results are needed to determine whether the effect of this novel method of treatment for osteonecrosis of the femoral head endures."	Pseudorandomization by day of week. SWT group trended towards lower pain ratings at baseline (p = 0.06). Lack of decreased pain in the surgery group differs from other studies. Data suggest SWT superior to coring with fibular grafting.
Gangji 2005 RCT	3.5	N = 13 (18 hips) Stages I or II osteo-necrosis	Core decompression procedure with vs. without autologous bone marrow mononuclear cell implantation	Significant pain reduction (p = 0.021) and WOMAC (p = 0.013) with autologous bone marrow cell implantation. At 24 months 5 of 8 control hips vs. 1/10 bone marrow hips deteriorated to stage III.	"Implantation of autologous bone-marrow mononuclear cells appears to be a safe and effective treatment for early stages of osteonecrosis of the femoral head. Although the findings of this study are promising, their interpretation is limited because of the small number of patients and the short duration of follow-up."	Small sample size. Sparse details. Sparse data. Study needs replicating with larger sample size and data reported.

HAMSTRING STRAINS: PATS

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Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Engebretsen 2008 RCT	3.5	N = 388 Soccer players with history of MSD of ankle, knee, hamstring or groin and high recurrence risk	Exercise program intervention (stepped increase in ankle, knee, groin, hamstring exercises up to 3 per week for 10 weeks) vs. control	505 injuries among 56% of players. Total injury incidence mean 3.2 (95% CI 2.5-3.9) in low-risk group, 5.3 (95% CI, 4.6-6.0) HR controls (p = 0.0001 vs LR controls), and 4.9 (95% CI, 4.3-5.6) HR intervention group (p = 0.50 vs. HR controls). For main outcome measure, sum of ankle, knee, hamstring, groin injuries, significantly lower injury risk in LR control vs. other 2 groups, no difference between HR intervention and HR controls. Compliance with training programs in HR intervention: 27.5% ankle, 29.2% knee, 21.1% hamstring, 19.4% groin.	"[P]layers with a significantly increased risk of injury were able to be identified through the use of a questionnaire, but player compliance with the training programs prescribed was low and any effect of the intervention on injury risk could not be detected."	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 RCT	3.5	Two infantry basic trainee companies (N = 148 and 150)	Three hamstring stretching sessions plus usual training fitness program vs. no hamstring stretching exercises added to usual training fitness program	Intervention group's hamstring flexibility increased (baseline/post) 41.7±8.3/34.7 vs. controls 45.9±6.5/42.9. 43 injuries in controls group (incidence rate 29.1%) vs. 25 injuries in intervention (IR = 16.7%), p = 0.02.	"[T]he number of lower extremity overuse injuries was significantly lower infantry basic trainees with increased hamstring flexibility."	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.

GROIN STRAINS AND ADDUCTOR-RELATED GROIN PAIN: PHYSICAL OR OCCUPATIONAL THERAPY

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Engebretsen 2008 RCT	3.5	N = 388 Soccer players with history of MSD of ankle, knee, hamstring or groin and high recurrence risk	Exercise program intervention (stepped increase in ankle, knee, groin, hamstring exercises up to 3 per week for 10 weeks) vs. control	Reported 505 injuries among 56% of players. Total injury incidence mean 3.2 (95% CI 2.5-3.9) in low-risk group, 5.3 (95% CI, 4.6-6.0) HR controls (p = 0 .0001 vs. LR controls), and 4.9 (95% CI, 4.3-5.6) HR intervention group (p = 0.50 vs. HR controls). For main outcome measure, sum of ankle, knee, hamstring, groin injuries also significantly lower injury risk LR control group vs. other 2 groups; no difference between HR intervention and HR controls. Compliance with training programs HR intervention: 27.5% ankle, 29.2% knee,	"[P]layers with a significantly increased risk of injury were able to be identified through the use of a questionnaire, but player compliance with the training programs prescribed was low and any effect of the intervention on injury risk could not be detected."	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.

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				21.1% hamstring, 19.4% groin.		

