Management of osteoarthritis of the knee

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Osteoarthritis of the knee causes pain, limits activity, and impairs quality of life. Although it cannot be cured, advances in understanding and treatment have improved the outlook for people with this condition. This review will outline evidence for management and emphasise the importance of a patient centred multidisciplinary approach, conservative non-drug interventions, judicious use of drugs, and appropriate surgical referral.

What is osteoarthritis and how common is it?

Osteoarthritis is a painful chronic joint disease characterised by structural changes to the whole joint, including loss of articular cartilage, development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity. It results from a complex interplay of genetic, metabolic, biomechanical, and biochemical factors. At the knee, osteoarthritis most commonly affects the medial tibiofemoral and patellofemoral joint compartments.

The reported incidence and prevalence of osteoarthritis of the knee varies, depending on population characteristics and disease definition. There are few population based incidence studies. The longest and most recent reported a relatively low annual cumulative radiographic incidence of 2.3% in middle aged women over a 15 year period.¹ In a systematic review, prevalence rates of radiographic disease ranged from 4.3% to 78.6%, whereas rates were lower for symptomatic disease (3.2-13.5%).²

Who gets osteoarthritis?

Osteoarthritis of the knee is more common in women and older people.³ Racial and ethnic differences also exist, with higher rates in black and Chinese people than in white people.⁴ Systemic and local risk factors have been identified (fig 1), with obesity and joint injury (particularly anterior cruciate ligament and meniscal injuries in sports people) being important modifiable factors. This last risk factor means that a proportion of those affected will be young active people in their 30s and 40s. Public health strategies targeted towards weight reduction and prevention of knee injuries could prevent large numbers of people developing the condition. Strong longitudinal evidence shows that knee malalignment (varus for medial knee osteoarthritis and valgus for lateral knee osteoarthritis) and obesity increase the risk of structural disease progression in those with established disease.⁵ In contrast, few studies have examined risk factors for functional decline and disability.

How is osteoarthritis diagnosed?

Clinically, osteoarthritis is diagnosed on the basis of a history and physical examination. Radiography is used to confirm clinical suspicion and exclude other conditions. When radiography is used along with physical examination, sensitivity and specificity are 91% and 86%, respectively.³ The osteoarthritis task force of the European League against Rheumatism suggests six criteria for a confident clinical diagnosis of osteoarthritis of the knee (box 1).³

Magnetic resonance imaging does not help in decisions about current interventions for osteoarthritis of the knee and should not be performed unless it will change management. This test may be useful when considering rare differential diagnoses such as osteochondritis dissecans, pigmented villonodular synovitis, or avascular necrosis (box 2). Inappropriate use of magnetic resonance imaging can lead to increased detection of incidental meniscal tears, which are common in older people,⁶⁷ and result in unnecessary arthroscopic knee surgery.

What are the principles of prevention and management?

Management of osteoarthritis of the knee has traditionally focused on treating pain and disability. However, a broader approach that includes prevention (reduction of risk factors—especially overweight or obesity, joint injury, and potentially smoking and vitamin D deficiency—to reduce disease incidence) and interventions that slow down disease progression is now recommended. Optimal management requires...
Summary points

- Osteoarthritis is a chronic disease; management should be patient centred and coordinated, with attention to modifiable risk factors and comorbidities.
- Focus on conservative non-drug treatment, particularly exercise; for overweight or obese patients weight loss is recommended.
- Management should be evidence-based; do not use interventions with high cost and risk that outweigh their benefits.
- Use paracetamol or non-steroidal anti-inflammatory drugs for pain relief, with due attention to precautions and contraindications.
- Refer patients to a physiotherapist for exercise, manual therapy, and gait aids; orthotist for bracing; psychologist for cognitive-behavioural therapy; and dietitian for nutritional advice.
- Do not use arthroscopy for pain management; refer patients for joint replacement only when symptoms are severe and other treatments have failed.

