BMJ Best Practice

Osteoarthritis

Straight to the point of care

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Summary

Osteoarthritis (OA) is a common and frequently debilitating joint disorder; prevalence increases with age.

The most commonly affected joints are the knee, hip, hands, feet, and lumbar and cervical spine.

Presents with joint pain and stiffness that is typically worse with activity.

Radiographs show loss of joint space, subchondral sclerosis, and osteophytes.

Treatments are nonpharmacologic and pharmacologic.

Joint replacement surgery is effective for controlling the pain of OA in advanced disease.

Definition

OA is the result of mechanical and biologic events that destabilize the normal process of degradation and synthesis of articular cartilage chondrocytes, extracellular matrix, and subchondral bone. It involves the entire joint, including the articular cartilage, subchondral bone, pericapsular muscles, capsule, and synovium. The condition leads to loss of cartilage, sclerosis and eburnation of the subchondral bone, osteophytes, and subchondral cysts. It is clinically characterized by joint pain, stiffness, and functional limitation.[1] [2]

Epidemiology

OA is the most common form of arthritis, affecting an estimated 302 million people globally, and 30.8 million adults in the US.[7] [8]

OA is more common in women than in men, with incidence increasing sharply around age 50 years, and leveling off after age 70 years.[9] [10] [11]

In the US, the incidence rate of knee OA is between 164 per 100,000 patient-years and 240 per 100,000 patient-years.[12] [13] The incidence of hand OA ranges from 2% to 4% per year.[1] The incidence rate of hip OA is between 47 per 100,000 patient-years and 88 per 100,000 patient-years.[12] [13]

The Johnston County OA Project reported annual incidence rates as 37 per 1000 person-years for hip symptoms, 24 per 1000 person-years for radiographic hip OA, 13 per 1000 person-years for symptomatic hip OA, and 2.9 per 1000 person-years for severe radiographic hip OA in adults of 45 years and above followed for a median of 5.5 years.[14]

The Framingham Osteoarthritis Study showed that the prevalence of radiographic OA increases with age from 27% in people younger than 60 years to 44% in those older than 70 years.[15] In addition, the Framingham study found that 2% of women (mean age 71 years) develop radiographic knee OA every year, and 1% of women develop symptomatic knee OA every year.[16] Rates of incident knee OA were 1.7 times higher in women than in men.[16] A subsequent Framingham Osteoarthritis Study publication reported that the prevalence of radiographic hip OA was 19.6% and that of symptomatic hip OA was 4.2% (in a population of 978 people over a 5-year period). Overall, men had significantly higher prevalence of radiographic hip OA compared with women, but no difference was seen between sexes for symptomatic hip OA.[17]

The Beijing Osteoarthritis Study reported a very low crude prevalence of radiographic hip OA in Chinese people ages 60-89 years (approximately 1% in both men and women); the prevalence of knee OA in Chinese women was higher when compared with US cohorts.[18] [19]

One population study in Spain concluded that rates of knee and hip OA increased continually with age, with the highest female-to-male ratio at age 70 to 75 years. However, the risk of OA of the hand peaked at 60 to 65 years, with the highest female-to-male ratio at 50 to 55 years.[10]

There is also evidence to suggest that osteoarthritis is more prevalent in low income and lower-middle income countries, with an estimated one in six of study participants reported to have OA.[20]

Etiology

OA is a complex and multifactorial disease with numerous genetic, biologic, and biochemical components that affect the entire joint, including synovium, meniscus (in the knee), periarticular ligaments, and subchondral bone.[21] The exact etiology is unknown.

Age, hereditary predisposition, female sex, joint anatomy and/or misalignment, and obesity are associated with increased risk of OA.[9] [10] [15] [16] [18] [19] [22] [23] [24] [25] [26] [27] [28]

Articular congenital deformities or trauma to the joint also increase the risk of developing OA.[23] [29] [30]

High bone mineral density and low estrogen status, such as in postmenopausal women, may be associated with higher risk of knee and hip OA.[10]

The preceding factors might lead to a joint environment that is susceptible to trauma and to external mechanical stressors that are exacerbated by certain physical activities.

Local mechanical factors, such as periarticular muscle weakness, joint anatomy and misalignment, and structural joint abnormality (e.g., meniscal tear), further facilitate the progression of the disease.[21] [23] [26] [27] [31] [32]

The internal and external factors combined lead eventually to a failed joint.[2] [33]

Pathophysiology

In the affected joint, there is a failure in maintaining the homeostatic balance of the cartilage matrix synthesis and degradation, resulting from reduced formation or increased catabolism.[34]

A number of factors may contribute:

- Inflammatory mediators play a role as potential drivers of joint tissue destruction. The number of proinflammatory mediators reported in the synovial fluid and tissue affected by OA is increasing.[35] [36] [37] [38] [39]
- Connective tissue growth factor (CTGF) is present in osteophytes of late-stage OA. CTFG is usually upregulated in synovial fluid of OA that stimulates the production of inflammatory cytokines. Evidence has demonstrated CTFG also activates nuclear factor-κB, increases the production of chemokines and cytokines, and upregulates matrix metalloproteinases-3 (MMP-3) that in turn leads to the reduction in proteoglycan contents in joint cartilage. Thereby creating an imbalance in cartilage homeostasis which may contribute to the pathogenesis of OA by developing synovial inflammation and cartilage degradation.[40]
- Matrix metalloproteinases (e.g., collagenase), enzymes that catalyze both collagen and proteoglycan degradation, are found in increased concentrations in OA cartilage.[41]
- Nitric oxide may activate metalloproteinases, thereby playing a role in cartilage degradation.
- Anabolic cytokine levels, such as those of insulin-like growth factors (IGF-I), are decreased in OA.[42] [43] [44]
- Aberrant chondrocyte metabolism is a response to changes in the inflammatory microenvironment and may play a key role in cartilage degeneration and OA progression. Under conditions of environmental stress, chondrocytes shift from oxidative phosphorylation to glycolysis, a process regulated by the AMP-activated protein kinase (AMPK) and mechanistic target of rapamycin (mTOR) pathways.[45]
- Leptin is able to modulate the production of inflammatory mediators in immune cells of patients with OA, and it has been demonstrated to participate in the onset and progression of OA. One meta-analysis reported greater levels of circulating leptin in OA patients compared with the control group, and that synovial leptin levels were greater in patients with OA compared with healthy participants.[46] In addition, LEPR rs113710 polymorphism was linked to an increased risk of developing OA.[46]

The osteoarthritic process involves not only the cartilage but also other joint structures, resulting in bone remodeling and bone marrow lesions of the subchondral bone, synovial inflammation, capsular stretching and periarticular muscle weakness, and ligament laxity.[21]

- The Janus Kinase 2 (JAK2)/Signal transducer and activator of transcription 3 (STAT3) is a signaling pathway which is instrumental in the osteoarticular system, including cartilage, subchondral bone, and synovium. There is evidence to suggest this signaling plays a significant role in the progression of OA.[47]

The above elements, in addition to trauma, can lead to focal stress and eventual cartilage loss. This can further alter the joint anatomy, predisposing it to the potentially detrimental effects of mechanical factors and physical activity, by redistributing and increasing the focal loading in the joint. For example, in knee OA, genu varum (bow-legs) and genu valgum (knock-knees) are associated with increased risk of structural deterioration of the joint.[33] [48]

Classification

Osteoarthritis classification by disease etiology[3] [4]

- Primary (idiopathic): no preceding injury to the joint; further categorized into localized OA, which mostly affects the hands, knee, hip, or foot (especially the first metatarsophalangeal), or generalized OA, usually affecting the hands and another joint.
- Secondary: an antecedent insult to the joint, such as a congenital abnormality (e.g., congenital hip dysplasia); trauma; inflammatory arthropathies (e.g., rheumatoid arthritis, chronic gout); and ongoing strenuous physical activities or occupations could lead to joint damage over time.

Kellgren-Lawrence radiographic classification of osteoarthritis[5] [6]

Has been used as a research tool in epidemiologic studies of osteoarthritis.

- Grade 0 (none): no radiologic findings of osteoarthritis
- Grade 1 (doubtful): doubtful joint space narrowing and possible osteophytic lipping
- Grade 2 (minimal): definite osteophytes and possible joint space narrowing
- Grade 3 (moderate): moderate multiple osteophytes, definite narrowing of joint space and some sclerosis, and possible deformity of bone ends
- Grade 4 (severe): large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone ends.

Case history

Case history #1

A 60-year-old woman presents complaining of bilateral knee pain almost daily for the past few months. The pain was gradual in onset. The pain is over the anterior aspect of the knee and gets worse with walking and going up and down stairs. She complains of stiffness in the morning that lasts for a few minutes, and a buckling sensation at times in the right knee. On exam, there is a small effusion, diffuse crepitus, and limited flexion of both knees. Joint tenderness is more prominent over the medial joint line bilaterally. She has a steady but slow gait, slightly favoring the right side.

Case history #2

A 55-year-old woman has had pain and swelling in several fingers of both hands for the past 2 months. She describes morning stiffness lasting 30 minutes. Her mother tells her that she had a similar condition at the same age. She denies any other joint pain or swelling. On exam, she has tenderness, slight erythema, and swelling in one proximal interphalangeal joint and two distal interphalangeal joints in

each hand. She has squaring at the base of her right thumb (the first carpometacarpal joint). There is no swelling or tenderness in her metacarpophalangeal joints.

Approach

The most common symptoms of OA are joint pain, stiffness, and sometimes swelling. OA most commonly affects the knee, hip, small hand joints (proximal interphalangeal [PIP] and distal interphalangeal [DIP] joints), and the spine (especially lumbar and cervical regions). In other joints (e.g., the ankle and wrist), OA is rare and there is usually an underlying etiology (e.g., crystal arthropathy, trauma).

History

More patients present in their 50s as OA is more common at this age, with a higher number of women presenting than men.[9] [10] [15] [16] [18] [19] [24] [56]

Patient history may include a physically demanding job or sport, with joint pain worsening during activities or weight bearing. Joint pain should not be present at night, except in advanced OA; if the patient has joint pain during the night, a differential diagnosis should be considered.

The distribution of joint involvement is important. Some women have inflammatory OA mainly affecting the proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints of the hands, which may be erythematous and swollen. The MCP joint can occasionally be affected by OA; however, if MCP symptoms are present, a differential diagnosis of calcium pyrophosphate dihydrate deposition (CPPD) disease, rheumatoid arthritis, or other secondary etiology should be considered.[72]

People with OA present with morning stiffness of no more than 30 minutes.[3] [73] If stiffness persists for longer than this, other diagnoses should be considered, such as rheumatoid arthritis.

Joint swelling and functional difficulties, such as a knee giving way or locking may be reported by patients. This can reflect an internal derangement, such as a partial meniscal tear or a loose body within the joint.

Physical examination

Weight and body mass index are important, as knee OA and, to a lesser degree, hip OA are common in overweight patients.[22] [23]

Swelling may be observed, with bony deformities and malalignment of the affected joint.[33] [48] [74] [32]

Bony deformities are particularly common in the hands and lead to enlargement of the PIP joints (Bouchard nodes) and DIP joints (Heberden nodes), as well as squaring at the base of the thumb (the first carpometacarpal joint).[75]

Bony malalignment is common, particularly in the knee, where OA causes both genu valgum (knock-knees) and genu varum (bow-legs).[33] In addition, a varus thrust, which is a worsening varus alignment in a weight-bearing knee, seems to further worsen the risk of progression of medial knee OA.[32]

In advanced knee OA, there may be new bone formation, causing bony swellings around the knee joint.[3] [76]

It is common to palpate crepitus during the range of motion of the joint. Limited range of motion, small effusions, and joint line tenderness may be elicited. An abnormal gait can be observed.

OA is essentially a clinical diagnosis

Guidelines recommend that OA is diagnosed clinically based on symptoms, patient age, and exam findings.[3] [73][77]

A clinical diagnosis can be considered in a patient with a typical OA presentation:[3] [73][77]

- Activity-related joint pain
- With either no morning joint-related stiffness or morning stiffness that lasts no longer than 30 minutes
- >45 years of age.

Atypical features that suggest an alternative or additional diagnosis include:[73]

- Prolonged morning joint-related stiffness
- History of recent trauma
- Palpable warmth over the joint
- Rapid worsening of symptoms
- Concerns that may suggest infection or malignancy.

Laboratory assessment

When an alternative or additional diagnosis of rheumatoid arthritis is suspected, inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]), rheumatoid factor, and anticyclic citrullinated peptide (anti-CCP) antibodies may be helpful as differential tests.[3] [78] These tests are normal in OA.

It should be noted that elevated inflammatory markers are also associated with age, increased weight, and other conditions; therefore, they should not be interpreted as definitive evidence of inflammatory conditions in the absence of other symptoms.

Imaging studies

Imaging studies are not routinely recommended for the diagnosis of OA, they should only be considered if the diagnosis is unclear or an alternative/additional diagnosis is suspected subsequent to initial investigations.[73]

Radiography

If imaging studies are required, radiography should be considered before other imaging modalities.[77] [79]

Conventional radiographic diagnosis of OA includes narrowing of the joint space, osteophytes, subchondral cysts, and subarticular sclerosis.[79] [80] If imaging the foot and ankle, avoid nonweightbearing radiographs if the patient is able to stand.[81]

Radiographs may also help to exclude less common etiologies for pain and in monitoring unexpected rapid progression or changes in symptoms that may be related to OA severity or an additional diagnosis.[77]

While radiographic evidence of OA is poorly correlated with the symptoms, one study suggested that radiologic progression in early symptomatic knee OA over 5 years was related to worsening pain and function.[82]

Magnetic resonance imaging (MRI)

Although more sensitive than plain radiographs in detecting OA changes, MRI is not indicated for the diagnosis of simple OA. If needed, MRI should be ordered if spinal OA with neurologic deficits is suspected, to identify and evaluate the extent and severity of spinal stenosis or nerve root entrapment.

MRI can be used to rule out other etiologies for hip or knee pain, such as avascular necrosis or other less common conditions such as pigmented villonodular synovitis or bone tumors.[77] [79] Although more sensitive than plain x-ray in detecting OA changes, MRI is not indicated for the diagnosis of simple OA in most joints.

Bone marrow lesions (edema), which are associated with knee pain in OA, are readily detected using MRI.[79] [83] [84] Medial and lateral compartment bone marrow lesions confer increased risk of progression of medial and lateral tibiofemoral OA, respectively.[85]

Other imaging modalities

Ultrasound (US) and computed tomography (CT) scans can be used to make additional diagnoses. Soft tissues are best imaged by US or MRI and bone by CT or MRI.[77] In practice, CT is not widely used for the diagnosis of OA.

History and exam

Key diagnostic factors

pain (common)

- OA-related joint pain is associated with activities or weight bearing. Joint pain should not be present at night, except in advanced OA; if the patient has joint pain during the night a differential diagnosis should be considered.

functional difficulties (common)

- Functional difficulties, such as a knee giving way or locking, can be present. This can reflect an internal derangement, such as a partial meniscal tear or a loose body within the joint.

knee, hip, hand, or spine involvement (common)

- Commonly involved joints are the knee, hip, hands, and lumbar and cervical spine.[3] [75] [78]

bony deformities (common)

- These are particularly common in the hands and lead to enlargement of the proximal interphalangeal (PIP) joints (Bouchard nodes) and distal interphalangeal (DIP) joints (Heberden nodes), as well as squaring at the base of the thumb (the first carpometacarpal joint).[75]
- In advanced knee OA, there may also be new bone formation, causing bony swellings around the knee joint.[3]

limited range of motion (common)

- Both active and passive range of joint movement is reduced in moderate to advanced OA, and this is usually associated with pain.

malalignment (common)

- Bony malalignment is common, particularly in the knee, where OA causes both genu valgum (knock-knees) and genu varum (bow-legs).[33] In addition, a varus thrust, which is a worsening varus alignment in a weight-bearing knee, seems to further worsen the risk of progression of medial knee OA.[32]

Other diagnostic factors

tenderness (common)

- OA can cause local tenderness over the joint line. The location of the tenderness can help differentiate OA from other local structures contributing to the pain, such as the pes anserine bursa in the knee and the greater trochanteric bursa in the hip.

crepitus (common)

- Crepitus is a palpable, and sometimes audible, creaking evident on active and passive movements of joints affected by OA.

stiffness (uncommon)

- Early morning stiffness is usually present for only a few minutes and, almost invariably, <30 minutes.[3] [73] This helps differentiate OA from other inflammatory arthritis, including rheumatoid arthritis.
- One exception is inflammatory OA of the hand, which causes more prominent stiffness during the early stages.

shoulder, elbow, wrist, or ankle involvement (uncommon)

- OA is less likely to involve joints such as the shoulder, elbows, wrists, or ankles, unless there is an underlying injury, occupational risk, or other etiology.

effusion (uncommon)

- An effusion is fluid within the joint cavity. In OA these are usually small and lack other inflammatory signs such as warmth and redness.
- In knee OA, a large effusion may reflect an underlying internal derangement such as a meniscal tear, or inflammatory arthritis such as gout or pseudogout.

antalgic gait (uncommon)

- Patients with lower limb OA often limp because of pain (antalgic gait), but spinal OA can also cause limping secondary to weakness, back pain, or radicular pain.