HIP FRACTURES

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Sonne-Holm 1982 RCT	3.5	N = 112 Femoral neck fractures	Hemiarthroplasty with and without bone cement	After 6 weeks, post-op cemented patients had less pain ($p < 0.05$); but no difference in hip mobility or gait function. Total hip index higher for cemented hemi-arthroplasties after 3 and 6 months. Twice as many with cemented vs. uncemented hemiarthroplasties had normal gait function after 3 and 6 months; by 1 year follow up 40% of all patients had normal gait function.	"Clinical results are improved with fixation of the prosthesis with cement, at least during the first 6 months following the operation."	Author suggests patients and observers were blinded. Lack of methodology details.
Raahave 1976 RCT	3.5	N = 16 Hernia repairs	Plastic skin drape vs. no plastic skin drape	Median bacterial densities of sounds (first stage/second stage): skin drape (4.6/10.4) vs. controls (4.2/6.0).	"[P]lastic skin drapes were without influence on the species and density of bacteria in operation wounds. Plastic wound drapes, on the other hand, considerably reduced not only exogenous but in particular endogenous bacteria which otherwise would have remained in the operation wounds."	Small sample size. Study suggests plastic drapes may be effective.
Jackson 1971 RCT	3.5	N = 921 Mixed surgical cases	Plastic skin drape vs. no plastic skin drape	For clean wounds, 5.4% of draped wounds became infected vs. 3.9%, $p > 0.5$.	"No significant difference was observed in the rate of wound infection between the two groups."	Suggests no differences.
Buciuto 1997 RCT	3.5	N = 233 Unstable trochanteric fractures	Fixed angle blade plate vs. compression hip screw	Follow-up study of previous randomized population reporting results 1-3 years post-surgical fixation of unstable trochanteric fractures. In follow-up, 20 patients had implant removed after fracture union; 7 of 20 cases, a spontaneous femoral neck fracture occurred average of 19 days post-removal (range, 7-60 days).	"The authors recommend consideration of additional and complementary radiologic investigations before implant removal in a patient with unspecified hip pain in whom standard radiographs show a healed trochanteric fracture."	The role of the implant position and subsequent removal and incidence of fracture are unclear.
Buciuto 1998 RCT	3.5	N = 233 Unstable trochanteric fractures	Fixed angle blade plate vs. compression hip screw	No differences in operative time or blood loss. Healing rates without complications: FAB 87% vs. CHS 68%, $p = 0.003$. Technical failures occurred in 13 vs. 38. More leg length discrepancies in CHS group (2 vs. 15, $p = 0.002$). Deaths at 1 year	"Our findings suggest that the RAB-plate is a safe implant for fixation of unstable trochanteric fractures and can be regarded as a good alternative to the compression hip screw."	Trends of better healing rates and lower technical failures, but more deaths in the FAB group.