Sources and selection criteria

We used recently published clinical guidelines for the management of osteoarthritis of the knee from the Osteoarthritis Research Society International, American College of Rheumatology, National Institute for Health and Clinical Excellence, European League against Rheumatism, American Academy of Orthopaedic Surgeons, Royal Australian College of General Practitioners, and the Ottawa Panel. We also searched the Cochrane Database of Systematic Reviews (without time limits) and performed PubMed and Embase searches (January 2008 to March 2012) using the keywords “knee” and “osteoarthritis”. We selected high quality systematic reviews, meta-analyses, and large randomised controlled trials. When such studies were unavailable, we considered relevant small randomised controlled trials, cohort studies, and observational studies.

Box 1 European League against Rheumatism recommendations on the diagnosis of knee osteoarthritis

These recommendations focus on six clinical signs and symptoms identified by a Delphi consensus approach across 12 countries. 1

**Symptoms**
- Persistent knee pain
- Limited knee stiffness (<30 min)
- Reduced function

**Signs**
- Crepitus
- Restricted movement
- Bony enlargement

Box 2 Differential diagnosis of knee pain and indications for magnetic resonance imaging (MRI)

**Common conditions that typically do not require MRI**
- Pes anserine bursitis
- Iliotibial band friction syndrome
- Patellar tendinosis
- Patellofemoral pain syndrome
- Prepatellar bursitis
- Semimembranosus bursitis

**Uncommon conditions where MRI may be helpful**
- Osteochondritis dissecans: usually presents with pain, swelling, and mechanical symptoms including catching, locking, popping noises, and giving way
- Pigmented villonodular synovitis: usually presents with sudden onset, unexplained joint swelling, and pain, with swelling disproportionate to the amount of pain
- Avascular necrosis: often asymptomatic early on with increasing joint pain as structure deteriorates; risk factors include long-term steroid use, excessive alcohol use, clotting disorders

What are the conservative treatment options?

To ensure safe and effective delivery of the many conservative non-drug treatments suitable for osteoarthritis of the knee, a multidisciplinary approach is needed, with judicious referral to allied health practitioners according to the patient’s needs and the healthcare setting (table). Core conservative treatments for a combination of conservative non-drug and drug treatments, with surgery reserved for severe clinical disease with structural changes. 2 Because the condition is chronic, education, self help, and patient driven treatments are important. Holistic assessment of the patient’s medical, social, and psychological needs can enable a tailored approach to treatment formulated in partnership with the patient (table). 3 4 The risks and benefits of treatment options should be communicated to patients in ways that can be understood. Periodic monitoring (every three months) for effects of treatment on pain, function, psychological status, and quality of life—as well as metrics of intervention, including body weight and muscle strength—can maximise treatment adherence and enable management to be tailored to the patient’s changing needs. 5
all patients include education and exercise, with weight loss for those who are overweight or obese.

Education about the disease process, pain mechanisms, and treatment options can be delivered in various ways, including informal discussion with the healthcare provider, provision of written materials, support groups, national association websites, and referral to self management programmes. However, meta-analyses show that in isolation these programmes have negligible effect sizes.3

Exercise is essential for all patients, irrespective of disease severity, age, comorbidity, pain severity, or disability. Meta-analyses show small to moderate effect sizes with exercise for pain and function, similar to those achieved with analgesics and non-steroidal anti-inflammatory drugs (NSAIDs).3 A Cochrane review found that, compared with fewer than 12 supervised exercise sessions, 12 or more directly supervised exercise sessions with a health professional significantly improved pain (effect size 0.46) and function (0.45) (pain 0.28, function 0.23). Local muscle strengthening and general aerobic exercise are recommended,2 7 whereas aquatic exercise may be better for people with serious mobility and functional limitations or those who cannot exercise on land.20 Tai chi is gaining popularity, and a systematic review of randomised controlled trials (RCTs) found encouraging but limited and not necessarily high quality evidence of benefit.20 Although exercise is beneficial, sports that involve twisting and high impact activities such as running should be avoided. Instead, advise younger active people who develop osteoarthritis after a knee injury to modify their activity and participate in low impact sports such as cycling, rowing, swimming, and deep water running. Finally, adherence to exercise and physical activity is vital for long term benefits (box 3).8