Risk factors

Strong

age >50 years

- Aging is the strongest risk factor associated with OA.[10] [15]
- The effect of aging on OA seems to be more pronounced in females.[10] Incidence increases sharply around age 50 years.[9] [10]

- In a prospective study of women from a UK population cohort, the oldest group of women (upper tertile) was at greatest risk of OA (adjusted odds ratio 2:41).[49]
- In a longitudinal study of aging, the incidence of radiographic features of hand OA in men increased with age.[50]

female sex

- Women are affected more than men.[10] [16] [18] [19] However, OA is a common disease that affects both sexes.

obesity

- Being overweight or obese increases the risk of OA; the strongest association is with knee OA.[22] [23]
- In the Framingham study, high body mass index at baseline exam was associated with increased risk for incident OA.[51] For women in the most overweight quintile, relative risk was 2.07.[52] Among obese men participating in the Framingham study, the age-adjusted relative risk of developing OA was 1.51.[52]

genetic factors

- Twin and family studies have shown that the genetic contribution to OA is about 40% to 50%.[24] [25]
- Certain hereditary disorders associated with OA, such as Stickler syndrome, are caused by defects in type-2 collagen, but the genetics and mechanisms in other forms of OA are poorly understood.[53] [54] [55]
- Hand OA is common in female siblings of people affected by OA.[24] Heberden nodes are more common in females with a family history of hand OA.[56]

joint anatomy and/or malalignment

- Evidence suggests that the antaomy and/or malalignment of knee or hip increases the risk of the development of OA and the subsequent progression of the disease.[26] [28] [31][32] [57]

physically demanding occupation/sport

- OA is common in manual workers, and there is a strong association between increased physical activity and lower limb OA.[58] [59] [60]
- Knee OA is common in miners, and hip OA is common in agricultural workers.[61] Heavy labor and activities can predispose specific joints to OA.
- Evidence suggests that certain sports including running, weight-lifting, and wrestling are associated with developing OA of the knee.[62]

post trauma/injury

- Previous trauma to the joint significantly increases the risk of developing OA.[23] [63]
- The prevalence of OA increases after an anterior cruciate ligament (ACL) reconstruction.[29] [30] [64]
- Evidence suggests that longer chronicity of ACL tear and older age at the time of surgery positively correlates with the development of OA, and that development of OA on the ipsilateral knee is more likely than OA on the contralateral side post ACL reconstruction.[29] [30]

Weak

high bone mineral density

- Several studies report higher bone mineral density in patients with hip and knee OA.[65] [66] [67]

- Eight-year follow-up of the Framingham Cohort found that incident OA (defined by the appearance of osteophytes) was lowest in those with the lowest bone mineral density.[16]

Tests

1st test to order

Test	Result
history and physical exam • OA is essentially a clinical diagnosis. Guidelines recommend a clinical diagnosis of OA based on symptoms, patient age, and examination findings.[3] [53] [73]	**activity-related joint pain, morning stiffness that lasts no longer than 30 minutes, >45 years of age**

Other tests to consider

Test	Result
x-ray of affected joints • OA is essentially a clinical diagnosis. • Imaging studies are not routinely recommended for the diagnosis of OA, they should only be considered if the diagnosis is unclear or an alternative/additional diagnosis is suspected subsequent to initial investigations.[73] • If imaging studies are required, radiography should be considered before other imaging modalities.[77] [79] If imaging the foot and ankle, avoid nonweightbearing radiographs if the patient is able to stand.[81] • Conventional radiographic diagnosis of OA includes narrowing of the joint space, osteophytes, subchondral cysts, and subarticular sclerosis.[79] [80] • Radiographs may also help to exclude less common etiologies for pain and in monitoring unexpected rapid progression or changes in symptoms that may be related to OA severity or an additional diagnosis.[77]	**new bone formation (osteophytes), joint space narrowing, and subchondral sclerosis and cysts**
serum CRP • OA is essentially a clinical diagnosis. • If there are atypical features that suggest an alternative or additional diagnosis, laboratory investigations may be warranted. • Inflammatory markers may be ordered if inflammatory arthritis, such as rheumoatoid arthritis (RA), is suspected.[3] [78] • It should be noted that elevated inflammatory markers are also associated with age, increased weight, and other conditions; therefore, they should not be interpreted as definitive evidence of inflammatory conditions in the absence of other symptoms.	**normal**
serum erythrocyte sedimentation rate (ESR) • OA is essentially a clinical diagnosis. • If there are atypical features that suggest an alternative or additional diagnosis, laboratory investigations may be warranted. • Inflammatory markers may be ordered if inflammatory arthritis, such as rheumatoid arthritis, is suspected.[3] [78] • It should be noted that elevated inflammatory markers are also associated with age, increased weight, and other conditions; therefore, they should not be interpreted as definitive evidence of inflammatory conditions in the absence of other symptoms.	**normal**
rheumatoid factor (RF) • OA is essentially a clinical diagnosis. • If there are atypical features that suggest an alternative or additional diagnosis, laboratory investigations may be warranted. • Indicated if rheumatoid arthritis (RA) cannot be excluded clinically, or if there is a suspicion that the patient might have both RA and OA.[3]	**negative**
anticyclic citrullinated peptide (anti-CCP) antibody • OA is essentially a clinical diagnosis. • If there are atypical features that suggest an alternative or additional diagnosis, laboratory investigations may be warranted. • Indicated if rheumatoid arthritis (RA) cannot be excluded clinically or if there is a suspicion that the patient might have both RA and OA.	**negative**

Test	Result
MRI of affected joints • Imaging studies are not routinely recommended for the diagnosis of OA, they should only be considered if the diagnosis is unclear or an alternative/additional diagnosis is suspected subsequent to initial investigations.[73] • Although more sensitive than plain radiographs in detecting OA changes, MRI is not indicated for the diagnosis of simple OA. If needed, MRI should be ordered if spinal OA with neurologic deficits is suspected, to identify and evaluate the extent and severity of spinal stenosis or nerve root entrapment. • MRI can be is used to rule out other etiologies for hip or knee pain, such as avascular necrosis or other less common conditions such as pigmented villonodular synovitis or bone tumors.[77] [79] • Bone marrow lesions (edema), which are associated with knee pain in OA, are readily detected using MRI.[79] [83] [84] Medial and lateral compartment bone marrow lesions confer increased risk of progression of medial and lateral tibiofemoral OA, respectively.[85]	**cartilage loss, bone marrow lesions, and meniscal tears**
ultrasound scan • OA is essentially a clinical diagnosis. • Imaging studies are not routinely recommended for the diagnosis of OA, they should only be considered if the diagnosis is unclear or an alternative/additional diagnosis is suspected subsequent to initial investigations.[73] • Ultrasound scans can be used to make additional diagnoses. • Soft tissues are best imaged by ultrasound or MRI.[77]	**effusion, synovial hypertrophy, cartilage loss**
CT • OA is essentially a clinical diagnosis. • Imaging studies are not routinely recommended for the diagnosis of OA, they should only be considered if the diagnosis is unclear or an alternative/additional diagnosis is suspected subsequent to initial investigations.[73] • CT can be used to make additional diagnoses. • Bones are best imaged by CT or MRI. • In practice, CT is not widely used for the diagnosis of OA.	**osteophytes, bone or cartilage loss**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Bursitis	• Greater trochanteric bursitis in the hip and pes anserine bursitis in the knee present with pain over the lateral aspect of the hip and over the medial aspect of the knee, respectively. There is local tenderness in these areas that is usually absent in simple OA.	• Local anesthetic and corticosteroid injection might be therapeutic and diagnostic if it relieves symptoms to a significant degree.
Gout	• The onset of arthritis in gout is usually more acute (over a period of a few hours), but could mimic an exacerbation of acute OA. • In acute attacks of gout, the affected joint is usually erythematous, hot, and acutely tender. • Gout commonly involves the foot, especially the first metatarsophalangeal (MTP) joint.	• Arthrocentesis and joint fluid analysis, which shows leukocytes >2000 cells/mm^3, and the presence of sodium monourate crystals.
Pseudogout	• The onset of arthritis in pseudogout (calcium pyrophosphate deposition [CPPD]) is usually more acute (over a period of a few hours), but could mimic an exacerbation of acute OA. Associated with other conditions (e.g., hemochromatosis) and results in secondary pseudo-OA, which often involves the metacarpophalangeal joints. • In acute attacks of pseudogout, the affected joint is usually erythematous, hot, and acutely tender. • Pseudogout often involves the wrist and knee, although it may affect almost any joint.	• Arthrocentesis and joint fluid analysis, which shows leukocytes >2000 cells/mm^3, and the presence of pyrophosphate crystals. • Radiographs: chondrocalcinosis; in cases of hemochromatosis, hooklike osteophytes in the second and third metacarpal heads.
Rheumatoid arthritis (RA)	• Number and distribution of the involved joints helps to differentiate RA from OA. • RA usually causes a symmetric small joint polyarthritis in the hands,	• In RA, erythrocyte sedimentation rate and CRP are abnormal and rheumatoid factor and anticyclic citrullinated antibodies are positive.

Condition	Differentiating signs / symptoms	Differentiating tests
	particularly affecting the metacarpophalangeal joints and sparing the distal interphalangeal joints. Typically, RA is associated with more prolonged morning stiffness than OA. Patients with acute RA may also feel generally ill, with fatigue and low mood. • Differentiation is sometimes challenging for hand involvement, and OA and RA can coexist.	Typical RA erosive changes are seen on x-ray, MRI, or ultrasound.
Psoriatic arthritis	• Psoriatic arthritis can occur in the absence of skin psoriasis and often affects the distal interphalangeal (DIP) joints. • In psoriatic arthritis, the joint involvement is usually asymmetric, but inflammatory OA can be difficult to distinguish from certain cases of psoriatic arthritis with only DIP involvement.	• In psoriatic arthritis, x-ray might show typical erosive changes. Ultrasound and MRI are usually more sensitive in showing enthesitis, tenosynovitis, and erosions.
Avascular necrosis (AVN)	• This is common in the hip and knee joints. • The onset is subacute and there is usually a risk factor such as corticosteroid use. Early on, the joint exam is unremarkable, except for possible localized bony tenderness in the knee.	• MRI is the most sensitive test for AVN. In the early stages, localized subchondral edema is characteristic. In 50% of all cases, accompanying joint effusion may be found. Due to necrosis of the cells of bone marrow and bone fibrovascular tissue, reactions with hyperemia can be delineated.[86]
Internal derangements (e.g., meniscal tears)	• The onset of meniscal tears is usually acute and debilitating, with preceding trauma, although the trauma can be minor. • Patients may describe true locking (normal flexion, but an inability to extend the affected knee).	• MRI is sensitive in detecting both acute meniscal and cruciate ligament tears, although degenerative meniscal tears are common in OA.

Criteria

American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the knee[3]

Clinical and laboratory diagnostic criteria:

- Knee pain plus at least 5 of the following 9 criteria: age >50 years; stiffness <30 minutes; crepitus; bony tenderness; bony enlargement; no palpable warmth; erythrocyte sedimentation rate (ESR) <40 mm/hour; rheumatoid factor <1.40; synovial fluid signs of OA.

Clinical and radiographic diagnostic criteria:

- Knee pain plus osteophytes, plus at least 1 of the following 3 criteria: age >50 years; stiffness <30 minutes; crepitus.

American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand[75]

Clinical criteria:

- Hard tissue enlargement involving at least 2 of 10 selected joints, swelling in <3 metacarpophalangeal (MCP) joints, and hard tissue enlargement of at least 2 distal interphalangeal (DIP) joints.
- If the patient has <2 enlarged DIP joints, then deformity of at least 1 of the 10 selected joints is necessary in order to classify the symptoms as being due to OA.

American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip[78]

Clinical and laboratory diagnostic criteria:

- Hip pain is present plus either 1) hip internal rotation ≥15°; pain present on internal rotation of the hip; morning stiffness of the hip for ≤60 minutes; age >50 years, or 2) hip internal rotation <15°; ESR ≤45 mm/hour. If no ESR was obtained, hip flexion ≤115° is substituted (sensitivity 86%, specificity 75%).

Clinical and radiographic diagnostic criteria:

- Hip pain plus 2 of the following 3 radiographic criteria: osteophytes (femoral or acetabular); joint space narrowing (superior, axial, and/or medial); ESR <20 mm/hour (sensitivity 89%, specificity 91%).

Approach

The main goal of treatment in OA is to control joint pain and stiffness, thereby improving function.

Management includes nonpharmacologic approaches (patient education, self-management, and exercise programs), pharmacologic therapies, and surgery. Therapy must be individualized; different treatments can be combined.

It is important to acknowledge the role of the placebo effect when considering any treatment in OA, as there is evidence that placebo is an effective treatment for people with OA.[89] [90]

The effect size of different types of placebo varies: for example, intra-articular placebo injections and topical placebo treatment might have a greater effect than oral placebos.[91]

Nonpharmacologic approaches

All patients should start treatment for OA with nonpharmacologic approaches.[7] [73] These include patient education, self-management, exercise programs (with reassurance that exercise, e.g., resistance training, tai chi, yoga, and water-based exercise, is not harmful to the joints), and they may also benefit from cognitive behavioral therapy in combination with physical therapy.[7] [73][92] [93] [94] [95] [96] [97] [98]

Physical and occupational therapy, as well as manual mobilization, are also recommended.[7] [73][99] [100] [101] [102]

Exercise and weight loss programs

Exercise is recommended for all patients with OA, though there is considerably more evidence for the use of exercise in the treatment of knee and hip OA than for hand OA.[7] Balance exercises or tai chi are recommended for patients with OA of the knee and/or hip, and yoga is suggested as an alternative for patients with OA of the knee.[7]

Weight loss is recommended for patients with OA of the knee and/or hip who are overweight.[7]

Two Cochrane reviews conclude that exercise programs have a small to moderate beneficial effect on pain and function for patients with knee and hip OA.[103] [104] However, the benefit from physical therapy on hip OA is unclear.[105] One meta-analysis showed a modest effect on pain, though no improvement in self-reported function for exercise in patients with OA of the hip.[106] Further meta-analyses reported that 14% more patients with hip OA responded to exercise therapy, compared with placebo, and that hip abductor muscle strengthening exercises significantly improved knee pain and other functional outcomes for patients with knee OA.[107] [108]

Evidence from randomized controlled trials (RCTs) suggests that quadricep strengthening exercises and weight loss are effective in controlling the pain of knee OA.[109] [110] Subsequent meta-analyses demonstrate that hip strengthening exercises are an effective rehabilitation treatment for patients with OA of the knee.[108] [111][112]

Exercise can improve quality of life by reducing pain and increasing function for patients with OA, especially those who are overweight or obese.[113] A combination of diet and exercise has been shown to reduce pain and increase muscle mass in patients with OA, and that diet alone or in combination with exercise can improve function.[114] [115]

Assistive devices

The American College of Rheumatology (ACR) recommends:[7]

- Cane use for patients with knee and/or hip OA in one or more joints, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use
- Tibiofemoral knee braces for patients with OA of the knee, in one or both knees, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use
- Hand orthoses for patients with OA of the first carpometacarpal (CMC) joint, or in joints apart from the first CMC joint of the hand
- Patellofemoral braces for patients with patellofemoral knee OA.

The ACR does not recommend modified shoes, or lateral and medial wedged insoles for patients with knee and/or hip OA.[7]

The National Institute of Health and Care Excellence (NICE) in the UK recommends:[73]

- Walking aids, such as canes, for people with lower limb OA
- Insoles, braces, tape, splints, or supports are not routinely recommended to OA patients, unless
    - there is joint instability or abnormal biomechanical loading AND
    - therapeutic exercise is ineffective or unsuitable without the addition of an aid or device AND
    - the addition of an aid or device is likely to improve movement.

One network meta-analysis reported that lateral wedge insoles in combination with knee bracing reduce peak knee adduction moment in patients with tibiofemoral OA, while gait training influenced both knee adduction angular impulse and knee adduction moment, so it is recommended for reducing biomechanical risk factors.[116]

There is conflicting evidence for the use of orthoses and/or braces for medial knee OA. There is evidence to suggest that lateral wedge insoles do not reduce pain or improve functionality in patients with medial knee OA, but conversely that lateral wedge insoles with arch support significantly improved pain and physical function in patients with knee OA.[117] [118] [119]

Knee valgus bracing has been demonstrated as an effective intervention to improve the quality of life and reduce pain during daily activities for patients with medial knee OA.[120] However, evidence suggests that valgus knee bracing may only be effective in the short term.[121] [122] [123] [124]

Combining both a knee brace and lateral wedge insoles has been shown to improve pain and function in patients with medial knee OA.[125]

Unloader shoes do not appear to confer benefit in medial knee OA.[126]

Patellar bracing or taping for patellofemoral pain can be considered. One RCT suggests the use of a knee brace may be helpful in reducing pain and bone marrow lesions in patellofemoral OA.[127] Results of one meta-analysis reported that a multimodal physical therapy intervention that included taping significantly reduced pain in the short term for patients with patellofemoral OA.[128]

One meta-analysis found that splinting in patients with thumb and carpometacarpal (CMC) joint OA reduced pain and improved function in the medium term (3-12 months), but not the short term.[129]

Dietary supplements

Glucosamine and chondroitin sulfate are not recommended for the management of patients with OA; decisions regarding the use of these agents should be discussed with patients.[7] [73] Despite this recommendation, glucosamine and chondroitin sulfate are commonly used by people with OA. Modest efficacy and low risk may explain the popularity of these supplements among patients.

Both agents have been associated with modest pain reduction in patients with knee OA, and are considered safe.[130] [131] [132] [133] [134] [135] However, many trials are of low quality.[133]

Results of studies on the efficacy of glucosamine or chondroitin vary. One meta-analysis found that glucosamine or chondroitin sulfate reduced pain in patients with knee OA individually, but found no additional benefit associated with combination treatment, whereas subsequent evidence suggests that combination treatment is effective for the treatment of knee OA, compared with placebo.[132] [136]

The inconsistencies between the labeling and actual contents of many dietary supplements should be considered; prescription-grade preparations should be sought.[135] [137]

Acupuncture and transcutaneous electrical nerve stimulation (TENS)

The ACR recommends acupuncture for patients with knee, hip, and/or hand OA.[7] However, NICE in the UK does not recommend acupuncture for the management of OA.[73] TENS is not recommended for the treatment of patients with OA due to insufficient evidence of benefit.[7] [73]

Evidence suggests that acupuncture may benefit patients with knee OA.[138] [139] [140] However, evidence of short-term benefit is based on low- to very-low-quality evidence, and may not be clinically important, when compared with control treatments.[141]

One Cochrane review concluded that acupuncture does not appear to reduce pain or improve function relative to sham acupuncture in people with hip OA.[142] However, subsequent meta-analysis suggest that acupuncture is reduced pain and improves function in patients with OA of the knee, and may be used as an adjunctive treatment.[143] [144]

The results of a Cochrane review reported that there is a lack of evidence to support the use of TENS to treat patients with OA of the knee, but there is also evidence to suggest that acupuncture significantly reduced pain, and improved walking ability in patients with OA of the knee.[145] [146]

Pharmacologic treatment

Pharmacologic management is required if nonpharmacologic approaches do not adequately control symptoms, although these can be used on an as-needed basis in some patients.

If pharmacologic treatments are needed, they should be used alongside nonpharmacologic treatments and to support therapeutic exercise, at the lowest effective dose for the shortest time possible.[73]

Topical analgesia

Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for patients with OA of the hand or knee, and can be considered for other affected joints.[7] [73] Other topical analgesics include capsaicin and methylsalicylate.[7] The ACR recommends topical capsaicin for patients with OA of the knee, but not for patients with OA of the hand.[7]

Topical NSAIDs effectively relieve pain in adults with knee or hand OA within 2 weeks of daily application. The results of systematic reviews and meta-analyses report that topical NSAIDs are the most effective

topical analgesic for pain relief for OA patients compared with oral NSAIDs, cyclo-oxygenase-2 [COX-2] inhibitors, and opioids, and that diclofenac transdermal patches may be the most effective and safest topical NSAID for pain relief.[147] [148]

Systematic reviews suggest that topical NSAIDs are relatively safe for the management of pain associated with OA.[149] [150] [151] [152] However, confirmation of the cardiovascular safety of topical NSAIDs requires further study.[149]

One Cochrane review found that arnica gel may improve symptoms as effectively as a topical NSAID, but with a potentially worse adverse effect profile.[153] In the same review, capsicum-extract gel (capsaicinoids ≤0.05%) did not significantly improve pain or function compared with placebo.[153] However, results of a network meta-analysis suggest that topical capsaicin may be as effective as topical NSAIDs at reducing pain in patients with OA.[154]

Oral analgesia

Guidance on oral analgesia for OA treatment varies, check local guidance.