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				were: FAB 13/111 (11.7%) vs. CHS 22/122 (18.0%).		
Mehdi 2000 RCT	3.0	N = 180 Extra-capsular fractures	Extramedullary hip screw vs. sliding hip screw	Average operating times 55 vs. 48 minutes (p = 0.9) respectively for IMHS and SHS. Mean EBL 247 and 270mL (p = 0.9). Acceptable screw position achieved in more SHS (p <0.05), attributed to greater technical difficulties with IMHS (p <0.05). Mean Harris hip scores at minimum 6 months not different between fracture severity groups (p = 0.3 and 0.5) and ASA groups (p >0.05).	"It is recommended for complex fractures in fit patients."	Abstract. Sparse study details
Benum 1994 RCT	3.0	N = 912 Sub-trochan-teric femoral fractures	Gamma nail vs. conventional hip screw	Average operative time GN 60.9 vs. CHS 56.4 minutes, p = 0.02. More peri-operative "problems and complications" with GN (11.1%) than CHS (4.0%), p = 0.00009. More reoperations in GN (6.8% vs. 1.5%, p = 0.00001).	"Due to a significantly higher rate of preoperative problems complications and reoperations in particular complicating femoral fractures, gamma nailing cannot be recommended as a standard procedure in intertrochanteric fractures."	Abstract. Details sparse. Large sample size.
Hogh 1993 RCT	3.0	N = 299 Trochan-teric and sub-tro-chanteric fractures	Gamma nail vs. DHS	No differences in operating time, blood loss. Compression screws cut out in 3 DHS vs. 10 GN cases. No differences over 6 months in walking. More pain in GN group.	"Immediate weight bearing was allowed for all patients in the gamma group. Significantly more patients in the gamma group had pain in the trochanter region."	Abstract. Sparse details.
Sadr 1977 RCT	2.5	N = 40 Sub-capital femoral fractures	Hemiarthroplasty with Thompson prosthesis with proplast coatings vs. standard Thompson with acrylic cement.	Loosening in 9 Proplast vs. 0 cemented. Operative mortality in 5/20 (25%) proplast vs. 2/20 (10%), p >0.05.	"At follow-up, which ranged from 3 to 17 months, there was substantial X-ray evidence of prosthetic loosening in the Proplast series."	Variable length follow-ups of 3 to 17 months
Calder 1995 RCT	2.5	N = 238 Dis-placed intra-capsular fractures	AHS vs. Monk vs. Thompson. Study assessed outcomes with mailed surveys	Rate of usable surveys 67.4%. Those younger completed more surveys (74.3% vs. 62.4%), as did those who were previously independent of walking aids (p = 0.005) and higher mental test scores (p <0.0001).	"Postal assessment using NHP gave a satisfactory response rate even in the elderly, and can provide an extra assessment to complement or replace hospital follow-up in some circumstances."	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,

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						especially adverse outcomes.
Herrera 2002 RCT	2.5	N = 125 Peritro-chanteric fractures	Gamma nail vs. proximal femoral nail	Surgical procedure length averaged PFN 49 minutes vs. Gamma nail 68 minutes (p <0.05). More transfusions for GN. Average healing time was 12 weeks for both. No differences in recovery of prior functional ability. No differences in mortality.	"The PFN seems to us to be a more dynamic system with a lower incidence of local and late complications."	Both techniques had significant limitations, but the study suggests PFN superior to Gamma nail.
Bannister 1990 RCT	2.5	N = 155 Trochan-teric fractures	AO dynamic hip screw vs. Jewett nail plate; open reduction permitted if unsatisfactory position	Of 155, complete data on 86 and 50 were DHS. Data not presented to denote how those in complete dataset differed from entire population or between intervention; 3 failed to unite, 2JNP and 1 DHS 8/50 (16%) DHS had evidence of mechanical failure vs. 25/36 (69%), p <0.001. At 1 year, 12% DHS vs. 25% JNP complained of hip pain.	"If the results of this study are projected, it is to be anticipated that the sliding screw will reduce reoperation by two-thirds and mild pain by one-half. While this represents welcome progress, it is unlikely to radically alter the face of trochanteric fracture management."	One-year mortality rate 37%. Most data aggregate, limiting conclusions on relative value of devices. Data suggest DHS superior.
Pitsaer 1993 RCT	2.5	N = 100 Inter-tro-chanteric fractures	Sliding hip screw vs. McLaughlin nail plate	Deaths in 33 patients within 6 months (32 unstable fractures) (NS between groups). No differences in early rehab, pain or regaining walking ability; 82% pain-free at 6 months. Functional outcome at 6 months did not correlate with prefracture walking score. Stable fractures developed less shortening (median 8.4 mm) than unstable fracture (median 17.1 mm). No differences between DHS and MCL groups. More breakage of McLaughlin nail-plate.	"[O]verall outcome was unrelated to the implant selected; although the Dynamic Hip Screw had a higher failure rate by 'cutting-out' we would advise against the use of the McLaughlin nail-plate due to its high incidence of implant breakage."	Sparse study details. Recommendation against McLaughlin Nail plate not based on functional outcomes but on complications (implant breakage).
Ekeland 1993 RCT	2.5	N = 378 Proximal femoral fractures	Gamma nail vs. hip compression screw	Fifteen re-operations (13GN vs. 2 HCS), p <0.003. 10 fractures, all with GN.	"The reoperation rate is significantly higher after Gamma nailing than after HCS. The risk of femoral shaft fractures after Gamma nailing is about 5%. Half of the fractures occurred early and were probably due to technical errors during Gamma nailing."	Abstract
Madsen 1996 RCT	2.0	N = 99 Unstable per-and	Gamma nail vs. compression hip screw vs. dynamic hip screw	No differences in DVTs, but more infections in Gamma (18%) and CHS (14%) vs. 2.4% in DHS/TSP, p = 0.02. Hospital stays	"The three different operation methods showed satisfactory results compared to previously reported	Abstract