A meta-analysis of a limited number of RCTs showed that a reduction in body weight of at least 5% at a rate of 0.24% per week over 20 weeks in overweight and obese people improved pain and disability, although the effect sizes were small (0.20-0.23). A high quality RCT also showed that weight loss improved all cause mortality in overweight or obese people with knee osteoarthritis by 10%.21 Furthermore, a computer simulation model of knee osteoarthritis and obesity using national US census and obesity data showed that a 0.6 unit reduction in mean body mass index (about 1.7 kg in a 1.7 m tall person) would reduce total knee replacements over the remaining lifespan of this population by 1.9%.22 Ottawa Panel guidelines have been developed specifically for overweight or obese people with osteoarthritis. These graded recommendations are based on a systematic review of evidence (RCTs, controlled clinical trials, cohort studies, and head to head studies) that consider the strength of evidence and rigour of experimental design. The review showed that, compared with either intervention alone or control, a combination of physical activity (aerobic exercise plus or minus strength training) and a weight reducing diet produced the most benefit on a range of clinical outcomes, with highest level recommendations for pain relief, functional status, strength, and quality of life.23 The panel recommends weight loss before weight bearing exercise is implemented to maintain joint integrity. A recent longitudinal study found that significant weight loss is accompanied by loss of leg muscle tissue and strength, so strengthening exercise should be undertaken alongside weight loss strategies.24 10

A variety of other interventions may be useful depending on the patient’s presentation and preferences. Despite gait aids being widely recommended, the first RCT of cane use has only just been published.25 It found that compared with no cane use, two months of daily cane use reduced pain and improved function (effect size 0.18 and 0.13, respectively). A recent RCT found that, compared with flat insoles, lateral wedge insoles had no effect on symptoms or cartilage loss over 12 months.11 RCTs show that unloading knee braces can improve malalignment and improve symptoms.12 13 but their use in clinical practice has been limited by important patient factors including adherence, comfort, and fitting.12 15 A small number of RCTs have shown that medically directed knee taping by a physiotherapist can reduce pain.1 A systematic review of 12 RCTs found that the addition of passive manual mobilisations to an exercise programme produced superior pain relief (effect size 0.69) to strengthening exercise (0.38) or combination exercise (0.34) alone.13

Because psychological factors can influence the pain experience, interventions such as cognitive behavioural therapy (training in pain coping skills) are recommended for some patients.7 However, the evidence is limited; a meta-analysis identified few clinical trials of cognitive behavioural therapy in knee arthritis and the effect size for pain reduction was small (0.18).14 The number of RCTs of acupuncture in the treatment of osteoarthritis of the knee has increased. These show significant and clinically relevant reductions in pain, although much of this is due to expectation (placebo effects).15 American College of Rheumatology guidelines recommend acupuncture only for patients with moderate to severe pain who are candidates for joint replacement but are unwilling or unable to have the operation.7 Similar recommendations were made for transcutaneous electrical nerve stimulation.7

What drugs are available to control pain in osteoarthritis of the knee?