In the US, acetaminophen, oral NSAIDs, tramadol, and duloxetine (an antidepressant with analgesic properties) are recommended for patients with knee, hip, and/or hand OA.[7] Opioids other than tramadol may be considered when other treatments are ineffective.[7]

In the UK, oral NSAIDs are recommended as first-line oral pharmacologic treatment, taking into account potential gastrointestinal, renal, liver, and cardiovascular toxicity, and any risk factors the patient may have, including age, pregnancy, current medication, and comorbidities.[73] Gastroprotection should be considered for patients on long-term NSAID therapy, especially those at risk of gastrointestinal bleeding.[73] Acetaminophen or weak opioids are not routinely offered to OA patients unless they are used infrequently for short-term pain relief, or all other oral analgesia is contraindicated, not tolerated or ineffective.[73]

Acetaminophen

Studies have demonstrated that acetaminophen has a small to modest benefit for patients with OA of the hip or knee, and is statistically inferior to all other drug categories for the management of OA pain (oral NSAIDs, topical NSAIDs, COX-2 inhibitors, and opioids).[147] [155] [156]

As such acetaminophen alone may not have a role in the treatment of hip or knee OA, irrespective of the dose used, but may be added for rescue analgesia, or if local therapies alone do not control symptoms.[137] [157]

With this evidence of limited efficacy, and with more data available regarding the potential adverse reactions of acetaminophen, careful consideration should taken about the use of acetaminophen for the treatment of OA.[155] [157] [158]

NSAIDs

Oral NSAIDs are more effective than acetaminophen for the management of OA pain; however, they are associated with gastrointestinal (GI) and renal toxicity.[147] [159] [160] Gastroprotection should be offered to patients on long-term NSAID therapy, especially those at risk of GI bleeding.[73] Evidence suggests that proton-pump inhibitors (PPIs) provide better protection against NSAID-induced peptic ulcer disease and gastritis compared with H2 antagonists.[161] Misoprostol is a prostaglandin E1 analog and is another

option for gastroprotection, but diarrhea is a common adverse effect, and the drug is less well tolerated than PPIs.[162] [163] [164]

Diclofenac or etoricoxib (not available in the US) may be the most effective NSAID for the treatment of pain in knee and hip OA, but potential benefit must be weighed against adverse effects, and may not be appropriate for patients with comorbidities or for long-term use.[157] [148]

Selective COX-2 inhibitors may be used as an alternative to nonselective NSAIDs. They are associated with reduced risk of GI adverse effects compared with nonselective NSAIDs, but similar renal toxicity.[165] [166] COX-2 inhibitors are effective for the management of pain associated with knee and hip OA, and may have a role in patients at increased risk for GI adverse effects.[137] [157] However, COX-2 inhibitors do not confer an advantage with respect to GI symptoms when compared with placebo, or NSAID and PPI used concomitantly for gastroprotection.[167] [168] The incidence of upper GI adverse effects did not differ between patients with knee OA who were treated with fixed-dose combination naproxen and esomeprazole or with celecoxib; the former reported significantly more heartburn-free days than those on celecoxib.[169]

Evidence suggests that NSAID use substantially contributes to the association between OA and cardiovascular disease (CVD), with increased risk reaching significance as early as 4 weeks into treatment.[170] [171] Several patient characteristics may be associated with increased CVD risk when taking an NSAID, such as age >80 years, history of CVD, rheumatoid arthritis, chronic obstructive pulmonary disease, renal disease, and hypertension.[172] One meta-analysis suggested that diclofenac and ibuprofen were associated with increased cardiovascular risk, while naproxen and celecoxib were not.[173] However, similar incident rates of cardiovascular events have been reported for ibuprofen, celecoxib, and naproxen.[174] GI and cardiovascular safety profiles of individual oral NSAIDs differ, and careful patient selection is required to maximize the risk:benefit ratio.[137] The lowest effective dose of NSAID should be used to minimize adverse effects.

Opioids

It should be noted that the potential clinical benefit of opioid treatment, regardless of preparation or dose, does not outweigh the harm opioid treatment may cause in patients with OA.[148] Opioids provide minimal relief of OA symptoms, and are known to cause discomfort in many patients. Clinicians should give careful consideration to the utility of opioids in the management of OA.[175]

Oral and transdermal opioids can decrease pain intensity and improve function in patients with OA of the knee or hip compared with placebo, but the observed benefits were small (12% absolute improvement in mean pain compared with placebo [various pain scales]; number needed to benefit of 10).[176] No studies of tramadol contributed to these results.

A subsequent meta-analysis reported that opioids did not demonstrate a clinically relevant reduction in pain or disability compared with placebo in patients with OA of the hip or knee in at 4-24 weeks. Number needed to treat for an additional dropout due to side effects was 5 (95% CI 4 to 7).[177]

Evidence suggests that tramadol is generally well tolerated and can be combined with acetaminophen and/or NSAIDs.[178] However, tramadol alone or in combination with acetaminophen is unlikely to have an important benefit on mean pain or function in patients with OA.[178] [179]

Duloxetine

Duloxetine is an antidepressant with analgesic properties.

Results from one systematic review suggest that duloxetine may be effective for the treatment of chronic pain associated with OA, with a number needed to benefit (clinically meaningful outcome at study end compared with placebo) of 7.[180]

Indirect comparisons between duloxetine and a number of post-first-line oral treatments for OA, including selective COX-2 inhibitors and opioids, found no difference in the total WOMAC composite scores (an inclusive set of OA outcomes) after approximately 12 weeks of treatment.[181] Some analyses suggested that etoricoxib (not available in the US) may be superior to duloxetine.[181]

Evidence from subsequent systematic reviews found that duloxetine moderately reduces pain compared with placebo, in patients with knee OA.[182] [183] [184] [185]

Commonly observed adverse effects reported among patients with OA treated with duloxetine include nausea, fatigue, constipation, and dry mouth.[182] There is a possible increased serotonergic effect if given with tramadol.

Acute exacerbation of symptoms despite regular analgesia

Intra-articular corticosteroid injections and intra-articular viscosupplementation are useful, particularly in the knee, for acute exacerbations of OA or when NSAIDs are contraindicated or not tolerated. These interventions can be used in addition to the nonpharmacologic therapies and analgesia.

Intra-articular corticosteroids and intra-articular viscosupplementation should be compared with injectable placebo to determine the incremental effect size in reducing pain and improving function that can be attributed to the therapeutic agent. In meta-analyses, administration of an intra-articular normal saline placebo injection to patients with knee or hip OA resulted in clinically meaningful improvements in pain and function at 6 months.[186] [187]

Not all placebos are the same; effect size varies with the method of delivering the drug.

Intra-articular corticosteroid injections

The ACR recommends intra-articular corticosteroid injections for patients with knee and/or hip OA, but only conditionally recommends this treatment for patients with OA of the hand.[7] In the UK, intra-articular corticosteroid injections are only recommended when other pharmacologic treatments are ineffective or unsuitable, or to support therapeutic exercise.[73]

Trials comparing intra-articular corticosteroid injections with sham or nonintervention controls are often small and of low methodological quality.[188] [189]

Intra-articular corticosteroid injections reduced pain and improved function in patients with OA of the knee at 6 weeks compared with placebo.[190] However, it appears that intra-articular corticosteroid injections do not reduce joint pain for patients with hand or temporomandibular OA compared with placebo.[191] [192]

It is unclear how long the benefit of intra-articular corticosteroids lasts in patients with OA. Results from meta-analyses vary, with reports of continued efficacy from 1 to 12 weeks in patients with OA of the hip.[188] [189] [193] [194] However, intra-articular corticosteroid may increase the risk of rapidly destructive hip disease, especially at higher doses.[195]

Meta-analysis of individual patient data suggests that patients with severe knee pain at baseline may derive greater short-term benefit (reduction in pain up to 4 weeks) from intra-articular corticosteroid injection than patients with less severe pain.[196]

Intra-articular triamcinolone every 12 weeks for 2 years failed to significantly reduce OA knee pain compared with intra-articular saline (-1.2 vs. -1.9; between-group difference -0.6, 95% CI -1.6 to 0.3) in a double-blind RCT.[197] Triamcinolone was associated with significantly greater cartilage volume loss than saline (mean change in index compartment cartilage thickness of -0.21 mm vs. -0.10 mm; between-group difference -0.11 mm, 95% CI -0.20 to -0.03), but the clinical significance of this finding is unclear.[197]

Time-limited adverse effects of intra-articular injection include post-injection pain, swelling, and post-injection flare. Intra-articular injection of corticosteroid was not associated with loss of joint space at 1- and 2-year follow-up in a placebo-controlled randomized trial of patients with knee arthritis.[198] Similarly, in meta-analysis intra-articular corticosteroids for knee OA had no effect on joint space narrowing beyond that of control interventions.[188]

Evidence suggests that recurrent intra-articular corticosteroid injections often provide inferior (or nonsuperior) symptom relief compared with other injectables (including placebo) at 3 months and beyond in patients with OA.[199]

Intra-articular viscosupplementation

Guidelines do not recommend intra-articular hyaluronic acid injections for the management of OA.[7] [73]

Despite this recommendation, it is commonly used for the management of symptomatic knee arthritis; studies variously report modest or no benefit.[200] [201] [202]

One literature review concludes that intra-articular hyaluronic acid should be considered as a treatment for patients with OA, tailored by disease stage and patient phenotype, despite recommendations to the contrary from international guidelines.[203]

One meta-analysis found that intra-articular viscosupplementation with hyaluronan or hylan derivatives is effective in the management of OA of the knee; improvement from baseline during the 5- to 13-week post-injection period was 28% to 54% for pain and 9% to 32% for function.[202] The analyses suggested that different hyaluronan/hylan products exert differential therapeutic effects, and that response is time dependent.[202]

Analyzing data only from placebo-controlled trials with low risk of bias, one meta-analysis indicated that intra-articular hyaluronic acid provides a modest, but real, benefit for patients with OA of the knee (pain intensity standardized mean difference [SMD] -0.21, 95% CI -0.32 to -0.10; function at 3 months SMD -0.12, 95% CI -0.22 to -0.02).[204]

However, in subsequent meta-analyses, intra-articular injection of hyaluronic acid was not associated with a clinically important difference in pain for patients with OA of the knee compared with placebo, but may increase the risk of serious adverse effects.[200] [205]

Surgery

Patients with OA pain that persists despite multiple treatment modalities and which substantially impacts their quality of life should be referred and considered for joint placement surgery.

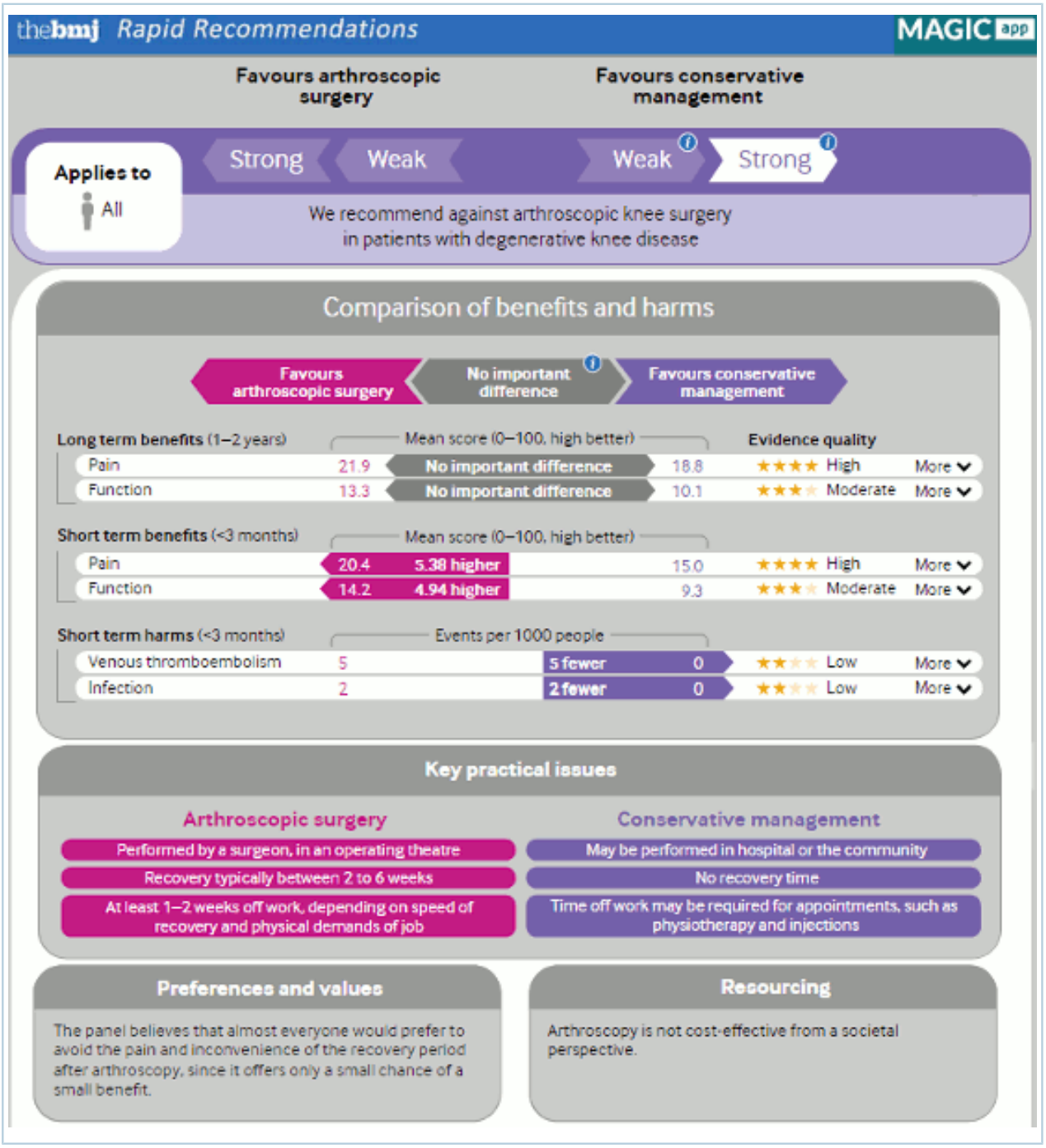
Total knee replacement followed by nonsurgical treatment resulted in significantly greater pain relief and functional improvement after 12 months than nonsurgical treatment alone (Knee Injury and Osteoarthritis Outcome Score [KOOS4] 32.5 vs. 16.0; adjusted mean difference 15.8, 95% CI 10.0 to 21.5) in an RCT of patients with moderate-to-severe knee OA who were eligible for unilateral total knee replacement.[206] Total knee replacement was associated with more serious adverse events.[206]

Unipartmental (partial) knee arthroplasty has been demonstrated to provide pain relief and satisfactory activity level for patients ages 60 years or younger. The results of one meta-analysis reported that 96.5% of implants survived at 10-year follow-up.[207]

There is no role of partial meniscectomy for meniscal tear in knee OA based on an RCT.[208]

Arthroscopic surgery is not effective for knee OA.[33] [209] [210] Clinical guidelines do not recommend the use of arthroscopic surgery in knee OA.[7] [73]

[BMJ Rapid Recommendations: arthroscopic surgery for degenerative knee arthritis and meniscal tears] (http://www.bmj.com/content/357/bmj.j1982) [MAGICapp: recommendations, evidence summaries and consultation decision aids] (https://www.magicapp.org/app#/guideline/1844)



BMJ Rapid Recommendations: arthroscopic surgery for degenerative knee arthritis and meniscal tears

Siemieniuk RAC, et al. BMJ. 2017 May 10;357:j1982

In patients with primary glenohumeral OA with an intact rotator cuff, total shoulder arthroplasty significantly improved postoperative patient-reported outcome measures (PROMs) compared with hemiarthroplasty.[211]

Evidence suggests that denervation may be an effective treatment for OA of the hand, especially for proximal interphalangeal (PIP) and trapeziometacarpal (TMC) joints.[212] [213]

Arthroplasty, trapeziectomy, and arthrodesis are options for thumb OA.[214] One meta-analysis concluded that there remains uncertainty about which procedure offers the best functional outcome and safety profile to treat OA of the thumb, the results of the systematic review suggest trapeziectomy with ligament

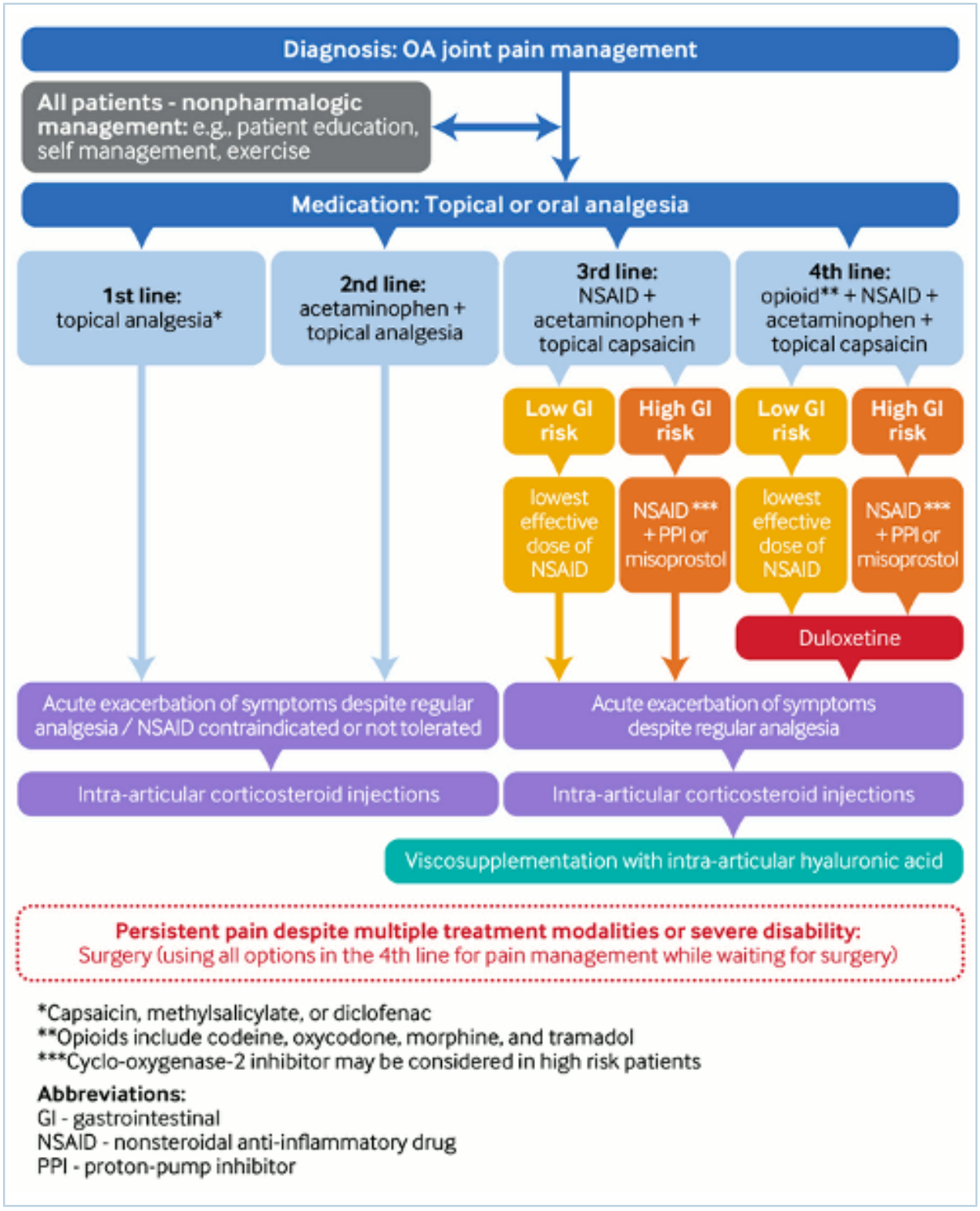
reconstruction and tendon interposition yielded good postoperative range of movement, while arthrodesis demonstrated a high rate of moderate-severe complications.[215]