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		sub-tro-chanteric fractures		Gamma 12.9 vs. CHS 10.2 vs. DHS/TSP 14.9 days, p >0.05.	series, both regarding postoperative complications and fracture healing."	
Hansen 1994 RCT	1.5	N = 23 Impacted, subcapital femoral neck fractures	Conservative treatment vs. dynamic hip screw	16 treated conservatively with secondary dislocation in 10 treated with hemiarthroplasty; 7 treated DHS, 6 healed well; 1 later had osteonecrosis. Successful conservatively treated younger (mean 69 years) than those with dislocations (82 years).	"[T]he advantages of primary osteo-synthesis predominate in the treatment of this type of fracture."	Abstract only. Details sparse. The groups are unequal for unknown reasons.
Aune 1993 RCT	1.5	N = 378 Proximal femoral fractures	Gamma nail vs. hip compression screw	13 reoperations with GN vs. 2 with HCS (p <0.003); 10 GN with femoral shaft fractures vs. 0 HCS.	"The reoperation rate was significantly higher after Gamma nailing than after HCS."	Abstract
Michos 2001 RCT	1.5	N = 52 Peritro-chanteric fractures	Gamma nail vs. sliding screw	EBL 730 for SS vs. 610mL for GN. Hospitalization for 14.5 days for SS vs. 12 days for GN. No non-union cases either group.	"[W]e recommend the selective use of the Gamma system. Its biomechanical benefits are required in subtrochanteric and unstable pertrochanteric fractures."	Abstract
Harrington 1999 RCT	1.0	N = 82 Unstable peritro-chanteric fractures	Compression hip screw (CHS) vs intramedullary hip screw (IMHS)	Duration of operation was significantly longer in IMHS group (mean 102 minutes) and blood loss significantly less than CHS group.	"We found no significant difference in functional outcome in patients treated with either CHS or the IMHS. However there were slightly more complications in the IMHS group."	Study reported in 4 paragraphs which resulted in sparse details. Unclear if part of population Harrington 2002 above.
Saudan 1999 RCT	0.5	N = 120 Inter and subtro-chanteric fractures	Proximal femoral nail vs. dynamic hip screw	Decreased EBL and operative time with PFN.	"PFN treatment for patients with trochanteric fracture has similar 6 month clinical results as treatment with DHS, with a briefer procedure and less blood loss, particularly among patients with complicated trochanteric fractures."	Short abstract.
Mott 1993 RCT	0.5	N = 69 Peri-trochan-teric hip fractures	Gamma nail vs. sliding hip screw	No differences in operative time, EBL, transfusions. 3 screw cutouts in GN vs. 1 in SHS.	"[T]he Gamma Nail appears to have unique morbidities associated with its use and its theoretical advantages have not been seen clinically."	Short abstract.