Analgesics can be useful. Paracetamol (acetaminophen), in doses of up to 4 g/day, is currently recommended for the initial treatment of mild to moderate pain in osteoarthritis of the knee.7 However, because of concerns about the risk of hepatotoxicity, an advisory committee of the US Food and Drug Administration recently recommended that the maximum adult daily dose should be less than 4 g/day and that the content in single doses of over the counter analgesics be limited to 650 mg.31 A systematic review of RCTs that provided a head to head comparison between paracetamol and NSAIDs showed better efficacy and patient preference for NSAIDs, although side effects were greater.3 No good evidence supports one NSAID over another with regard to efficacy for symptoms. Cardiovascular safety concerns with highly potent cyclo-oxygenase-2 selective inhibitors have led to some of these drugs being taken off the market and have drawn attention to similar concerns for non-selective NSAIDs as well as gastrointestinal safety risks. Practitioners must therefore be aware of the warnings, precautions, and contraindications associated with the use of these agents. If it is deemed necessary to prescribe an oral NSAID for people with risk factors for gastrointestinal toxicity, consider the use of a cyclo-oxygenase-2 selective inhibitor or combined use of a non-selective NSAID with a gastroprotective agent (proton pump inhibitor). For people over 75 years, the American College of Rheumatology strongly recommends the use of topical rather than oral NSAIDs (box 4).7 Because some people with osteoarthritis of the knee also have depression and neuropathic pain symptoms (shooting or burning pain, pins and needles), the role of centrally active agents, including selective serotonin and noradrenaline reuptake inhibitors, has been of interest. At this stage, duloxetine is the only agent to have been examined in a high quality RCT.36 In this study, 65% of participants in the duloxetine group reported...
more than a 30% reduction in pain compared with 44% in the placebo group. This was the result of a primary analgesic effect and not elevation in mood or changes in anxiety or depression. These centrally active agents may be useful in subgroups of people with osteoarthritis of the knee.

**Are intra-articular injections beneficial in osteoarthritis?**

Intra-articular corticosteroids are used widely in the management of osteoarthritis of the knee. A Cochrane review found that the reduction in pain lasts for only one to two weeks. Given this short duration of benefit, the cost, and the potential adverse effects, their use may not be merited in a chronic disease such as osteoarthritis. Despite their appeal for use in patients with clinical features of inflammation (such as a large effusion), the evidence to support this is limited. However, they do have a role in patients who also have pseudogout and calcium pyrophosphate dihydrate crystals.

Intra-articular injections of viscosupplements (hyaluronic acid) usually given weekly for three to five weeks, have been extensively researched. A recent meta-analysis found that trials are generally of low quality and that viscosupplementation is associated with a small and clinically irrelevant reduction in pain and an increased risk of serious adverse events. A recent RCT showed a marked carryover effect for at least one year and that symptoms improved between cycles, compared with placebo, suggesting that repeated injection cycles might be effective.

**New drugs for osteoarthritis of the knee**

Newer analgesics, including nerve growth factor inhibitors, are being developed. High quality RCTs have shown that these drugs reduce pain in osteoarthritis of the knee. However, this optimism has been clouded by potential safety concerns—a small number of patients treated with tanezumab have developed rapid joint destruction.

Unfortunately, none of the drugs used in osteoarthritis of the knee has convincing structural disease modifying efficacy. New drugs are being developed for osteoarthritis, with trials mainly testing pro-anabolics (growth factors and hormones), with a
modest selection of anti-catabolics (interleukin 1, inhibitor of xB kinase (IkK)), and inducible nitric oxide synthase inhibitors) and cell therapy (mainly mesenchymal stem cells from bone marrow or adipose tissue).1113

What is the evidence for glucosamine and other complementary medicines?

The most commonly used alternative treatment is glucosamine. In RCTs, glucosamine has a similar effect to placebo on pain, with industry independent trials showing smaller effects than commercially funded ones.1 Evidence for a possible structure modifying effect remains controversial. In contrast, a meta-analysis (just three RCTs over two years’ duration) found that chondroitin had a small effect on symptoms and structure (effect size 0.23).23 A Cochrane review of herbal therapy in osteoarthritis found two studies with promising results for avocado soybean unsaponifiables,23 and there is some low level evidence of efficacy for diacerein, roshup, and methylsulfonylmethane.3 However, high quality trials are urgently needed before any conclusions can be drawn about the usefulness of such treatments. American College of Rheumatology guidelines conditionally recommend that healthcare providers do not use nutritional supplements (such as glucosamine) or topical capsicam.7

What is the role of surgery?