Preoperative interventions and preparation

Presurgical obesity is associated with worse clinical outcomes following hip or knee arthroplasty in patients with OA; weight loss prior to elective surgery for knee or hip OA may improve postsurgical outcomes and reduce the risk of patient harm.[216]

Low- to moderate-quality evidence suggests that preoperative exercise reduces pain in patients with hip or knee OA prior to joint replacement, and may improve activity after hip replacement.[217]

Many orthopedists recommend delaying joint replacement surgery for at least 3 months following intra-articular corticosteroid injection to reduce the risk of postoperative peri-prosthetic infections.[218] [219]



Osteoarthritis treatment flowchart

Created by BMJ Knowledge Centre

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute		(summary)
joint pain: medical management		
	1st	topical analgesia
	plus	nonpharmacologic approaches
	adjunct	intra-articular corticosteroid injections
	2nd	acetaminophen + topical analgesia
	plus	nonpharmacologic approaches
	adjunct	intra-articular corticosteroid injections
	3rd	NSAID + acetaminophen + topical capsaicin
	plus	nonpharmacologic approaches
	adjunct	gastroprotection
	adjunct	intra-articular corticosteroid injections
	adjunct	viscosupplementation with intra-articular hyaluronic acid
	4th	opioid + NSAID + acetaminophen + topical capsaicin
	adjunct	duloxetine
	plus	nonpharmacologic approaches
	adjunct	gastroprotection
	adjunct	intra-articular corticosteroid injections
	adjunct	viscosupplementation with intra-articular hyaluronic acid

Ongoing		(summary)
persistent pain despite multiple treatment modalities or with severe disability		
	1st	**surgery**
	adjunct	**topical and oral analgesia**
	adjunct	**duloxetine**
	adjunct	**gastroprotection**
	adjunct	**viscosupplementation with intra-articular hyaluronic acid**
	adjunct	**intra-articular corticosteroid injections**

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

joint pain: medical management

1st **topical analgesia**

Primary options

» capsaicin topical: (0.025 to 0.075%) apply to the affected area(s) three to four times daily when required

OR

» diclofenac topical: (1% gel) upper extremity joints: apply 2 g to the affected area(s) four times daily, maximum 8 g/joint/day up to 32 g/day total; (1% gel) lower extremity joints: apply 4 g to the affected area(s) four times daily, maximum 16 g/joint/day up to 32 g/day total; (1.5% solution) knee joints: apply 40 drops to each affected knee four times daily; (2% solution) knee joints: apply 40 mg (2 sprays) to each affected knee twice daily

OR

» diclofenac epolamine topical: (1.3% patch) apply one patch to the affected area twice daily

OR

» methylsalicylate topical: apply to the affected area(s) three to four times daily when required

» Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for patients with OA of the hand or knee, and can be considered for other affected joints.[7] [73] Other topical analgesics include capsaicin and methylsalicylate.[7] The ACR recommends topical capsaicin for patients with OA of the knee, but not for patients with OA of the hand.[7]

» Topical NSAIDs effectively relieve pain in adults with knee or hand OA within 2 weeks of daily application. The results of systematic reviews and meta-analyses report that topical NSAIDs are the most effective topical analgesic for pain relief for OA patients compared with oral NSAIDs, cyclo-oxygenase-2 [COX-2] inhibitors,

Acute

and opioids, and that diclofenac transdermal patches may be the most effective and safest topical NSAID for pain relief.[147] [148]

» Systematic reviews suggest that topical NSAIDs are relatively safe for the management of pain associated with OA.[149] [150] [151] [152] However, confirmation of the cardiovascular safety of topical NSAIDs requires further study.[149]

» One Cochrane review found that arnica gel may improve symptoms as effectively as a topical NSAID, but with a potentially worse adverse effect profile.[153] In the same review, capsicum-extract gel (capsaicinoids ≤0.05%) did not significantly improve pain or function compared with placebo.[153] However, results of a network meta-analysis suggest that topical capsaicin may be as effective as topical NSAIDs at reducing pain in patients with OA.[154]

plus **nonpharmacologic approaches**

Treatment recommended for ALL patients in selected patient group

» All patients should start treatment for OA with nonpharmacologic approaches.[135] [137] These include patient education, self-management, exercise programs (with reassurance that exercise, e.g., resistance training, tai chi, yoga, and water-based exercise, is not harmful to the joints), and they may also benefit from cognitive behavioral therapy in combination with physical therapy.[7] [73] [92] [93] [94] [96] [95] [97] [98]

» Exercise is recommended for all patients with OA, though there is considerably more evidence for the use of exercise in the treatment of knee and hip OA than for hand OA.[7] Balance exercises or tai chi are recommended for patients with OA of the knee and/or hip, and yoga is suggested as an alternative for patients with OA of the knee.[7]

» Weight loss is recommended for patients with OA of the knee and/or hip who are overweight.[7]

» Two Cochrane reviews conclude that exercise programs have a small to moderate beneficial effect on pain and function for patients with knee and hip OA.[103] [104] However, the benefit from physical therapy on hip OA is unclear.[105] One meta-analysis showed a modest effect on pain, though no improvement in self-reported function for exercise in patients with OA of the hip.[106] Further meta-analyses reported that

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14% more patients with hip OA responded to exercise therapy compared with placebo, and that hip abductor muscle strengthening exercises as significantly improved knee pain and other functional outcomes for patients with knee OA.[107] [108]

» Evidence from randomized controlled trials (RCTs) suggests that quadricep strengthening exercises and weight loss are effective in controlling the pain of knee OA.[109] [110] Subsequent meta-analyses demonstrate that hip strengthening exercises are an effective rehabilitation treatment for patients with OA of the knee.[111] [108] [112]

» Exercise can improve quality of life by reducing pain and increasing function for patients with OA, especially those who are overweight or obese.[113] A combination of diet and exercise has been shown to reduce pain and increase muscle mass in patients with OA, and that diet alone or in combination with exercise can improve function.[114] [115]

» The American College of Rheumatology (ACR) recommends cane use for patients with knee and/or hip OA in one or more joints, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; tibiofemoral knee braces for patients with OA of the knee, in one or both knees, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; hand orthoses for patients with OA of the first carpometacarpal (CMC) joint, or in joints apart from the first CMC joint of the hand; patellofemoral braces for patients with patellofemoral knee OA.[7]

» The ACR does not recommend modified shoes, or lateral and medial wedged insoles for patients with knee and/or hip OA.[7]

» The National Institute of Health and Care Excellence (NICE) in the UK recommends walking aids, such as canes, for people with lower limb OA; insoles, braces, tape, splints, or supports are not routinely recommended to patients with OA, unless there is joint instability or abnormal biomechanical loading AND therapeutic exercise is ineffective or unsuitable without the addition of an aid or device AND the addition of an aid or device is likely to improve movement.[73]

» One network meta-analysis reported that lateral wedge insoles in combination with knee

Acute

bracing reduce peak knee adduction moment in patients with tibiofemoral OA, while gait training influenced both knee adduction angular impulse and knee adduction moment, so it is recommended for reducing biomechanical risk factors.[116]

» There is conflicting evidence for the use of orthoses and/or braces for medial knee OA. There is evidence to suggest that lateral wedge insoles do not reduce pain or improve functionality in patients with medial knee OA, but conversely that lateral wedge insoles with arch support significantly improved pain and physical function in patients with knee OA.[117] [118] [119]

» Knee valgus bracing has been demonstrated as an effective intervention to improve the quality of life and reduce pain during daily activities for patients with medial knee OA.[120] However, evidence suggests that valgus knee bracing may only be effective in the short term.[121] [122] [123] [124]

» Combining both a knee brace and lateral wedge insoles has been shown to improve pain and function in patients with medial knee OA.[125]

» Unloader shoes do not appear to confer benefit in medial knee OA.[126]

» Patellar bracing or taping for patellofemoral pain can be considered. One RCT suggests the use of a knee brace may be helpful in reducing pain and bone marrow lesions in patellofemoral OA.[127] Results of one meta-analysis reported that a multimodal physical therapy intervention that included taping significantly reduced pain in the short term for patients with patellofemoral OA.[128]

» One meta-analysis found that splinting in patients with thumb and CMC joint OA reduced pain and improved function in the medium term (3-12 months), but not the short term.[129]

» Glucosamine and chondroitin sulfate are not recommended for the management of patients with OA; decisions regarding the use of these agents should be discussed with patients.[7] [73] Despite this recommendation, glucosamine and chondroitin sulfate are commonly used by people with OA. Modest efficacy and low risk may explain the popularity of these supplements among patients.

Acute

» Both agents have been associated with modest pain reduction in patients with knee OA and are considered safe.[130] [131] [132] [133] [134] [135] However, many trials are of low quality.[133]

» Results of studies on the efficacy of glucosamine or chondroitin varies. One meta-analysis found that glucosamine or chondroitin sulfate reduced pain in patients with knee OA individually, but found no additional benefit associated with combination treatment, whereas subsequent evidence suggests that combination treatment is effective for the treatment of knee OA compared with other placebo.[132] The inconsistencies between the labeling and actual contents of many dietary supplements should be considered; prescription-grade preparations should be sought.[135] [137]

» The ACR recommends acupuncture for patients with knee, hip, and/or hand OA.[7] However, NICE in the UK does not recommend acupuncture for the management of OA.[73] [136]

» TENS is not recommended to treat patients with OA due to insufficient evidence of benefit.[7] [73]

» Evidence suggests that acupuncture may benefit patients with knee OA.[138] [139] [140] [220] However, evidence of short-term benefit is based on low- to very-low-quality evidence, and may not be clinically important, when compared with control treatments.[141] One Cochrane review concluded that acupuncture does not appear to reduce pain or improve function relative to sham acupuncture in people with hip OA.[142] However, subsequent meta-analysis suggest that acupuncture is reduced pain and improves function in patients with OA of the knee, and may be used as an adjunctive treatment.[143] [144]

» The results of a Cochrane review reported that there is a lack of evidence to support the use of TENS to treat patients with OA of the knee, but there is also evidence to suggest that acupuncture significantly reduced pain, and improved walking ability in patients with OA of the knee.[145] [146]

adjunct **intra-articular corticosteroid injections**

Treatment recommended for SOME patients in selected patient group

Primary options

Acute

» methylprednisolone acetate: 4-80 mg intra-articularly as a single dose

OR

» triamcinolone acetonide: 2.5 to 40 mg intra-articularly as a single dose

» Intra-articular corticosteroid injections are useful, particularly in the knee, for acute exacerbations of OA or when nonsteroidal anti-inflammatory drugs are contraindicated or not tolerated, and can be used in addition to the nonpharmacologic therapies and analgesia.

» The ACR recommends intra-articular corticosteroid injections for patients with knee and/or hip OA, but only conditionally recommends this treatment for patients with OA of the hand.[7] In the UK, intra-articular corticosteroid injections are only recommended when other pharmacologic treatments are ineffective or unsuitable, or to support therapeutic exercise.[73]

» Trials comparing intra-articular corticosteroid injections with sham or nonintervention controls are often small and of low methodological quality.[188] [189]

» Intra-articular corticosteroid injections reduced pain and improved function in patients with OA of the knee at 6 weeks compared with placebo.[190] However, it appears that intra-articular corticosteroid injections do not reduce joint pain for patients with hand or temporomandibular OA compared with placebo.[191] [192]

» It is unclear how long the benefit of intra-articular corticosteroids lasts in patients with OA. Results from meta-analyses vary, with reports of continued efficacy from 1 to 12 weeks in patients with OA of the hip.[188] [189] [193] [194] However, intra-articular corticosteroid may increase the risk of rapidly destructive hip disease, especially at higher doses.[195]

» Meta-analysis of individual patient data suggests that patients with severe knee pain at baseline may derive greater short-term benefit (reduction in pain up to 4 weeks) from intra-articular corticosteroid injection than patients with less severe pain.[196]

» Intra-articular triamcinolone every 12 weeks for 2 years failed to significantly reduce OA knee pain compared with intra-articular saline

Acute

(-1.2 vs. -1.9; between-group difference -0.6, 95% CI -1.6 to 0.3) in a double-blind RCT.[197] Triamcinolone was associated with significantly greater cartilage volume loss than saline (mean change in index compartment cartilage thickness of -0.21 mm vs. -0.10 mm; between-group difference -0.11 mm, 95% CI -0.20 to -0.03), but the clinical significance of this finding is unclear.[197]

» Time-limited adverse effects of intra-articular injection include post-injection pain, swelling, and post-injection flare. Intra-articular injection of corticosteroid was not associated with loss of joint space at 1- and 2-year follow-up in a placebo-controlled randomized trial of patients with knee arthritis.[198] Similarly, in meta-analysis intra-articular corticosteroids for knee OA had no effect on joint space narrowing beyond that of control interventions.[188]

» Evidence suggests that recurrent intra-articular corticosteroid injections often provide inferior (or nonsuperior) symptom relief compared with other injectables (including placebo) at 3 months and beyond in patients with OA.[199]

» Dose depends upon size of joint and degree of inflammation present.

»

2nd **acetaminophen + topical analgesia**

Primary options

» acetaminophen: 325-1000 mg orally every 6 hours when required, maximum 4000 mg/day

--AND--

» capsaicin topical: (0.025 to 0.075%) apply to the affected area(s) three to four times daily when required

-or-

» diclofenac topical: (1% gel) upper extremity joints: apply 2 g to the affected area(s) four times daily, maximum 8 g/joint/day up to 32 g/day total; (1% gel) lower extremity joints: apply 4 g to the affected area(s) four times daily, maximum 16 g/joint/day up to 32 g/day total; (1.5% solution) knee joints: apply 40 drops to each affected knee four times daily; (2% solution) knee joints: apply 40 mg (2 sprays) to each affected knee twice daily

-or-

» diclofenac epolamine topical: (1.3% patch) apply one patch to the affected area twice daily

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Acute

-or-

» methylsalicylate topical: apply to the affected area(s) three to four times daily when required

» While topical analgesics should be used as first-line therapy (e.g., capsaicin, nonsteroidal anti-inflammatory drugs [NSAIDs] such as diclofenac, methylsalicylate), acetaminophen could be added if topical therapies alone do not control symptoms.

» Studies have demonstrated that acetaminophen has a small to modest benefit for patients with OA of the hip or knee, and is statistically inferior to all other drug categories for the management of OA pain (oral NSAIDs, topical NSAIDs, COX-2 inhibitors, and opioids).[155] [147] [156]

» As such acetaminophen alone may not have a role in the treatment of hip or knee OA, irrespective of the dose used, but may be added for rescue analgesia, or if local therapies alone do not control symptoms.[137] [157]

» With this evidence of limited efficacy, and with more data available regarding the potential adverse reactions of acetaminophen, careful consideration should taken about the use of acetaminophen for the treatment of OA.[155] [157] [158]

»

plus **nonpharmacologic approaches**

Treatment recommended for ALL patients in selected patient group

» All patients should start treatment for OA with nonpharmacologic approaches.[135] [137] These include patient education, self-management, exercise programs (with reassurance that exercise, e.g., resistance training, tai chi, yoga, and water-based exercise, is not harmful to the joints), and they may also benefit from cognitive behavioral therapy in combination with physical therapy.[7] [73] [92] [93] [94] [96] [95] [97] [98]

» Exercise is recommended for all patients with OA, though there is considerably more evidence for the use of exercise in the treatment of knee and hip OA than for hand OA.[7] Balance exercises or tai chi are recommended for patients with OA of the knee and/or hip, and yoga is suggested as an alternative for patients with OA of the knee.[7]

Acute

» Weight loss is recommended for patients with OA of the knee and/or hip who are overweight.[7]

» Two Cochrane reviews conclude that exercise programs have a small to moderate beneficial effect on pain and function for patients with knee and hip OA.[103] [104] However, the benefit from physical therapy on hip OA is unclear.[105] One meta-analysis showed a modest effect on pain, though no improvement in self-reported function for exercise in patients with OA of the hip.[106] Further meta-analyses reported that 14% more patients with hip OA responded to exercise therapy compared with placebo, and that hip abductor muscle strengthening exercises as significantly improved knee pain and other functional outcomes for patients with knee OA.[107] [108]

» Evidence from randomized controlled trials (RCTs) suggests that quadricep strengthening exercises and weight loss are effective in controlling the pain of knee OA.[109] [110] Subsequent meta-analyses demonstrate that hip strengthening exercises are an effective rehabilitation treatment for patients with OA of the knee.[111] [108] [112]

» Exercise can improve quality of life by reducing pain and increasing function for patients with OA, especially those who are overweight or obese.[113] A combination of diet and exercise has been shown to reduce pain and increase muscle mass in patients with OA, and that diet alone or in combination with exercise can improve function.[114] [115]

» The American College of Rheumatology (ACR) recommends cane use for patients with knee and/or hip OA in one or more joints, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; tibiofemoral knee braces for patients with OA of the knee, in one or both knees, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; hand orthoses for patients with OA of the first carpometacarpal (CMC) joint, or in joints apart from the first CMC joint of the hand; patellofemoral braces for patients with patellofemoral knee OA.[7]

» The ACR does not recommend modified shoes, or lateral and medial wedged insoles for patients with knee and/or hip OA.[7]

» The National Institute of Health and Care Excellence (NICE) in the UK recommends

Acute

walking aids, such as canes, for people with lower limb OA; insoles, braces, tape, splints, or supports are not routinely recommended to patients with OA, unless there is joint instability or abnormal biomechanical loading AND therapeutic exercise is ineffective or unsuitable without the addition of an aid or device AND the addition of an aid or device is likely to improve movement.[73]

» One network meta-analysis reported that lateral wedge insoles in combination with knee bracing reduce peak knee adduction moment in patients with tibiofemoral OA, while gait training influenced both knee adduction angular impulse and knee adduction moment, so it is recommended for reducing biomechanical risk factors.[116]

» There is conflicting evidence for the use of orthoses and/or braces for medial knee OA. There is evidence to suggest that lateral wedge insoles do not reduce pain or improve functionality in patients with medial knee OA, but conversely that lateral wedge insoles with arch support significantly improved pain and physical function in patients with knee OA.[117] [118] [119]

» Knee valgus bracing has been demonstrated as an effective intervention to improve the quality of life and reduce pain during daily activities for patients with medial knee OA.[120] However, evidence suggests that valgus knee bracing may only be effective in the short term.[121] [122] [123] [124]

» Combining both a knee brace and lateral wedge insoles has been shown to improve pain and function in patients with medial knee OA.[125]

» Unloader shoes do not appear to confer benefit in medial knee OA.[126]

» Patellar bracing or taping for patellofemoral pain can be considered. One RCT suggests the use of a knee brace may be helpful in reducing pain and bone marrow lesions in patellofemoral OA.[127] Results of one meta-analysis reported that a multimodal physical therapy intervention that included taping significantly reduced pain in the short term for patients with patellofemoral OA.[128]

» One meta-analysis found that splinting in patients with thumb and CMC joint OA reduced

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pain and improved function in the medium term (3-12 months), but not the short term.[129]

» Glucosamine and chondroitin sulfate are not recommended for the management of patients with OA; decisions regarding the use of these agents should be discussed with patients.[7] [73] Despite this recommendation, glucosamine and chondroitin sulfate are commonly used by people with OA. Modest efficacy and low risk may explain the popularity of these supplements among patients.