HIP ARTHROPLASTY

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments

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Lindberg 1991 RCT	3.5	N = 47 Cemented THA	High vs. low viscosity cement both with gentamicin	At 48 hours, gentamicin concentrations were: high viscosity (±SEM) 0.03±0.0 vs. 0.13±0.01. Other intervals similar results (p <0.01).	"The improved mechanical fixation and the high concentration of gentamicin of the bone cement interface favours the use of low viscosity cement, especially in revision for deep infection."	Study assessed release of gentamicin from 2 different cement preps, with more systemic release of low viscosity cement.
Vendittoli 2006 RCT	2.5	N = 210 De-generative hip disease, ages 23-65years	Total hip arthroplasty (CLS Spotorno, Allofit, Metasul, Zimmer head) vs. resurfacing arthroplasty (Durom, Zimmer)	Intra-operative stability in 89 (87.3%) THRs vs. 98 (95%) resurfacing (p = 0.21). No difference in diameters of last reamer used (p = 0.77). Acetabular component size correlated with male gender (p <0.0001) and higher 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."	Implant survival not main study purpose. Some methods details sparse. Baseline BMI higher in THR (p = 0.01). Data suggest comparable results to total arthroplasty; however, maximum follow-up less than 3 years; 4 hips converted intra-operative to THR.

ANTIBIOTICS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Nelson 1993 RCT	2.5	N = 28 Infected total hip or knee arthro-plasties	All debrided. Implantation of gentamicin-poly-methyl-methacrylate (PMMA) beads vs. conventional parenteral systemic antibiotics.	Infection recurred in 2 patients treated by gentamicin-PMMA beads (15%) vs. 4 (30%) in systemic antibiotic therapy. All recurrences occurred in patients who had infected total hip arthroplasties; none occurred in patients in 6 with total knee arthroplasties.	"These data… support the concept that debridement combined with gentamicin – PMMA bead implantation followed by a second-stage joint reconstruction is comparable with debridement and conventional parental antibiotic therapy followed by secondary reconstruction."	Methods sparse. Multiple co-interventions weaken conclusions.
McQueen 1990 RCT	2.0	N = 378 Total joint arthro-plasty	1.5g of cefuroxime intravenously plus 2 doses of 750mg intra-muscularly at 6 and 12 hours after operation vs. 1.5g cefuroxime powder mixed with CMW type 1 cement powder	No statistically significant difference in superficial wound infections. Early deep infection rate was 1% and not different. There were no late deep infections.	"[C]efuroxime given systemically or in bone cement is an effective antibiotic in the prophylaxis of infection after total joint arthroplasty."	Methods sparse.

PRE-OPERATIVE EDUCATION

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Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
McGregor 2004 RCT	3.5	N = 35 THR	Standard care (B) vs. standard care plus hip class 2 to 4 weeks before surgery and information booklet (A)	Preoperative class and booklet, had lower hospital stays by 3 days (15 vs. 18 days), significantly reducing costs. Group A reported prediction of surgical results with 93.9%±8.9% accuracy at discharge, decreasing to 89.6%±3.2% at 3-months. Group B had 79.1%±19.2% success in predicting outcome at discharge, decreasing to 69.4%±30.9% at 3 months.	"Patients attending the class reported higher levels of satisfaction (99% satisfied in the preoperative rehabilitation class compared with 80% in the control group 3 months postoperatively) and had more realistic expectations of surgery."	Details sparse. Length of stay may not be generalizable beyond U.K. Exercise intervention apparently to ensure ability to perform exercises post-op, rather than perform pre-op exercises.
Lilja 1998 RCT	3.5	N=101 55 THR; 46 breast cancer	Control group informed about pre- and post-operative routines by ward nurse vs. intervention group given extended information by an anesthetic nurse (0.5 hours day before surgery)	No significant differences between intervention and control group for breast cancer patients or THR patients. Breast cancer patients in intervention group significantly more anxious than THR patients in intervention group ($p < 0.01$). Breast cancer patients in intervention group showed highest anxiety scores on Hospital Anxiety and Depression Scale (HADS) scale on day of surgery.	"[E]tended preoperative information given by anaesthetic nurses will decrease anxiety, cortisol and pain in…THR patients, was not supported. The other assumption, that anxiety, cortisol and pain would decrease more for the THR patients than for breast cancer patients was confirmed."	Baseline data not provided.
Wong 1990 RCT	2.5	N = 146 THR	Group I (experimental) – early discharged, experimental program participants (pamphlet, videotape, home nurse visits); Group II (experimental) – conventional discharged, experimental program participants; and Group III (control) – conventional discharged, traditional program participants.	Lengths of stay were 8.8, 13.8 and 12.8 days respectively. Patients in both experimental groups had a higher score in Perceived Preparedness for Discharge Scale ($p <0.01$) and Exercise compliance scores ($p <0.05$), but no significant difference was found between groups I and III on the Compliant behavior index ($p <0.05$).	"The findings suggest that a programme of after-care combines' educational and follow-up home-visit strategies for the early discharged patients provides outcomes that are comparable to the traditional discharge planning for the conventionally discharged patients. It also points out that patients who have been adequately informed of their conditions are more likely to comply with prescribed treatment."	Sparse details. Results suggest earlier discharge and education are effective. Interventions began 3 to 6 days after surgery, likely limiting utility of the findings.
Santavirta 1994 RCT	2.5	N = 60 Primary THR	All received educational booklet. Trial was educational booklet vs. booklet plus	Knowledge of complications was poor, with no differences between the intensive education and control groups. Intensive educational group better	"[T]he experimental group showed greater interest in obtaining more information about their replaced hip. Patients in the experimental group showed significantly	Randomized, but compliance with assignments was low in the experimental group. Contact