The surgical treatment of choice depends mainly on symptoms, disability, radiographic severity, and the patient’s age. The American Academy of Orthopaedic Surgeons recommends that arthroscopic lavage or debridement (or both) and meniscal resection be performed only in patients with mechanical symptoms, such as sudden onset of inability to fully extend the knee or repeated disabling catching or locking.24 This operation has no demonstrable effect on pain in osteoarthritis of the knee, with the latest RCT showing similar benefits to optimised physical and medical treatment.24

Joint arthroplasty is reserved for patients with severe disease defined as persistent moderate to severe pain, functional limitation, and reduced quality of life despite optimal conservative treatment, together with radiological disease. Patients should be referred to an orthopaedic surgeon at the time when joint replacement is needed and preferably before substantive functional decline has occurred because this may not be regained after surgery. Although there are no RCTs, higher quality prospective studies of consecutive unselected patients find that joint arthroplasty is generally successful, with 80% of patients reporting reductions in pain.616 Weight loss before surgery is important because obesity increases the risk of surgical complications and is associated with poorer longer term outcomes.31 Preoperative exercise for two to three months can optimise the physical status of patients awaiting joint replacement. It is not clear whether this enhances postoperative functional recovery—a recent meta-analysis of 12 quasi-randomised or randomised controlled trials found no benefits.10 However, the authors thought that the exercise programmes in these trials had poor therapeutic validity and that this may have masked the potential benefits.

In patients under 60 years, the main concern in performing joint arthroplasty is implant wear because revision arthroplasty is less successful than primary arthroplasty. Although there is no definitive answer as to how young is too young for this surgical procedure, the decision should be based on whether benefits outweigh risks for each individual. Only low impact activities such as cycling, swimming, and walking are recommended after joint arthroplasty because implant wear seems to be partly related to the amount and type of activity. Alternative operation in younger or more active patients with unicompartimental disease is a high tibial osteotomy, which decreases symptoms, slows down the osteoarthritis process, and delays the need for arthroplasty by unloading the osteoarthritic compartment. A recent meta-analysis of cohort studies found that nine to 12 years after a valgus high tibial osteotomy only 16% of patients had needed joint arthroplasty.23

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Tips for non-specialists

Osteoarthritis of the knee can be reliably diagnosed using clinical signs and symptoms. Screen for the presence of comorbidities such as depression and anxiety and treat if present; consider using duloxetine if depression and neuropathic symptoms present. Although there is no cure, tell patients that disease does not always progress, radiographic findings do not relate to symptoms, and many effective treatments are available. Take a patient centred multidisciplinary approach and encourage patients to self manage their condition. All patients should exercise regularly regardless of the severity of symptoms or radiographic changes; a combination of strengthening and aerobic exercise is recommended. Aquatic exercise may be useful for some people. Advise against high impact physical activities and sports that involve twisting and repetitive loading. Help patients who are overweight or obese to lose weight—a goal of at least 5% of body weight is recommended. Consider referral to skilled therapists to help with physical, dietary, and psychological interventions where appropriate. Start with paracetamol (caution with maximal dose) or non-steroidal anti-inflammatory drugs (NSAIDs), but take into account gastrointestinal and cardiovascular safety concerns and comorbidities. Consider topical NSAIDs in patients over 75 years. Arthroscopic surgery is not useful for treating pain and is reserved for patients with mechanical symptoms, such as locking or catching. Consider referral to an orthopaedic surgeon when patients have severe symptoms, have failed conservative management, and joint replacement is needed—preferably before substantive functional decline has occurred.