» Both agents have been associated with modest pain reduction in patients with knee OA and are considered safe.[130] [131] [132] [133] [134] [135] However, many trials are of low quality.[133]

» Results of studies on the efficacy of glucosamine or chondroitin varies. One meta-analysis found that glucosamine or chondroitin sulfate reduced pain in patients with knee OA individually, but found no additional benefit associated with combination treatment, whereas subsequent evidence suggests that combination treatment is effective for the treatment of knee OA compared with other placebo.[132] The inconsistencies between the labeling and actual contents of many dietary supplements should be considered; prescription-grade preparations should be sought.[135] [137]

» The ACR recommends acupuncture for patients with knee, hip, and/or hand OA.[7] However, NICE in the UK does not recommend acupuncture for the management of OA.[137] [136]

» TENS is not recommended to treat patients with OA due to insufficient evidence of benefit.[7] [73]

» Evidence suggests that acupuncture may benefit patients with knee OA.[138] [139] [140] [220] However, evidence of short-term benefit is based on low- to very-low-quality evidence, and may not be clinically important, when compared with control treatments.[141] One Cochrane review concluded that acupuncture does not appear to reduce pain or improve function relative to sham acupuncture in people with hip OA.[142] However, subsequent meta-analysis suggest that acupuncture is reduced pain and improves function in patients with OA of the knee, and may be used as an adjunctive treatment.[143] [144]

Acute

» The results of a Cochrane review reported that there is a lack of evidence to support the use of TENS to treat patients with OA of the knee, but there is also evidence to suggest that acupuncture significantly reduced pain, and improved walking ability in patients with OA of the knee.[145] [146]

adjunct **intra-articular corticosteroid injections**

Treatment recommended for SOME patients in selected patient group

Primary options

» methylprednisolone acetate: 4-80 mg intra-articularly as a single dose

OR

» triamcinolone acetonide: 2.5 to 40 mg intra-articularly as a single dose

» Intra-articular corticosteroid injections are useful, particularly in the knee, for acute exacerbations of OA or when nonsteroidal anti-inflammatory drugs are contraindicated or not tolerated, and can be used in addition to the nonpharmacologic therapies and analgesia.

» The ACR recommends intra-articular corticosteroid injections for patients with knee and/or hip OA, but only conditionally recommends this treatment for patients with OA of the hand.[7] In the UK, intra-articular corticosteroid injections are only recommended when other pharmacologic treatments are ineffective or unsuitable, or to support therapeutic exercise.[73]

» Trials comparing intra-articular corticosteroid injections with sham or nonintervention controls are often small and of low methodological quality.[188] [189]

» Intra-articular corticosteroid injections reduced pain and improved function in patients with OA of the knee at 6 weeks compared with placebo.[190] However, it appears that intra-articular corticosteroid injections do not reduce joint pain for patients with hand or temporomandibular OA compared with placebo.[191] [192]

» It is unclear how long the benefit of intra-articular corticosteroids lasts in patients with OA. Results from meta-analyses vary, with reports of continued efficacy from 1 to 12 weeks in patients with OA of the hip.[188] [189] [193]

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[194] However, intra-articular corticosteroid may increase the risk of rapidly destructive hip disease, especially at higher doses.[195]

» Meta-analysis of individual patient data suggests that patients with severe knee pain at baseline may derive greater short-term benefit (reduction in pain up to 4 weeks) from intra-articular corticosteroid injection than patients with less severe pain.[196]

» Intra-articular triamcinolone every 12 weeks for 2 years failed to significantly reduce OA knee pain compared with intra-articular saline (-1.2 vs. -1.9; between-group difference -0.6, 95% CI -1.6 to 0.3) in a double-blind RCT.[197] Triamcinolone was associated with significantly greater cartilage volume loss than saline (mean change in index compartment cartilage thickness of -0.21 mm vs. -0.10 mm; between-group difference -0.11 mm, 95% CI -0.20 to -0.03), but the clinical significance of this finding is unclear.[197]

» Time-limited adverse effects of intra-articular injection include post-injection pain, swelling, and post-injection flare. Intra-articular injection of corticosteroid was not associated with loss of joint space at 1- and 2-year follow-up in a placebo-controlled randomized trial of patients with knee arthritis.[198] Similarly, in meta-analysis intra-articular corticosteroids for knee OA had no effect on joint space narrowing beyond that of control interventions.[188]

» Evidence suggests that recurrent intra-articular corticosteroid injections often provide inferior (or nonsuperior) symptom relief compared with other injectables (including placebo) at 3 months and beyond in patients with OA.[199]

» Dose depends upon size of joint and degree of inflammation present.

»

3rd **NSAID + acetaminophen + topical capsaicin**

Primary options

» acetaminophen: 325-1000 mg orally every 6 hours when required, maximum 4000 mg/day

--AND--

» capsaicin topical: (0.025 to 0.075%) apply to the affected area(s) three to four times daily when required

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--AND--

» naproxen: 250-500 mg orally twice daily when required, maximum 1250 mg/day
-or-
» ibuprofen: 400-800 mg orally every 6-8 hours when required, maximum 3200 mg/day
-or-
» diclofenac potassium: 50 mg orally (immediate-release) twice or three times daily when required
-or-
» diclofenac sodium: 100 mg orally (extended-release) once daily when required

Secondary options

» acetaminophen: 325-1000 mg orally every 6 hours when required, maximum 4000 mg/day

--AND--

» capsaicin topical: (0.025 to 0.075%) apply to the affected area(s) three to four times daily when required

--AND--

» celecoxib: 200 mg orally once daily; or 100 mg orally twice daily
-or-
» meloxicam: 7.5 to 15 mg orally once daily

» Oral nonsteroidal anti-inflammatory drugs (NSAIDs) can be added to acetaminophen and topical analgesics (e.g., capsaicin), to reduce pain and improve function.

» Oral NSAIDs are more effective than acetaminophen for the management of OA pain; however, they are associated with gastrointestinal (GI) and renal toxicity.[147] [159] [160]

» Diclofenac or etoricoxib (not available in the US) may be the most effective NSAID for the treatment of pain in knee and hip OA, but potential benefit must be weighed against adverse effects, but may not be appropriate for patients with comorbidities or for long-term use. [148] [157]

» Selective COX-2 inhibitors may be used as an alternative to nonselective NSAIDs. They are associated with reduced risk of GI adverse effects compared with nonselective NSAIDs, but similar renal toxicity.[165] [166] COX-2 inhibitors are effective for the management of pain associated with knee and hip OA, and may have a role in patients at increased risk for GI adverse

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effects.[137] [157] However, COX-2 inhibitors do not confer an advantage with respect to GI symptoms when compared with placebo, or NSAID and proton-pump inhibitor (PPI) used concomitantly for gastroprotection.[73] [167] [168] The incidence of upper GI adverse effects did not differ between patients with knee OA who were treated with fixed-dose combination naproxen and esomeprazole or with celecoxib; the former reported significantly more heartburn-free days than those on celecoxib.[169]

» Evidence suggests that NSAID use substantially contributes to the association between OA and cardiovascular disease (CVD), with increased risk reaching significance as early as 4 weeks into treatment.[170] [171] Several patient characteristics may be associated with increased CVD risk when taking an NSAID, such as age >80 years, history of CVD, rheumatoid arthritis, chronic obstructive pulmonary disease, renal disease, and hypertension.[172] One meta-analysis suggested that diclofenac and ibuprofen were associated with increased cardiovascular risk while naproxen and celecoxib were not.[173] However, similar incident rates of cardiovascular events have been reported for ibuprofen, celecoxib, and naproxen.[174]

» GI and cardiovascular safety profiles of individual oral NSAIDs differ, and careful patient selection is required to maximize the risk:benefit ratio.[137] The lowest effective dose of NSAID should be used to minimize adverse effects.

»

plus **nonpharmacologic approaches**

Treatment recommended for ALL patients in selected patient group

» All patients should start treatment for OA with nonpharmacologic approaches.[135] [137] These include patient education, self-management, exercise programs (with reassurance that exercise, e.g., resistance training, tai chi, yoga, and water-based exercise, is not harmful to the joints), and they may also benefit from cognitive behavioral therapy in combination with physical therapy.[7] [73] [92] [93] [94] [96] [95] [97] [98]

» Exercise is recommended for all patients with OA, though there is considerably more evidence for the use of exercise in the treatment of knee and hip OA than for hand OA.[7] Balance exercises or tai chi are recommended for patients with OA of the knee and/or hip, and

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yoga is suggested as an alternative for patients with OA of the knee.[7]

» Weight loss is recommended for patients with OA of the knee and/or hip who are overweight.[7]

» Two Cochrane reviews conclude that exercise programs have a small to moderate beneficial effect on pain and function for patients with knee and hip OA.[103] [104] However, the benefit from physical therapy on hip OA is unclear.[105] One meta-analysis showed a modest effect on pain, though no improvement in self-reported function for exercise in patients with OA of the hip.[106] Further meta-analyses reported that 14% more patients with hip OA responded to exercise therapy compared with placebo, and that hip abductor muscle strengthening exercises as significantly improved knee pain and other functional outcomes for patients with knee OA.[107] [108]

» Evidence from randomized controlled trials (RCTs) suggests that quadricep strengthening exercises and weight loss are effective in controlling the pain of knee OA.[109] [110] Subsequent meta-analyses demonstrate that hip strengthening exercises are an effective rehabilitation treatment for patients with OA of the knee.[111] [108] [112]

» Exercise can improve quality of life by reducing pain and increasing function for patients with OA, especially those who are overweight or obese.[113] A combination of diet and exercise has been shown to reduce pain and increase muscle mass in patients with OA, and that diet alone or in combination with exercise can improve function.[114] [115]

» The American College of Rheumatology (ACR) recommends cane use for patients with knee and/or hip OA in one or more joints, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; tibiofemoral knee braces for patients with OA of the knee, in one or both knees, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; hand orthoses for patients with OA of the first carpometacarpal (CMC) joint, or in joints apart from the first CMC joint of the hand; patellofemoral braces for patients with patellofemoral knee OA.[7]

» The ACR does not recommend modified shoes, or lateral and medial wedged insoles for patients with knee and/or hip OA.[7]

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» The National Institute of Health and Care Excellence (NICE) in the UK recommends walking aids, such as canes, for people with lower limb OA; insoles, braces, tape, splints, or supports are not routinely recommended to patients with OA, unless there is joint instability or abnormal biomechanical loading AND therapeutic exercise is ineffective or unsuitable without the addition of an aid or device AND the addition of an aid or device is likely to improve movement.[73]

» One network meta-analysis reported that lateral wedge insoles in combination with knee bracing reduce peak knee adduction moment in patients with tibiofemoral OA, while gait training influenced both knee adduction angular impulse and knee adduction moment, so it is recommended for reducing biomechanical risk factors.[116]

» There is conflicting evidence for the use of orthoses and/or braces for medial knee OA. There is evidence to suggest that lateral wedge insoles do not reduce pain or improve functionality in patients with medial knee OA, but conversely that lateral wedge insoles with arch support significantly improved pain and physical function in patients with knee OA.[117] [118] [119]

» Knee valgus bracing has been demonstrated as an effective intervention to improve the quality of life and reduce pain during daily activities for patients with medial knee OA.[120] However, evidence suggests that valgus knee bracing may only be effective in the short term.[121] [122] [123] [124]

» Combining both a knee brace and lateral wedge insoles has been shown to improve pain and function in patients with medial knee OA.[125]

» Unloader shoes do not appear to confer benefit in medial knee OA.[126]

» Patellar bracing or taping for patellofemoral pain can be considered. One RCT suggests the use of a knee brace may be helpful in reducing pain and bone marrow lesions in patellofemoral OA.[127] Results of one meta-analysis reported that a multimodal physical therapy intervention that included taping significantly reduced pain in the short term for patients with patellofemoral OA.[128]

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» One meta-analysis found that splinting in patients with thumb and CMC joint OA reduced pain and improved function in the medium term (3-12 months), but not the short term.[129]

» Glucosamine and chondroitin sulfate are not recommended for the management of patients with OA; decisions regarding the use of these agents should be discussed with patients.[7] [73] Despite this recommendation, glucosamine and chondroitin sulfate are commonly used by people with OA. Modest efficacy and low risk may explain the popularity of these supplements among patients.

» Both agents have been associated with modest pain reduction in patients with knee OA and are considered safe.[130] [131] [132] [133] [134] [135] However, many trials are of low quality.[133]

» Results of studies on the efficacy of glucosamine or chondroitin varies. One meta-analysis found that glucosamine or chondroitin sulfate reduced pain in patients with knee OA individually, but found no additional benefit associated with combination treatment, whereas subsequent evidence suggests that combination treatment is effective for the treatment of knee OA compared with other placebo.[132] The inconsistencies between the labeling and actual contents of many dietary supplements should be considered; prescription-grade preparations should be sought.[135] [137]

» The ACR recommends acupuncture for patients with knee, hip, and/or hand OA.[7] However, NICE in the UK does not recommend acupuncture for the management of OA.[73][136]

» TENS is not recommended to treat patients with OA due to insufficient evidence of benefit.[7] [73]

» Evidence suggests that acupuncture may benefit patients with knee OA.[138] [139] [140] [220] However, evidence of short-term benefit is based on low- to very-low-quality evidence, and may not be clinically important, when compared with control treatments.[141] One Cochrane review concluded that acupuncture does not appear to reduce pain or improve function relative to sham acupuncture in people with hip OA.[142] However, subsequent meta-analysis suggest that acupuncture is reduced pain and improves function in patients with OA of the knee, and may be used as an adjunctive treatment.[143] [144]

Acute

» The results of a Cochrane review reported that there is a lack of evidence to support the use of TENS to treat patients with OA of the knee, but there is also evidence to suggest that acupuncture significantly reduced pain, and improved walking ability in patients with OA of the knee.[145] [146]

adjunct **gastroprotection**

Treatment recommended for SOME patients in selected patient group

Primary options

» omeprazole: 20 mg orally once daily

OR

» esomeprazole: 20 mg orally once daily

OR

» pantoprazole: 40 mg orally once daily

OR

» rabeprazole: 20 mg orally once daily

Secondary options

» misoprostol: 100-200 micrograms orally four times daily

» Gastroprotection should be offered to patients on long-term NSAID therapy, especially those at risk of GI bleeding.[73] Evidence suggests that proton-pump inhibitors (PPIs) provide better protection against NSAID-induced peptic ulcer disease and gastritis compared with H2 antagonists.[161] Misoprostol is a prostaglandin E1 analog and is another option for gastroprotection, but diarrhea is a common adverse effect, and the drug is less well tolerated than PPIs.[162] [163] [164]

adjunct **intra-articular corticosteroid injections**

Treatment recommended for SOME patients in selected patient group

Primary options

» methylprednisolone acetate: 4-80 mg intra-articularly as a single dose

OR

Acute

» triamcinolone acetonide: 2.5 to 40 mg intra-articularly as a single dose

» Intra-articular corticosteroid injections are useful, particularly in the knee, for acute exacerbations of OA or when nonsteroidal anti-inflammatory drugs are contraindicated or not tolerated, and can be used in addition to the nonpharmacologic therapies and analgesia.

» The ACR recommends intra-articular corticosteroid injections for patients with knee and/or hip OA, but only conditionally recommends this treatment for patients with OA of the hand.[7] In the UK, intra-articular corticosteroid injections are only recommended when other pharmacologic treatments are ineffective or unsuitable, or to support therapeutic exercise.[73]

» Trials comparing intra-articular corticosteroid injections with sham or nonintervention controls are often small and of low methodological quality.[188] [189]

» Intra-articular corticosteroid injections reduced pain and improved function in patients with OA of the knee at 6 weeks compared with placebo.[190] However, it appears that intra-articular corticosteroid injections do not reduce joint pain for patients with hand or temporomandibular OA compared with placebo.[191] [192]

» It is unclear how long the benefit of intra-articular corticosteroids lasts in patients with OA. Results from meta-analyses vary, with reports of continued efficacy from 1 to 12 weeks in patients with OA of the hip.[188] [189] [193] [194] However, intra-articular corticosteroid may increase the risk of rapidly destructive hip disease, especially at higher doses.[195]

» Meta-analysis of individual patient data suggests that patients with severe knee pain at baseline may derive greater short-term benefit (reduction in pain up to 4 weeks) from intra-articular corticosteroid injection than patients with less severe pain.[196]

» Intra-articular triamcinolone every 12 weeks for 2 years failed to significantly reduce OA knee pain compared with intra-articular saline (-1.2 vs. -1.9; between-group difference -0.6, 95% CI -1.6 to 0.3) in a double-blind RCT.[197] Triamcinolone was associated with significantly greater cartilage volume loss than saline (mean change in index compartment cartilage thickness

Acute

of -0.21 mm vs. -0.10 mm; between-group difference -0.11 mm, 95% CI -0.20 to -0.03), but the clinical significance of this finding is unclear.[197]

» Time-limited adverse effects of intra-articular injection include post-injection pain, swelling, and post-injection flare. Intra-articular injection of corticosteroid was not associated with loss of joint space at 1- and 2-year follow-up in a placebo-controlled randomized trial of patients with knee arthritis.[198] Similarly, in meta-analysis intra-articular corticosteroids for knee OA had no effect on joint space narrowing beyond that of control interventions.[188]

» Evidence suggests that recurrent intra-articular corticosteroid injections often provide inferior (or nonsuperior) symptom relief compared with other injectables (including placebo) at 3 months and beyond in patients with OA.[199]

» Dose depends upon size of joint and degree of inflammation present.