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			intensive education (20-60 minute teaching session)	followed the exercise program (p = 0.02).	better adherence to the instructions for the postoperative rehabilitation programme."	time varied significantly. 37% could not name a relevant complication.
Burns 1992 RCT	2.0	N = 108 (?) "Approxi-mately 108 patients were included." Females with hip fractures	Controls in acute orthopaedic ward (both therapists responsible for other wards) vs. trial group transferred to continuing care hospital with occupational therapy, kitchen, physiotherapy area.	"At discharge, significantly more patients in the treatment group were independent in terms of activities of daily living, than the control group: 41 v. 25. Their median stay was 24 days compared with 41 days in the control group."	"This trial confirms the effectiveness of rehabilitative aftercare for elderly woman with hip fracture. Without provision of such aftercare, these patients would occupy a rising, proportion of hospital beds and achieve a lesser degree of independence."	Sparse description of study and results.

PREVENTION OF VENOUS THROMBOEMBOLIC DISEASE

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Kew 1999 RCT	3.5	N = 78 Hip fractures	Low molecular weight heparin (Fraxiparine) vs. control	"There was a significantly increased occurrence of DVTs on the operated side in both groups (p<0.001)."	"[Low molecular weight heparin] may thus be effective in preventing thigh DVTs and significant pulmonary emboli."	Sparse information. No demographics. No dose of medicine.
Kim 2003 J Bone Joint Surg Br RCT	3.5	N = 200 THR	Cemented vs. cementless implants	Bilateral THR 200 (100%) with DVT vs. unilateral 100 (100%) with DVT. No differences between groups for any factors. Of 200 with bilateral total hip replacement, 52 (26%) positive for thrombi. Cementless vs. cemented no statistical difference for thrombi (p = 0.654).	"[A]ll thrombi regardless of their site or size resolved completely and spontaneously without causing pulmonary embolism."	Mostly an incidence study not a comparison of treatments.
Horbach 1996 RCT	3.5	N = 305 THR	LMWH 3000IU and DHE 0.5mg subcutaneously once daily for 14 days vs. 3 subcutaneous injections of unfractionated heparin/day starting with 5000 IU per administration, adjusted to keep PTT 50 seconds for 14 days	16 patients excluded. DVT in 12.0% of LMWH/DHE vs. 8.8% of UFH, p = 0.76. Blood transfusion not significant between groups.	"Single daily subcutaneous injections of LMWH/DHE appeared to be safe and efficacious compared to adjusted-dose UFH for prophylaxis of DVT in high risk patients."	Some baseline differences with more obesity in UFH should bias against UFH. No difference between LMWH and unfractionated heparin.

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Zhao 2005 RCT	3.0	N = 62 Hip fractures	Osteoking 25ml once every other day at evening in fasting vs. Sanchi-dansheng tablet 3 times a day, 3 tablets each time for 10 days	Difference in round length between left and right sides, either for thighs or shanks, less in Osteoking than Sanchi-dansheng group, p <0.05. 9.4% of Osteoking vs. 30% Sancchi-dansheng group diagnosed with DVT (p <0.05).	"Osteoking has a satisfactory effect in preventing postoperational DVT in patients with ITF (intertrochanteric fracture."	Many methodological weaknesses. Dropouts not mentioned.
Jain 004 Prospective case series	1.5	N = 45 Total hip patients and 26 knee patients	No prophylaxis	2 patients developed proximal DVT; no distal DVT was found.	"[T]he incidence of DVT in Indian patients is very low and is not comparable with American and European populations. It is therefore not cost effective to advise prophylaxis in Indian patients undergoing THA/ TKA who have no known risk factors for DVT."	Not an RCT or crossover. Biases not discussed.

POST-OPERATIVE ACTIVITY LIMITATIONS AND REHABILITATION PROGRAMS: HIP ARTHROPLASTY

Author/Year Study Type	Score	Sample Size	Comparison Group	Results	Conclusion	Comments
Jan 2004 RCT	3.0	N = 53 Hip arthroplasty at least 1.5 years previously	Home exercise 12 weeks of hip flexion ROM, strengthening exercises, 30-minute daily walk vs. no additional instruction controls	Strength improved in the high compliance group (p <0.05). Walking speed and functional scores also improved in the compliant group (p <0.05). Low compliant group had no improvements, as did the control group.	"The designed home program was effective in improving hip muscle strength, walking speed, and function in patients after THR who practiced the program at least 3 times a week, but adherence to this home program may be a problem."	High compliance defined as at least 50%. Results negative except when not compliant subtracted from analyses. Study intervention long after surgery.

POST-OPERATIVE ACTIVITY LIMITATIONS AND REHABILITATION PROGRAMS: HIP FRACTURE

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Swanson 1998 RCT	3.5	N = 71 Elderly patients with proximal femoral fractures	Early intervention (early surgery, multidisciplinary approach, minimal narcotics, intense daily therapy) vs. usual care	Early intervention had shorter hospital stays (21 vs. 32.5 days, p <0.01).	"This early intervention program in an acute care setting results in significantly shorter length of hospital stay for elderly patients with femoral fractures."	Multiple co-interventions limits strength of conclusions on any given component. Generalizability from Australia is unclear.
Day 2001 RCT	3.5	N = 71 All proximal femoral fractures; same as	Accelerated rehabilitation (in acute care ward) vs. standard care (specialist	Rates of chest infections, cardiac problems, bed sores higher standard care (39.4% vs. 15.8%, p = 0.03), mean length of hospital stay favored	"Accelerated rehabilitation for patients with a proximal femoral fracture in a major teaching hospital can be accomplished safely."	Some baseline differences of uncertain significance. Data suggest early