»

adjunct **viscosupplementation with intra-articular hyaluronic acid**

Treatment recommended for SOME patients in selected patient group

Primary options

» sodium hyaluronate: 20 mg (2 mL) intra-articularly once weekly for 3-5 weeks

OR

» hylan GF 20: 16 mg (2 mL) intra-articularly once weekly for 3 weeks, total of 3 injections; 6 mL intra-articularly as single injection

» Guidelines do not recommend intra-articular hyaluronic acid injections for the management of OA.[7] [73]

» Despite this recommendation, it is commonly used for the management of symptomatic knee arthritis; studies variously report modest or no benefit.[200] [201] [202]

» One literature review concludes that intra-articular hyaluronic acid should be considered as a treatment for patients with OA, tailored by disease stage and patient phenotype, despite recommendations to the contrary from international guidelines.[203]

Acute

» One meta-analysis found that intra-articular viscosupplementation with hyaluronan or hylan derivatives is effective in the management of OA of the knee; improvement from baseline during the 5- to 13-week post-injection period was 28% to 54% for pain and 9% to 32% for function.[202] The analyses suggested that different hyaluronan/hylan products exert differential therapeutic effects, and that response is time dependent.[202]

» Analyzing data only from placebo-controlled trials with low risk of bias, one meta-analysis indicated that intra-articular hyaluronic acid provides a modest, but real, benefit for patients with OA of the knee (pain intensity standardized mean difference [SMD] -0.21, 95% CI -0.32 to -0.10; function at 3 months SMD -0.12, 95% CI -0.22 to -0.02).[204]

» However, in subsequent meta-analyses intra-articular injection of hyaluronic acid was not associated with a clinically important difference in pain for patients with OA of the knee compared with placebo, but it may increase the risk of serious adverse effects.[200] [205]

»

4th **opioid + NSAID + acetaminophen + topical capsaicin**

Primary options

» acetaminophen: 325-1000 mg orally every 6 hours when required, maximum 4000 mg/day

--AND--

» capsaicin topical: (0.025 to 0.075%) apply to the affected area(s) three to four times daily when required

--AND--

» naproxen: 250-500 mg orally twice daily when required, maximum 1250 mg/day
-or-
» ibuprofen: 400-800 mg orally every 6-8 hours when required, maximum 3200 mg/day
-or-
» diclofenac potassium: 50 mg orally (immediate-release) twice or three times daily when required
-or-
» diclofenac sodium: 100 mg orally (extended-release) once daily when required
-or-
» celecoxib: 200 mg orally once daily; or 100 mg orally twice daily

Acute

-or-

» meloxicam: 7.5 to 15 mg orally once daily

--AND--

» tramadol: 50-100 mg orally (immediate-release) every 4-6 hours when required, maximum 400 mg/day

-or-

» oxycodone: 5-10 mg orally (immediate-release) every 4-6 hours when required; 10 mg orally (controlled-release) twice daily when required

-or-

» codeine sulfate: 15-60 mg orally every 4-6 hours when required, maximum 360 mg/day

-or-

» morphine sulfate: 10-30 mg orally (immediate-release) every 4 hours when required; 15 mg orally (controlled-release) every 8-12 hours when required

» Opioids are reserved for pain relief in patients whose symptoms are inadequately controlled, or in whom the other agents are inadequate or contraindicated.[73]

» Opioids can be added to topical analgesics (e.g., capsaicin), acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs) (or cyclo-oxygenase-2 [COX-2] inhibitors).

» It should be noted that the potential clinical benefit of opioid treatment, regardless of preparation or dose, does not outweigh the harm opioid treatment may cause in patients with OA.[148] Opioids provide minimal relief of OA symptoms, and are known to cause discomfort in a many patients. Clinicians should give careful consideration to the utility of opioids in the management of OA.[175]

» Oral and transdermal opioids can decrease pain intensity and improve function in patients with OA of the knee or hip compared with placebo, but the observed benefits were small (12% absolute improvement in mean pain compared with placebo [various pain scales]; number needed to benefit of 10).[176] No studies of tramadol contributed to these results.

» A subsequent meta-analysis reported that opioids did not demonstrate a clinically relevant reduction in pain or disability compared with placebo in patients with OA of the hip or knee in at 4-24 weeks. Number needed to treat for an additional dropout due to side effects was 5 (95% CI 4 to 7).[177]

Acute

» Evidence suggests that tramadol is generally well tolerated and can be combined with acetaminophen and/or NSAIDs.[178] However, tramadol alone or in combination with acetaminophen is unlikely to have an important benefit on mean pain or function in patients with OA.[178] [179]

» Opioids are used at the smallest possible dose and shortest possible course to avoid adverse effects, especially in older people.

» Patients requiring opioid analgesia are considered for surgery.

»

adjunct **duloxetine**

Treatment recommended for SOME patients in selected patient group

Primary options

» duloxetine: 30 mg orally once daily initially, increase according to response, maximum 120 mg/day

» Duloxetine is an antidepressant with analgesic properties.

» Results from one systematic review suggest that duloxetine may be effective for the treatment of chronic pain associated with OA, with a number needed to benefit (clinically meaningful outcome at study end compared with placebo) of 7.[180]

» Indirect comparisons between duloxetine and a number of post-first-line oral treatments for OA, including selective COX-2 inhibitors and opioids, found no difference in the total WOMAC composite scores (an inclusive set of OA outcomes) after approximately 12 weeks of treatment.[181] Some analyses suggested that etoricoxib (not available in the US) may be superior to duloxetine.[181]

» Evidence from subsequent systematic reviews found that duloxetine moderately reduces pain compared with placebo, in patients with knee OA.[182] [183] [184] [185]

» Commonly observed adverse effects reported among patients with OA treated with duloxetine include nausea, fatigue, constipation, and dry mouth.[182] There is a possible increased serotonergic effect if given with tramadol.

plus **nonpharmacologic approaches**

Acute

Treatment recommended for ALL patients in selected patient group

» All patients should start treatment for OA with nonpharmacologic approaches.[135] [137] These include patient education, self-management, exercise programs (with reassurance that exercise, e.g., resistance training, tai chi, yoga, and water-based exercise, is not harmful to the joints), and they may also benefit from cognitive behavioural therapy in combination with physical therapy.[7] [73] [92] [93] [94] [96] [95] [97] [98]

» Exercise is recommended for all patients with OA, though there is considerably more evidence for the use of exercise in the treatment of knee and hip OA than for hand OA.[7] Balance exercises or tai chi are recommended for patients with OA of the knee and/or hip, and yoga is suggested as an alternative for patients with OA of the knee.[7]

» Weight loss is recommended for patients with OA of the knee and/or hip who are overweight.[7]

» Two Cochrane reviews conclude that exercise programs have a small to moderate beneficial effect on pain and function for patients with knee and hip OA.[103] [104] However, the benefit from physical therapy on hip OA is unclear.[105] One meta-analysis showed a modest effect on pain, though no improvement in self-reported function for exercise in patients with OA of the hip.[106] Further meta-analyses reported that 14% more patients with hip OA responded to exercise therapy compared with placebo, and that hip abductor muscle strengthening exercises as significantly improved knee pain and other functional outcomes for patients with knee OA.[107] [108]

» Evidence from randomized controlled trials (RCTs) suggests that quadricep strengthening exercises and weight loss are effective in controlling the pain of knee OA.[109] [110] Subsequent meta-analyses demonstrate that hip strengthening exercises are an effective rehabilitation treatment for patients with OA of the knee.[111] [108] [112]

» Exercise can improve quality of life by reducing pain and increasing function for patients with OA, especially those who are overweight or obese.[113] A combination of diet and exercise has been shown to reduce pain and increase muscle mass in patients with OA, and that

Acute

diet alone or in combination with exercise can improve function.[114] [115]

» The American College of Rheumatology (ACR) recommends cane use for patients with knee and/or hip OA in one or more joints, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; tibiofemoral knee braces for patients with OA of the knee, in one or both knees, which is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant their use; hand orthoses for patients with OA of the first carpometacarpal (CMC) joint, or in joints apart from the first CMC joint of the hand; patellofemoral braces for patients with patellofemoral knee OA.[7]

» The ACR does not recommend modified shoes, or lateral and medial wedged insoles for patients with knee and/or hip OA.[7]

» The National Institute of Health and Care Excellence (NICE) in the UK recommends walking aids, such as canes, for people with lower limb OA; insoles, braces, tape, splints, or supports are not routinely recommended to patients with OA, unless there is joint instability or abnormal biomechanical loading AND therapeutic exercise is ineffective or unsuitable without the addition of an aid or device AND the addition of an aid or device is likely to improve movement.[73]

» One network meta-analysis reported that lateral wedge insoles in combination with knee bracing reduce peak knee adduction moment in patients with tibiofemoral OA, while gait training influenced both knee adduction angular impulse and knee adduction moment, so it is recommended for reducing biomechanical risk factors.[116]

» There is conflicting evidence for the use of orthoses and/or braces for medial knee OA. There is evidence to suggest that lateral wedge insoles do not reduce pain or improve functionality in patients with medial knee OA, but conversely that lateral wedge insoles with arch support significantly improved pain and physical function in patients with knee OA.[117] [118] [119]

» Knee valgus bracing has been demonstrated as an effective intervention to improve the quality of life and reduce pain during daily activities for patients with medial knee OA.[120] However, evidence suggests that valgus knee bracing may

Acute

only be effective in the short term.[121] [122] [123] [124]

» Combining both a knee brace and lateral wedge insoles has been shown to improve pain and function in patients with medial knee OA.[125]

» Unloader shoes do not appear to confer benefit in medial knee OA.[126]

» Patellar bracing or taping for patellofemoral pain can be considered. One RCT suggests the use of a knee brace may be helpful in reducing pain and bone marrow lesions in patellofemoral OA.[127] Results of one meta-analysis reported that a multimodal physical therapy intervention that included taping significantly reduced pain in the short term for patients with patellofemoral OA.[128]

» One meta-analysis found that splinting in patients with thumb and CMC joint OA reduced pain and improved function in the medium term (3-12 months), but not the short term.[129]

» Glucosamine and chondroitin sulfate are not recommended for the management of patients with OA; decisions regarding the use of these agents should be discussed with patients.[7] [73] Despite this recommendation, glucosamine and chondroitin sulfate are commonly used by people with OA. Modest efficacy and low risk may explain the popularity of these supplements among patients.

» Both agents have been associated with modest pain reduction in patients with knee OA and are considered safe.[130] [131] [132] [133] [134] [135] However, many trials are of low quality.[133]

» Results of studies on the efficacy of glucosamine or chondroitin varies. One meta-analysis found that glucosamine or chondroitin sulfate reduced pain in patients with knee OA individually, but found no additional benefit associated with combination treatment, whereas subsequent evidence suggests that combination treatment is effective for the treatment of knee OA compared with other placebo.[132] The inconsistencies between the labeling and actual contents of many dietary supplements should be considered; prescription-grade preparations should be sought.[135] [137]

» The ACR recommends acupuncture for patients with knee, hip, and/or hand OA.[7]

Acute

However, NICE in the UK does not recommend acupuncture for the management of OA.[73][136]

» TENS is not recommended to treat patients with OA due to insufficient evidence of benefit.[7] [73]

» Evidence suggests that acupuncture may benefit patients with knee OA.[138] [139] [140] [220] However, evidence of short-term benefit is based on low- to very-low-quality evidence, and may not be clinically important, when compared with control treatments.[141] One Cochrane review concluded that acupuncture does not appear to reduce pain or improve function relative to sham acupuncture in people with hip OA.[142] However, subsequent meta-analysis suggest that acupuncture is reduced pain and improves function in patients with OA of the knee, and may be used as an adjunctive treatment.[143] [144]

» The results of a Cochrane review reported that there is a lack of evidence to support the use of TENS to treat patients with OA of the knee, but there is also evidence to suggest that acupuncture significantly reduced pain, and improved walking ability in patients with OA of the knee.[145] [146]

adjunct **gastroprotection**

Treatment recommended for SOME patients in selected patient group

Primary options

» omeprazole: 20 mg orally once daily

OR

» esomeprazole: 20 mg orally once daily

OR

» pantoprazole: 40 mg orally once daily

OR

» rabeprazole: 20 mg orally once daily

Secondary options

» misoprostol: 100-200 micrograms orally four times daily

» Gastroprotection should be offered to patients on long-term NSAID therapy, especially those

Acute

at risk of GI bleeding.[73] Evidence suggests that proton-pump inhibitors (PPIs) provide better protection against NSAID-induced peptic ulcer disease and gastritis compared with H2 antagonists.[161] Misoprostol is a prostaglandin E1 analog and is another option for gastroprotection, but diarrhea is a common adverse effect, and the drug is less well tolerated than PPIs.[162] [163] [164]

adjunct **intra-articular corticosteroid injections**

Treatment recommended for SOME patients in selected patient group

Primary options

» methylprednisolone acetate: 4-80 mg intra-articularly as a single dose

OR

» triamcinolone acetonide: 2.5 to 40 mg intra-articularly as a single dose

» Intra-articular corticosteroid injections are useful, particularly in the knee, for acute exacerbations of OA or when nonsteroidal anti-inflammatory drugs are contraindicated or not tolerated, and can be used in addition to the nonpharmacologic therapies and analgesia.

» The ACR recommends intra-articular corticosteroid injections for patients with knee and/or hip OA, but only conditionally recommends this treatment for patients with OA of the hand.[7] In the UK, intra-articular corticosteroid injections are only recommended when other pharmacologic treatments are ineffective or unsuitable, or to support therapeutic exercise.[73]

» Trials comparing intra-articular corticosteroid injections with sham or nonintervention controls are often small and of low methodological quality.[188] [189]

» Intra-articular corticosteroid injections reduced pain and improved function in patients with OA of the knee at 6 weeks compared with placebo.[190] However, it appears that intra-articular corticosteroid injections do not reduce joint pain for patients with hand or temporomandibular OA compared with placebo.[191] [192]

» It is unclear how long the benefit of intra-articular corticosteroids lasts in patients with OA. Results from meta-analyses vary, with

Acute

reports of continued efficacy from 1 to 12 weeks in patients with OA of the hip.[188] [189] [193] [194] However, intra-articular corticosteroid may increase the risk of rapidly destructive hip disease, especially at higher doses.[195]

» Meta-analysis of individual patient data suggests that patients with severe knee pain at baseline may derive greater short-term benefit (reduction in pain up to 4 weeks) from intra-articular corticosteroid injection than patients with less severe pain.[196]

» Intra-articular triamcinolone every 12 weeks for 2 years failed to significantly reduce OA knee pain compared with intra-articular saline (-1.2 vs. -1.9; between-group difference -0.6, 95% CI -1.6 to 0.3) in a double-blind RCT.[197] Triamcinolone was associated with significantly greater cartilage volume loss than saline (mean change in index compartment cartilage thickness of -0.21 mm vs. -0.10 mm; between-group difference -0.11 mm, 95% CI -0.20 to -0.03), but the clinical significance of this finding is unclear.[197]

» Time-limited adverse effects of intra-articular injection include post-injection pain, swelling, and post-injection flare. Intra-articular injection of corticosteroid was not associated with loss of joint space at 1- and 2-year follow-up in a placebo-controlled randomized trial of patients with knee arthritis.[198] Similarly, in meta-analysis intra-articular corticosteroids for knee OA had no effect on joint space narrowing beyond that of control interventions.[188]

» Evidence suggests that recurrent intra-articular corticosteroid injections often provide inferior (or nonsuperior) symptom relief compared with other injectables (including placebo) at 3 months and beyond in patients with OA.[199]

» Dose depends upon size of joint and degree of inflammation present.