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		Swanson 98 above	care, transfer to geriatric ward for rehab)	accelerated rehab (32.5 vs. 21 days, p = 0.02). Short-/long-term mortality did not differ.		rehabilitation program superior to standard care.
Gilchrist 1988 RCT	3.5	N = 222 All females over 65years with femoral fractures	Randomization to orthopaedic geriatric unit (orthopaedic surgical staff care, weekly combined ward round with geriatrician, orthopaedic senior registrar and senior ward nurse then PT, OT and social worker at case conference) vs. controls (similar nursing but no case conference)	Inpatient mortality was 4(4%) orthopaedic geriatric unit vs. 13 (10%) orthopaedic ward (p = 0.06). Lengths of stays did not differ statistically, although they favored the orthopaedic geriatric unit (e.g., 41.7 vs. 52.1 days for those admitted from home and discharged home).	"[D]esignated orthopaedic geriatric units can provide medical care to these patients and should be administered without additional cost."	Randomization to different types of care units in the UK may limit generalizability.
Jette 1987 RCT	2.5	N = 75 50 inter-trochan-teric and 25 subcapital hip fractures	Standard vs. intensive rehab; standard program of progressive weight bearing and exercises. Intensive included same exercises, plus education geriatric team meetings, 1 home visit	No differences in morality, hospital discharge or functional recovery; 33% vs. 21% regained function (NS).	"There were no statistically significant differences in mortality, hospital discharge status, or pattern and level of functional recovery, between patients receiving experimental and standard approaches to hospital rehabilitation."	Methods details sparse. Unclear if numbers of appointments differed in 2 programs. Programs appear to be exercise vs. exercise plus education.
Graham 1968 RCT	2.5	N = 175 Hip fractures	Weight bearing at 2 weeks vs. 10 weeks	Mortality rate at 3 years was 25.1%; 76.8 % of patients achieved bony union 3 years after operation. Most failures occurred within 12 months of operation. Severity of fracture percent failed type III/type IV: 15.2%/28.8%.	"[F]ull weight-bearing two weeks after operation did not increase the incidence of failure of fixation or of non-union."	Suggests early weight bearing may be superior.
Abrami 1964 RCT	2.0	N = 124 Trans-cervical femoral fracture	Early weight bearing at 2 weeks vs. 10 weeks	No significant difference between those weight bearing exercises starting at 2 weeks or 10 weeks postoperatively.	"[N]o harmful effect on the early post-operative stability of this fracture when a sliding nail-plate is used for fixation."	Few details. Outcome measure is crude, which likely reduces power.
Tsauo 2005 RCT	2.0	N = 25 Hip fracture	Home-based physical therapy (8 home visits) vs. bedside education	No difference between baseline characteristics for 2 treatments. Harris score of home-based PT group progressed 58.6±8.5 to 90.1±5.4 at Month 3, vs. control group progression 54.6±14.5 to 77.4±10.0 (p <0.01). Scores of	"Home-based PT programs could help patients regain function and HRQOL earlier."	Small sample size and sparse details. Suggests home PT superior to education.

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				psychologic domain of HRQOL (health-related quality of life) for home-based PT group significantly better Month 1 ($p < 0.05$) and 3 ($p < 0.01$) after discharge. Physical domain score of home-based PT group significantly better ($p < 0.05$) 3 months after discharge.		
Baker 1991 RCT	0.5	N = 40 Female femoral neck fracture	Treadmill gait retraining vs. conventional training	Treadmill group more mobile at discharge ($p < 0.05$). 65% of treadmill group vs. 40% controls regained prefracture mobility rating ($p < 0.05$). Treadmill group hospitalized 54 vs. 67 days. Unlimited mobility at discharge was 45% within the treadmill group compared to 10% in conventional group.	[S]ignificantly better mobility outcomes, as measured by temporal-distance gait parameters and mobility level, more subjects receiving conventional gait retraining. Furthermore, the superior mobility outcome was achieved sooner."	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 RCT	0.5	N = 74 Elderly hip fracture patients	Intensive exercise vs. home-based exercise	Changes from baseline and 6 months: physical performance test score exercise training group 7.0±4.3, $p < 0.000$; functional status questionnaire score exercise training group 6.1±5.1, $p = 0.009$; knee extension exercise training group 21.3±15.0, $p = 0.0$; Berg Balance score exercise training group 5.0±8.1 $p = 0.009$. Significant changes in exercise training group in all 4 variables compared to no change in control group.	"Intensive exercise training after a hip fracture can induce greater improvements in functional performance, and reduce disability, more than a low-intensity home exercise program."	Abstract suggests intensive exercise program may be superior.
Lauridsen 2002 RCT	0.5	N = 88 Hip fracture	3.6 hours of PT a week vs. 1.9 hours	24 patients in the intensive 3.6 hours a week PT withdrew after 15 days compared to 13 patients from control group after 22 days	"The considerable drop-out rate suggests that intensive physical therapy may be of limited value when attempting to reduce the duration of rehabilitation following hip fracture."	Suggests compliance problems may be important.

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