»

adjunct **viscosupplementation with intra-articular hyaluronic acid**

Treatment recommended for SOME patients in selected patient group

Primary options

» sodium hyaluronate: 20 mg (2 mL) intra-articularly once weekly for 3-5 weeks

OR

Acute

» hylan GF 20: 16 mg (2 mL) intra-articularly once weekly for 3 weeks, total of 3 injections; 6 mL intra-articularly as single injection

» Guidelines do not recommend intra-articular hyaluronic acid injections for the management of OA.[7] [73]

» Despite this recommendation, it is commonly used for the management of symptomatic knee arthritis; studies variously report modest or no benefit.[200] [201] [202]

» One literature review concludes that intra-articular hyaluronic acid should be considered as a treatment for patients with OA, tailored by disease stage and patient phenotype, despite recommendations to the contrary from international guidelines.[203]

» One meta-analysis found that intra-articular viscosupplementation with hyaluronan or hylan derivatives is effective in the management of OA of the knee; improvement from baseline during the 5- to 13-week post-injection period was 28% to 54% for pain and 9% to 32% for function.[202] The analyses suggested that different hyaluronan/hylan products exert differential therapeutic effects, and that response is time dependent.[202]

» Analysing data only from placebo-controlled trials with low risk of bias, one meta-analysis indicated that intra-articular hyaluronic acid provides a modest, but real, benefit for patients with OA of the knee (pain intensity standardized mean difference [SMD] -0.21, 95% CI -0.32 to -0.10; function at 3 months SMD -0.12, 95% CI -0.22 to -0.02).[204]

» However, in subsequent meta-analyses intra-articular injection of hyaluronic acid was not associated with a clinically important difference in pain for patients with OA of the knee compared with placebo, but it may increase the risk of serious adverse effects.[200] [205]

»

Ongoing

persistent pain despite multiple treatment modalities or with severe disability

1st **surgery**

» Patients with OA pain that persists despite multiple treatment modalities and which substantially impacts their quality of life should be referred and considered for joint placement surgery.[73]

» Total knee replacement followed by nonsurgical treatment resulted in significantly greater pain relief and functional improvement after 12 months than nonsurgical treatment alone (Knee Injury and Osteoarthritis Outcome Score [KOOS4] 32.5 vs. 16.0; adjusted mean difference 15.8, 95% CI 10.0 to 21.5) in a randomized controlled trial of patients with moderate-to-severe knee OA who were eligible for unilateral total knee replacement.[206] Total knee replacement was associated with more serious adverse events.[206]

» Unipartmental (partial) knee arthroplasty has been demonstrated to provides pain relief and satisfactory activity level for patients ages 60 years or younger. The results of one meta-analysis reported that 96.5% of implants survived at 10-year follow-up.[207]

» There is no role of partial meniscectomy for meniscal tear in knee OA based on a randomized controlled trial.[208]

» Arthroscopic surgery is not effective for knee OA.[33] [209] [210] Clinical guidelines do not recommend the use of arthroscopic surgery in knee OA.[7] [73] [BMJ Rapid Recommendations: arthroscopic surgery for degenerative knee arthritis and meniscal tears] (http://www.bmj.com/content/357/bmj.j1982) [MAGICapp: recommendations, evidence summaries and consultation decision aids] (https://www.magicapp.org/app#/guideline/1844)

» In patients with primary glenohumeral OA with an intact rotator cuff, total shoulder arthroplasty significantly improved postoperative patient-reported outcome measures (PROMs) compared with hemiarthroplasty.[211]

» Evidence suggests that denervation may be an effective treatment for OA of the hand, especially for proximal interphalangeal (PIP) and trapeziometacarpal (TMC) joint OA.[212] [213]

Ongoing

» Arthroplasty, trapeziectomy, and arthrodesis are options for thumb OA.[214] One meta-analysis concluded that there remains uncertainty about which procedure offers the best functional outcome and safety profile to treat OA of the thumb, the results of the systematic review suggest trapeziectomy with ligament reconstruction and tendon interposition yielded good postoperative range of movement, while arthrodesis demonstrated a high rate of moderate-severe complications.[215]

»

adjunct **topical and oral analgesia**

Treatment recommended for SOME patients in selected patient group

Primary options

» acetaminophen: 325-1000 mg orally every 6 hours when required, maximum 4000 mg/day

--AND--

» capsaicin topical: (0.025 to 0.075%) apply to the affected area(s) three to four times daily when required

--AND--

» naproxen: 250-500 mg orally twice daily when required, maximum 1250 mg/day
-or-
» ibuprofen: 400-800 mg orally every 6-8 hours when required, maximum 3200 mg/day
-or-
» diclofenac potassium: 50 mg orally (immediate-release) twice or three times daily when required
-or-
» diclofenac sodium: 100 mg orally (extended-release) once daily when required
-or-
» celecoxib: 200 mg orally once daily; or 100 mg orally twice daily
-or-
» meloxicam: 7.5 to 15 mg orally once daily

--AND--

» tramadol: 50-100 mg orally (immediate-release) every 4-6 hours when required, maximum 400 mg/day
-or-
» oxycodone: 5-10 mg orally (immediate-release) every 4-6 hours when required; 10 mg orally (controlled-release) twice daily when required
-or-

MANAGEMENT

Ongoing

» codeine sulfate: 15-60 mg orally every 4-6 hours when required, maximum 360 mg/day
-or-
» morphine sulfate: 10-30 mg orally (immediate-release) every 4 hours when required; 15 mg orally (controlled-release) every 8-12 hours when required

» Topical and oral analgesia should be continued as required while awaiting joint replacement and can be used in combination.

» Studies have demonstrated that acetaminophen has a small to modest benefit for patients with OA of the hip or knee, and is statistically inferior to all other drug categories for the management of OA pain (oral NSAIDs, topical NSAIDs, COX-2 inhibitors, and opioids).[155] [147] [156] As such acetaminophen alone may not have a role in the treatment of hip or knee OA, irrespective of the dose used, but may be added for rescue analgesia, or if local therapies alone do not control symptoms.[137] [157]

» With this evidence of limited efficacy, and with more data available regarding the potential adverse reactions of acetaminophen, careful consideration should taken about the use of acetaminophen for the treatment of OA.[155] [157] [158]

» Oral NSAIDs are more effective than acetaminophen for the management of OA pain; however, they are associated with gastrointestinal (GI) and renal toxicity.[147] [159] [160]

» Diclofenac or etoricoxib (not available in the US) may be the most effective NSAID for the treatment of pain in knee and hip OA, but potential benefit must be weighed against adverse effects, but may not be appropriate for patients with comorbidities or for long-term use.[148] [157]

» Selective COX-2 inhibitors may be used as an alternative to nonselective NSAIDs. They are associated with reduced risk of GI adverse effects compared with nonselective NSAIDs, but similar renal toxicity.[165] [166] COX-2 inhibitors are effective for the management of pain associated with knee and hip OA, and may have a role in patients at increased risk for GI adverse effects.[137] [157] However, COX-2 inhibitors do not confer an advantage with respect to GI symptoms when compared with placebo, or NSAID and proton-pump inhibitor (PPI) used

Ongoing

concomitantly for gastroprotection.[73] [167] [168] The incidence of upper GI adverse effects did not differ between patients with knee OA who were treated with fixed-dose combination naproxen and esomeprazole or with celecoxib; the former reported significantly more heartburn-free days than those on celecoxib.[169]

» Evidence suggests that NSAID use substantially contributes to the association between OA and cardiovascular disease (CVD), with increased risk reaching significance as early as 4 weeks into treatment.[170] [171] Several patient characteristics may be associated with increased CVD risk when taking an NSAID, such as age >80 years, history of CVD, rheumatoid arthritis, chronic obstructive pulmonary disease, renal disease, and hypertension.[172] One meta-analysis suggested that diclofenac and ibuprofen were associated with increased cardiovascular risk, while naproxen and celecoxib were not.[173] However, similar incident rates of cardiovascular events have been reported for ibuprofen, celecoxib, and naproxen.[174]

» GI and cardiovascular safety profiles of individual oral NSAIDs differ, and careful patient selection is required to maximize the risk:benefit ratio.[137] The lowest effective dose of NSAID should be used to minimize adverse effects.

» It should be noted that the potential clinical benefit of opioid treatment, regardless of preparation or dose, does not outweigh the harm opioid treatment may cause in patients with OA.[148] Opioids provide minimal relief of OA symptoms, and are known to cause discomfort in a many patients. Clinicians should give careful consideration to the utility of opioids in the management of OA.[175]

» Oral and transdermal opioids can decrease pain intensity and improve function in patients with OA of the knee or hip compared with placebo, but the observed benefits were small (12% absolute improvement in mean pain compared with placebo [various pain scales]; number needed to benefit of 10).[176] No studies of tramadol contributed to these results.

» A subsequent meta-analysis reported that opioids did not demonstrate a clinically relevant reduction in pain or disability compared with placebo in patients with OA of the hip or knee in at 4-24 weeks. Number needed to treat for an additional dropout due to side effects was 5 (95% CI 4 to 7).[177]

Ongoing

» Evidence suggests that tramadol is generally well tolerated and can be combined with acetaminophen and/or NSAIDs.[178] However, tramadol alone or in combination with acetaminophen is unlikely to have an important benefit on mean pain or function in patients with OA.[178] [179]

»

adjunct **duloxetine**

Treatment recommended for SOME patients in selected patient group

Primary options

» duloxetine: 30 mg orally once daily initially, increase according to response, maximum 120 mg/day

» May be continued while awaiting joint replacement.

» Duloxetine inhibits the reuptake of both serotonin and norepinephrine and can be used to reduce pain and improve function.

» Results from one systematic review suggest that duloxetine may be effective for the treatment of chronic pain associated with OA, with a number needed to benefit (clinically meaningful outcome at study end compared with placebo) of 7.[180]

» Indirect comparisons between duloxetine and a number of post-first-line oral treatments for OA, including selective COX-2 inhibitors and opioids, found no difference in the total WOMAC composite scores (an inclusive set of OA outcomes) after approximately 12 weeks of treatment.[181] Some analyses suggested that etoricoxib (not available in the US) may be superior to duloxetine.[181]

» Evidence from subsequent systematic reviews found that duloxetine moderately reduces pain compared with placebo, in patients with knee OA.[182] [183] [184] [185]

» Commonly observed adverse effects reported among patients with OA treated with duloxetine include nausea, fatigue, constipation, and dry mouth.[182] There is a possible increased serotonergic effect if given with tramadol.

adjunct **gastroprotection**

Treatment recommended for SOME patients in selected patient group

Ongoing

Primary options

» omeprazole: 20 mg orally once daily

OR

» esomeprazole: 20 mg orally once daily

OR

» pantoprazole: 40 mg orally once daily

OR

» rabeprazole: 20 mg orally once daily

Secondary options

» misoprostol: 100-200 micrograms orally four times daily

» Gastroprotection should be offered to patients on long-term NSAID therapy, especially those at risk of GI bleeding.[73] Evidence suggests that proton-pump inhibitors (PPIs) provide better protection against NSAID-induced peptic ulcer disease and gastritis compared with H2 antagonists.[161] Misoprostol is a prostaglandin E1 analog and is another option for gastroprotection, but diarrhea is a common adverse effect, and the drug is less well tolerated than PPIs.[162] [163] [164]

adjunct **viscosupplementation with intra-articular hyaluronic acid**

Treatment recommended for SOME patients in selected patient group

Primary options

» sodium hyaluronate: 20 mg (2 mL) intra-articularly once weekly for 3-5 weeks

OR

» hylan GF 20: 16 mg (2 mL) intra-articularly once weekly for 3 weeks, total of 3 injections; 6 mL intra-articularly as single injection

» May be continued while awaiting joint replacement.

» Guidelines do not recommend intra-articular hyaluronic acid injections for the management of OA.[7] [73]

Ongoing

» Despite this recommendation, it is commonly used for the management of symptomatic knee arthritis; studies variously report modest or no benefit.[200] [201] [202]

» One literature review concludes that intra-articular hyaluronic acid should be considered as a treatment for patients with OA, tailored by disease stage and patient phenotype, despite recommendations to the contrary from international guidelines.[203]

» One meta-analysis found that intra-articular viscosupplementation with hyaluronan or hylan derivatives is effective in the management of OA of the knee; improvement from baseline during the 5- to 13-week post-injection period was 28% to 54% for pain and 9% to 32% for function.[202] The analyses suggested that different hyaluronan/hylan products exert differential therapeutic effects, and that response is time dependent.[202]

» Analysing data only from placebo-controlled trials with low risk of bias, one meta-analysis indicated that intra-articular hyaluronic acid provides a modest, but real, benefit for patients with OA of the knee (pain intensity standardized mean difference [SMD] -0.21, 95% CI -0.32 to -0.10; function at 3 months SMD -0.12, 95% CI -0.22 to -0.02).[204]

» However, in subsequent meta-analyses intra-articular injection of hyaluronic acid was not associated with a clinically important difference in pain for patients with OA of the knee compared with placebo, but it may increase the risk of serious adverse effects.[200] [205]

»

adjunct **intra-articular corticosteroid injections**

Treatment recommended for SOME patients in selected patient group

Primary options

» methylprednisolone acetate: 4-80 mg intra-articularly as a single dose

OR

» triamcinolone acetonide: 2.5 to 40 mg intra-articularly as a single dose

» May be continued while awaiting joint replacement.

Ongoing

» Intra-articular corticosteroid injections are useful, particularly in the knee, for acute exacerbations of OA or when nonsteroidal anti-inflammatory drugs are contraindicated or not tolerated, and can be used in addition to the nonpharmacologic therapies and analgesia.

» The ACR recommends intra-articular corticosteroid injections for patients with knee and/or hip OA, but only conditionally recommends this treatment for patients with OA of the hand.[7] In the UK, intra-articular corticosteroid injections are only recommended when other pharmacologic treatments are ineffective or unsuitable, or to support therapeutic exercise.[73]

» Trials comparing intra-articular corticosteroid injections with sham or nonintervention controls are often small and of low methodological quality.[188] [189]

» Intra-articular corticosteroid injections reduced pain and improved function in patients with OA of the knee at 6 weeks compared with placebo.[190] However, it appears that intra-articular corticosteroid injections do not reduce joint pain for patients with hand or temporomandibular OA compared with placebo.[191] [192]

» It is unclear how long the benefit of intra-articular corticosteroids lasts in patients with OA. Results from meta-analyses vary, with reports of continued efficacy from 1 to 12 weeks in patients with OA of the hip.[188] [189] [193] [194] However, intra-articular corticosteroid may increase the risk of rapidly destructive hip disease, especially at higher doses.[195]

» Meta-analysis of individual patient data suggests that patients with severe knee pain at baseline may derive greater short-term benefit (reduction in pain up to 4 weeks) from intra-articular corticosteroid injection than patients with less severe pain.[196]

» Intra-articular triamcinolone every 12 weeks for 2 years failed to significantly reduce OA knee pain compared with intra-articular saline (-1.2 vs. -1.9; between-group difference -0.6, 95% CI -1.6 to 0.3) in a double-blind RCT.[197] Triamcinolone was associated with significantly greater cartilage volume loss than saline (mean change in index compartment cartilage thickness of -0.21 mm vs. -0.10 mm; between-group difference -0.11 mm, 95% CI -0.20 to -0.03),

Ongoing

but the clinical significance of this finding is unclear.[197]

» Time-limited adverse effects of intra-articular injection include post-injection pain, swelling, and post-injection flare. Intra-articular injection of corticosteroid was not associated with loss of joint space at 1- and 2-year follow-up in a placebo-controlled randomized trial of patients with knee arthritis.[198] Similarly, in meta-analysis intra-articular corticosteroids for knee OA had no effect on joint space narrowing beyond that of control interventions.[188]

» Evidence suggests that recurrent intra-articular corticosteroid injections often provide inferior (or nonsuperior) symptom relief compared with other injectables (including placebo) at 3 months and beyond in patients with OA.[199]

» Dose depends upon size of joint and degree of inflammation present.

»

Emerging

Extracorporeal shockwave therapy (ESWT)

Extracorporeal shockwave therapy has been demonstrated to reduce pain and improve functionality in patients with OA of the knee at up to 12 months, with only minor adverse effects.[227] [228] [229] However, there remains a lack of clarity regarding the frequency and dose levels of ESWT required to achieve the maximum improvement.[229] Further long-term trials are needed.

Autologous conditioned serum (ACS)

Randomized controlled trials and observational studies suggest that autologous conditioned serum may be of some benefit with respect to pain control and functional recovery in patients with OA, but a disease-modifying effect has not been convincingly demonstrated.[230] [231] [232] [233]

Platelet-rich plasma (PRP) intra-articular injections

Meta-analyses suggest that PRP intra-articular injections may provide symptomatic relief in OA.[234] [235] [236] [237] [238] [239] [240] The UK National Institute for Health and Care Excellence reports that evidence on PRP injections for knee OA is limited in quality, and therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.[241] The American College of Rheumatology (ACR) does not recommend PRP intra-articular injections for patients with knee or hip OA.[7] Meta-analyses comparing PRP with hyaluronic acid and other injectable options in patients with OA of the knee suggest that PRP is either more beneficial than hyaluronic acid and other injectables, or patients can expect a similar beneficial short-term outcomes with PRP compared with hyaluronic acid.[242] [243] [244] [245] The benefits of PRP for the treatment of knee OA may increase over time, becoming clinically significant after 6-12 months.[245] However, the improvement remains partial and is supported by low-level evidence. Further research is needed to confirm the benefits of PRP and identify the best formulation and indications for PRP injections in knee OA.[242] [245] Evidence on the effectiveness of PRP to treat OA of the ankle varies. One meta-analysis demonstrated an improvement of pain and function for patients with OA of the ankle in the short term (12 weeks), while a second meta-analysis reported no improvement of symptoms or function for PRP at 52 weeks compared with placebo.[240] [246]

Radiofrequency ablation

Radiofrequency ablation, a minimally invasive treatment option, employs a high temperature probe to target nervous tissue of interest. Meta-analyses report significant improvement in pain for up to 12 months when used to treat knee OA.[247] [248] [249] [250] [251] [252] [253] Concerns exist regarding procedural protocols, study sample size and quality, and patient follow-up; further, high-quality studies are warranted.[251] Genicular nerve thermal radiofrequency ablation has been demonstrated to be more effective compared with nonsteroidal anti-inflammatory drugs and intra-articular corticosteroid injections at reducing pain, improving function and quality of life in patients with OA of the knee.[254] Two subsequent meta-analyses found that genicular artery embolization is an effective treatment for reducing pain for patients with mild, moderate, or severe knee OA refractory to conservative management, without any serious complications.[255] [256]

Tapentadol

Tapentadol is a centrally acting analgesic mu-opioid receptor agonist and norepinephrine reuptake inhibitor. Pooled analysis of two double-blind, randomized, placebo- and oxycodone (controlled release)-controlled studies found that prolonged-release tapentadol provided significantly more effective pain relief than oxycodone (controlled release) in patients with moderate-to-severe chronic OA knee pain.[257] Tapentadol appears to be associated with reduced risk for vomiting, constipation, nausea, somnolence, and pruritus compared with oxycodone.[257]

Ketorolac

Randomized controlled trials suggest that intra-articular ketorolac injection provides comparable improvement in patient-reported outcome measures to intra-articular corticosteroid in patients with knee or hip OA.[258] [259] In one trial, pain remained significantly decreased from baseline at 24 weeks in both treatment arms.[259]

Cell-mediated gene therapy

Phase 2 and phase 3 studies of cell-mediated gene therapy in patients with knee OA report statistically significant improvements in function and pain.[260] [261] Larger, multicenter trials are required.

Stem cell therapy

Meta-analyses suggest that intra-articular mesenchymal stem cell therapy reduces pain in patients with OA of the knee, but that evidence of disease-modifying effects (e.g., cartilage repair) remains limited.[262] [263] [264] [265] [266] [267] [268] The ACR does not recommend stem cell injections for patients with knee or hip OA.[7]

Combined intra-articular injections

One systematic review reported that combined intra-articular injections of a corticosteroid and hyaluronic acid reduced WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain scores at 2 to 4 weeks, 24 to 26 weeks, and 52 weeks, compared with hyaluronic acid injections alone in patients with OA of the knee.[269] A comparison of combined intra-articular injections of PRP and hyaluronic acid reported that the combined intra-articular injection improved patient-reported outcomes compared with hyaluronic acid alone, but it was not more effective when compared with PRP alone for patients with OA of the knee.[270] One meta-analysis demonstrated that combined intra-articular injection of mesenchymal stem cells (MSCs) with PRP improved pain and function scores at 6 months, but not at 12 months, compared with hyaluronic acid or PRP alone in patients with OA of the knee.[271]

Antinerve growth factor antibodies

Fasinumab, an antinerve growth factor monoclonal antibody, appeared to improve pain and function in a 36-week phase 2b/3 double-blind, placebo-controlled, randomized trial of patients with knee or hip OA with history of inadequate response or intolerance to analgesics.[272] The US National Library of Medicine clinical trials register suggests that there are no active clinical trials of fasinumab in patients with OA.[273] The Food and Drug Administration's Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee considered that the risk for joint destruction or rapidly progressive osteoarthritis (RPOA) associated with tanezumab, a humanized antinerve growth factor monoclonal antibody (for moderate to severe OA pain in adults for whom the use of other analgesics is ineffective or inappropriate) was too great. The European Medicines Agency's Committee for Medicinal Products for Human Use also recommended refusing a marketing application for tanezumab.

Primary prevention

Obesity is strongly linked to the development of knee OA; therefore, obese patients should be encouraged to lose weight.[22] [23]

One guideline suggests that by targeting specific patients with post-traumatic knee injury, OA may be prevented by initiating appropriate rehabilitation approaches and interventions at a specified time, recommendations include:[68]

- Person-centered interventions to promote education, self-management, and exercises that mitigate known modifiable risk factors for re-injury and nontraumatic OA.
- Education and exercise therapy based rehabilitation for patients with anterior cruciate ligament tear, with optional reconstruction if a patient cannot achieve their acceptable functional level.
- Monitoring knee pain and other symptoms, adverse events, knee-related quality of life and cognitive behavioral factors (fear, self-efficacy, and confidence), self-reported knee function, quadriceps and

hamstring muscle function (strength), functional performance (hop battery), and physical activity/sport participation.

However, there are no therapeutic interventions or medical treatments that are guaranteed to prevent or delay the development of OA. Doxycycline may delay joint space narrowing, but the modest benefit of treatment, which is of questionable clinical significance, may be outweighed by safety issues.[69] [70] Some evidence suggests that long-term use of glucosamine and chondroitin sulfate (≥2 years) may modestly delay radiographic progression of OA of the knee, but these results are controversial.[70] [71]

Secondary prevention

Losing weight, even in modest amounts (5 to 10 lb), helps prevent OA of the knees and helps reduce the pain in overweight people.[292]

Appropriate exercises and activities help preserve functional abilities.

Identification of biochemical biomarkers may enable diagnosis of OA at earlier stages, potentially preventing disease progression in some patients.[293] [294]

No medical treatments are available to prevent OA.

Patient discussions

Patients are asked to consult their physician if they have persistent pain in their joints on most days for more than 1 month.

If they are diagnosed with OA, a combination of exercise, physical therapy, healthy lifestyle, and medications as recommended by their physician is appropriate.

Patients should be referred to a rheumatologist and/or orthopedist if they have significant pain or limitation in their activities.

Monitoring

Monitoring

Patients are monitored for progression of disease and response to treatment, in addition to any adverse effects. They are asked about their pain response to treatment, function, and limitation in their activities due to their disease.

Patients are examined for declining range of motion in the affected joint and for other signs reflecting advanced disease.

If the patient is taking a nonsteroidal anti-inflammatory drug (NSAID) or a cyclo-oxygenase-2 (COX-2) inhibitor, tests for renal function and a complete blood count are obtained every 3 to 6 months.[7] [73]

FOLLOW UP

Complications

Complications	Timeframe	Likelihood
functional decline and inability to perform activities of daily living	**long term**	**high**
If no improvement with nonpharmacologic and pharmacologic therapy, referral to an orthopedist should be considered.		
spinal stenosis in cervical and lumbar OA	**long term**	**medium**
Spinal stenosis may result from degenerative changes, typically in the lumbar spine but also in the cervical spine. Neurogenic claudication is characterized by back and leg pain, and the patient may complain of paresthesia in the lower limbs that is worse on walking and improved by sitting. A referral for orthopedic spinal opinion to consider decompression surgery is warranted.		
NSAID-related gastrointestinal bleeding	**variable**	**medium**
Long-term use of nonsteroidal anti-inflammatory drug (NSAID) analgesia can cause gastric irritation, peptic ulceration, and upper gastrointestinal bleeding in some patients. This risk can be decreased with the use of proton-pump inhibitors.		
effusion	**variable**	**medium**
Arthrocentesis and corticosteroid injection, and/or referral to rheumatology, should be considered.		
NSAID-related renal dysfunction	**variable**	**low**
Nonsteroidal anti-inflammatory drug (NSAID) analgesia decreases the production of renal prostaglandins, which act as vasodilators to maintain renal perfusion pressure. In a healthy person these prostaglandins have only a minor role, but they become progressively more important in people with glomerular disease and renal insufficiency. A resulting fall in hemodynamic pressure can cause acute renal failure. NSAIDs may also cause acute interstitial nephritis as a result of decreased prostaglandin synthesis.		

Prognosis

OA is a chronic, slowly progressive disease and is common with advancing age.

A combination of different modalities of treatment can provide adequate pain control and preserve function and quality of life for many patients. Despite treatment, most patients continue to have some degree of pain and functional limitation affecting their desired activities and quality of life.

Complications of medication, particularly nonsteroidal anti-inflammatory drugs (NSAIDs), are problematic.

In patients who do not respond to medical and nonmedical therapies, total joint replacement provides good long-term pain relief for most people.

Diagnostic guidelines

International

ACR appropriateness criteria: chronic extremity joint pain-suspected inflammatory arthritis, crystalline arthritis, or erosive osteoarthritis (https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria) [87]

Published by: American College of Radiology **Last published:** 2022

ACR appropriateness criteria: chronic hip pain (https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria) [88]

Published by: American College of Radiology **Last published:** 2022

Imaging in the clinical management of peripheral joint osteoarthritis (https://www.eular.org/recommendations-management) [77]

Published by: European League Against Rheumatism **Last published:** 2017

Osteoarthritis in over 16s: diagnosis and management (https://www.nice.org.uk/guidance/ng226) [73]

Published by: National Institute for Health and Care Excellence (UK) **Last published:** 2022

Treatment guidelines

International

APA clinical practice guideline for psychological and other nonpharmacological treatment of chronic musculoskeletal pain in adults (https://www.apa.org/about/offices/directorates/guidelines/clinical-practice) [274]

Published by: American Psychological Association **Last published:** 2024

Management of osteoarthritis of the hip (https://www.orthoguidelines.org/guidelines) [275]

Published by: American Academy of Orthopaedic Surgeons **Last published:** 2023

Clinical practice guideline for the optimal timing of elective total hip or knee arthroplasty for patients with symptomatic moderate to severe osteoarthritis or osteonecrosis who have failed nonoperative therapy (https://rheumatology.org/clinical-practice-guidelines) [276]

Published by: American College of Rheumatology (ACR) and American Association of Hip and Knee Surgeons (AAHKS) **Last published:** 2023

Treatment for shoulder OA with intact rotator cuff and severe glenoid retroversion: appropriate use criteria (https://www.aaos.org/quality/quality-programs) [277]

Published by: American Academy of Orthopedic Surgeons **Last published:** 2023

Appropriate use criteria on the management of osteoarthritis of the knee (non-arthroplasty) (https://www.aaos.org/quality/quality-programs) [278]

Published by: American Academy of Orthopaedic Surgeons **Last published:** 2022

Guideline for the perioperative management of antirheumatic medication in patients with rheumatic diseases undergoing elective total hip or total knee arthroplasty (https://rheumatology.org/clinical-practice-guidelines) [279]

Published by: American College of Rheumatology/American Association of Hip and Knee Surgeons **Last published:** 2022

Surgical management of osteoarthritis of the knee (https://www.orthoguidelines.org/guidelines) [280]

Published by: American Academy of Orthopaedic Surgeons **Last published:** 2022

Management of osteoarthritis of the knee (non-arthroplasty) (https://www.orthoguidelines.org/guidelines) [281]

Published by: American Academy of Orthopaedic Surgeons **Last published:** 2021

Guideline for the management of osteoarthritis of the hand, hip, and knee (https://www.eular.org/recommendations-management) [7]

Published by: American College of Rheumatology **Last published:** 2020

International

VA/DoD clinical practice guideline for the non-surgical management of hip and knee osteoarthritis (https://www.healthquality.va.gov) [282]

Published by: US Department of Veterans Affairs; US Department of Defense **Last published:** 2020

The Ottawa Panel guidelines on programmes involving therapeutic exercise for the management of hand osteoarthritis (https://www.ncbi.nlm.nih.gov/pubmed/29911409) [283]

Published by: Ottawa Panel **Last published:** 2018

Noninvasive treatments for acute, subacute, and chronic low back pain (https://www.acponline.org/clinical-information/guidelines) [284]

Published by: American College of Physicians **Last published:** 2017

Responsible, safe, and effective prescription of opioids for chronic non-cancer pain (https://asipp.org/guidelines) [285]

Published by: American Society of Interventional Pain Physicians **Last published:** 2017

An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain (https://asipp.org/guidelines) [286]

Published by: American Society of Interventional Pain Physicians **Last published:** 2013

OARSI guidelines for the non-surgical management of knee osteoarthritis (https://oarsi.org/education/oarsi-guidelines-0) [287]

Published by: Osteoarthritis Research Society International **Last published:** 2019

ESMO management of toxicities from immunotherapy: clinical practice guideline for diagnosis, treatment and follow-up (https://www.esmo.org/guidelines) [288]

Published by: European Society for Medical Oncology **Last published:** 2022

EULAR recommendations regarding lifestyle behaviors and work participation to prevent progression of rheumatic and musculoskeletal diseases (https://www.eular.org/recommendations-management) [289]

Published by: European League Against Rheumatism **Last published:** 2021

EULAR recommendations for intra-articular therapies (https://www.eular.org/recommendations-management) [290]

Published by: European League Against Rheumatism **Last published:** 2021

Management of knee osteoarthritis (https://www.esceo.org/publications/esceo-guidance-position-and-scientific-papers) [137]

Published by: European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) **Last published:** 2019

International

EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis (https://www.eular.org/recommendations-management) [291]

Published by: European League Against Rheumatism **Last published:** 2013

Osteoarthritis in over 16s: diagnosis and management (https://www.nice.org.uk/guidance/ng226) [73]

Published by: National Institute for Health and Care Excellence (UK) **Last published:** 2022

Online resources

1. BMJ Rapid Recommendations: arthroscopic surgery for degenerative knee arthritis and meniscal tears (http://www.bmj.com/content/357/bmj.j1982) *(external link)*

2. MAGICapp: recommendations, evidence summaries and consultation decision aids (https://www.magicapp.org/app#/guideline/1844) *(external link)*

Key articles

- Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2020 Feb;72(2):149-62. Full text (https://onlinelibrary.wiley.com/doi/10.1002/acr.24131) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31908149?tool=bestpractice.bmj.com)
- National Institute for Health and Care Excellence. Osteoarthritis in over 16s: diagnosis and management. Oct 2022 [internet publication]. Full text (https://www.nice.org.uk/guidance/ng226)
- Bruyère O, Honvo G, Veronese N, et al. An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Semin Arthritis Rheum. 2019 Dec;49(3):337-50. Full text (https://www.sciencedirect.com/science/article/pii/S0049017219300435) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31126594?tool=bestpractice.bmj.com)

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Images

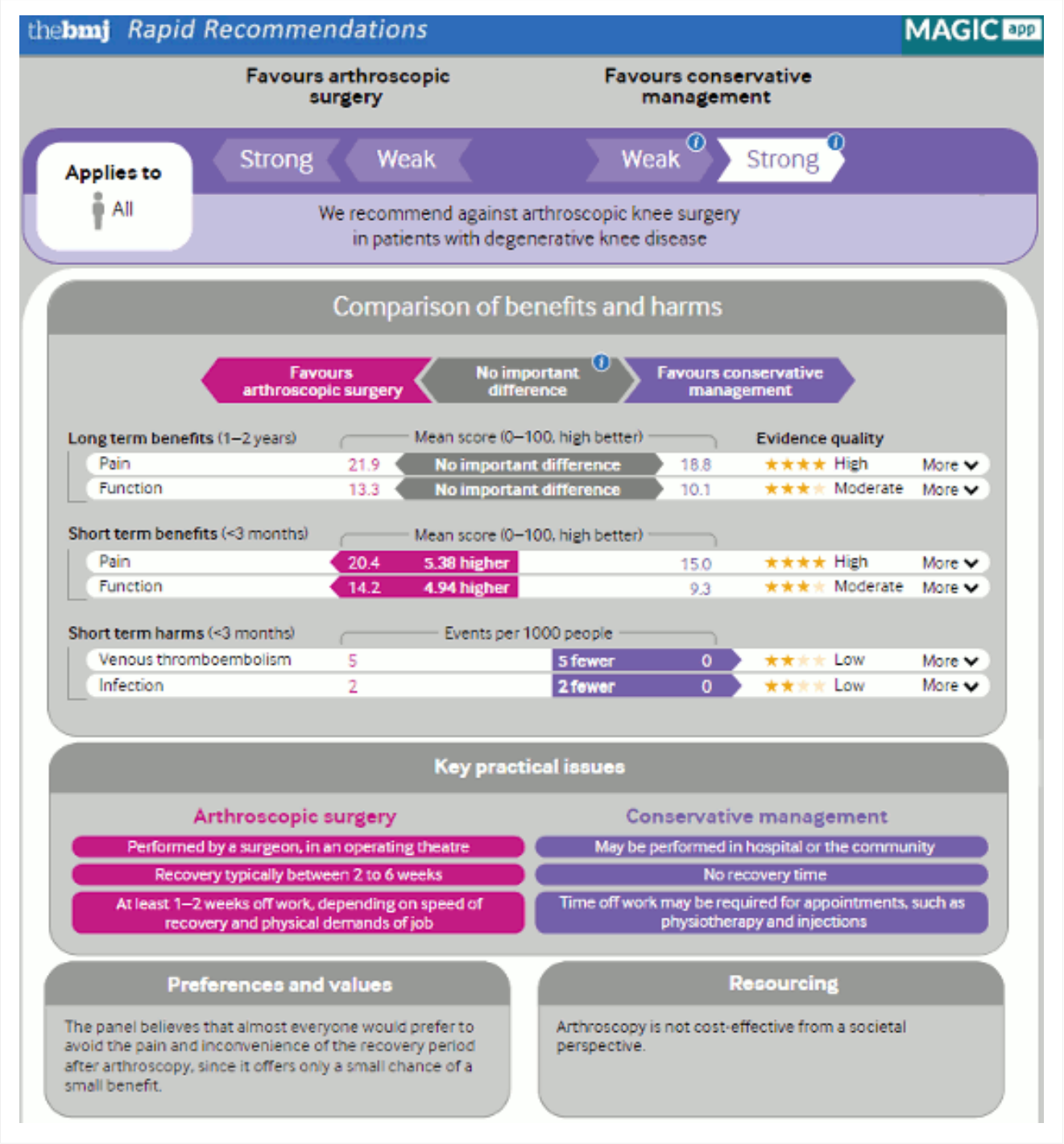

Figure 1: BMJ Rapid Recommendations: arthroscopic surgery for degenerative knee arthritis and meniscal tears

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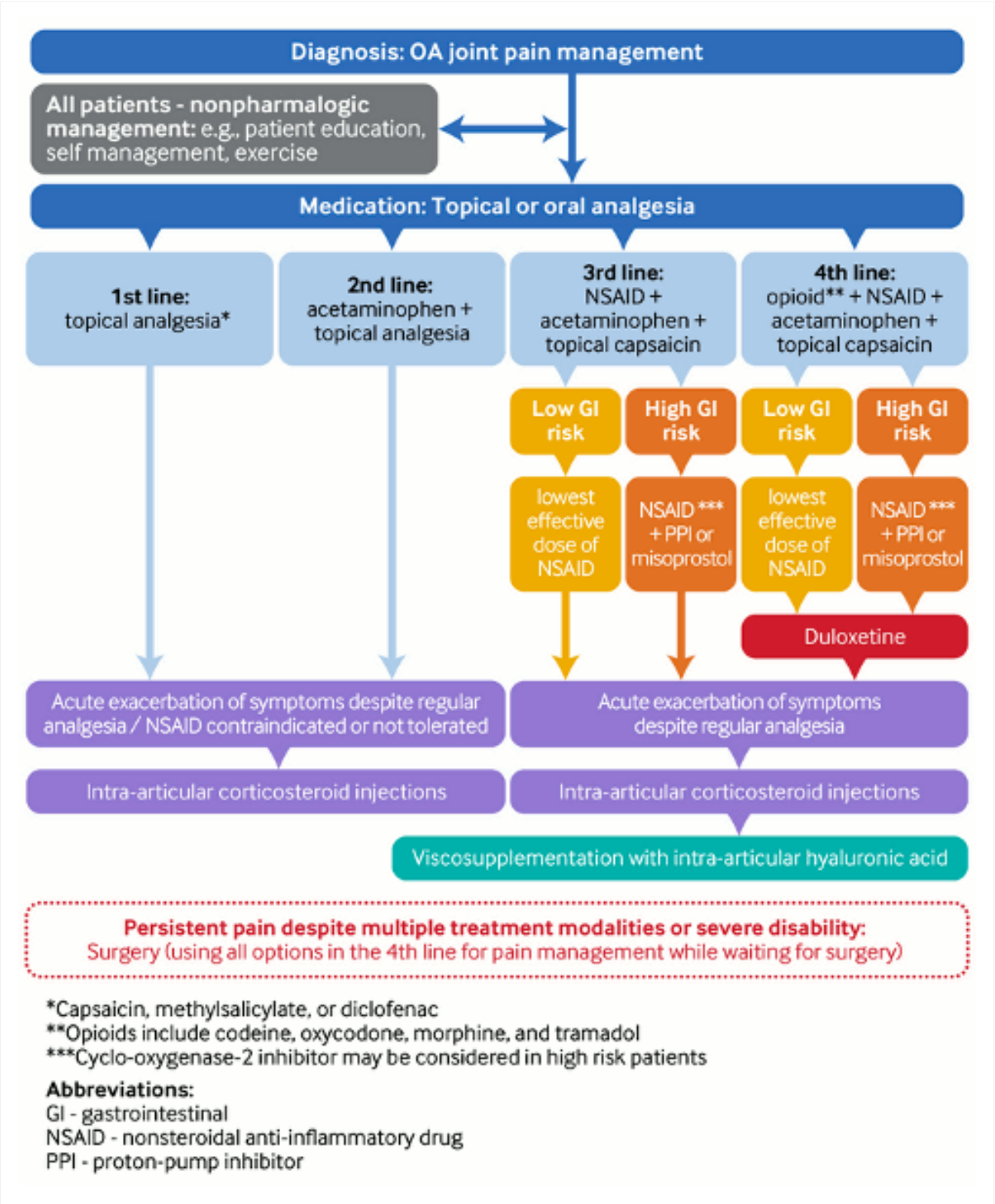

Figure 2: Osteoarthritis treatment flowchart

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Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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