Questions for future research

How can we maximise adherence to conservative management options such as exercise?
Can load modifying interventions, such as braces, modified footwear, and gait retraining, slow down disease progression?
How can we improve the uptake of optimal management by healthcare professionals?
What models of care are most effective and cost effective in managing people with osteoarthritis of the knee in different settings?
What is the efficacy of the various complementary and alternative medicines available?
What are the barriers to the implementation of primary prevention measures, such as injury prevention and weight reduction?
Can we identify an effective and safe pain relieving modality?
Can we avoid long term systemic toxicity and identify people at risk of rapid structural progression?
What is the efficacy of the various complementary and alternative medicines available?
What are the barriers to the implementation of primary prevention measures, such as injury prevention and weight reduction?
Can we identify an effective and safe pain relieving modality?
Can we avoid long term systemic toxicity and identify people at risk of rapid structural progression?

Additional educational resources

Resources for healthcare professionals

Osteoarthritis Research Society International (www.oarsi.org)—Recent OARSI guidelines on the management of knee osteoarthritis, together with educational resources, meetings, and a slide library.
National Institute for Health and Clinical Excellence (www.nice.org.uk)—Recent NICE guidelines on the management of knee osteoarthritis.
European League against Rheumatism (www.eular.org)—Recent EULAR guidelines and educational resources, including videos on physical examination of patients with musculoskeletal conditions.
American Academy of Orthopaedic Surgeons (www.aaos.org)—Recent AAOS treatment guidelines for osteoarthritis and educational resources.
American College of Rheumatology (www.rheumatology.org)—Updated treatment guidelines for osteoarthritis released in April 2012.

Resources for patients

Arthritis Foundation USA (www.arthritis.org)—Education for the public, patients, and health professionals.
Arthritis Care United Kingdom (www.arthritis.org.uk)—Education for the public, patients, and health professionals.
10 000 Steps (www.10000steps.org.au)—Free health promotion programme that encourages the use of step counting pedometers to help monitor and increase daily physical activity.

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## Table

### Table 1 | Comprehensive assessment of patients with osteoarthritis of the knee and practical implications for management

<table>
<thead>
<tr>
<th>Assessment elements</th>
<th>Practical implications</th>
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<tbody>
<tr>
<td>Joint symptoms and signs such as joint pain, giving way, stiffness, locking or catching, effusion, range of motion, tenderness on palpation, joint laxity, knee alignment in standing</td>
<td>Helps with differential diagnosis and establishes whether radiography and magnetic resonance imaging are needed (box 2). Neuropathic symptoms (shooting, burning pain, and pins and needles) may indicate need for a centrally active agent. Changes in pain allow assessment of treatment response. If patient has disabling locking or catching consider orthopaedic referral. If giving way and laxity, consider a gait aid, physiotherapy for muscle strengthening, and referral to an orthotist for bracing. If knee malalignment, bracing may be beneficial</td>
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<tr>
<td>Comorbidities such as cardiovascular disease, diabetes, peptic ulcer, renal, liver disease, depression</td>
<td>Influence contraindications and precautions for treatment, in particular prescription of drugs (box 4)</td>
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<tr>
<td>Functional ability, activities of daily living (such as walking, stair climbing, sit to stand, balance), and history of falls</td>
<td>If difficulty with walking, function, balance, or more than 1 fall in past 12 months, consider gait aid, attention to footwear, and referral to a physiotherapist for treatment including exercise prescription and manual therapy. If a varus thrust is seen during walking (visible dynamic worsening of varus alignment during stance phase), consider referral to a physiotherapist for exercise programme and possibly orthotist for bracing</td>
</tr>
<tr>
<td>Muscle mass and strength, particularly of the quadriceps</td>
<td>If weak, prescribe muscle strengthening exercises—consider referral to a physiotherapist or exercise specialist</td>
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<tr>
<td>Foot posture</td>
<td>If abnormalities, consider referral to a podiatrist for orthotics and footwear advice</td>
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<tr>
<td>Psychosocial factors, such as mood disorders (depression and anxiety), sleep, social support, ability to cope, participation in leisure activities, relationships, and employment</td>
<td>If mood disorder present, consider referral to psychologist or prescription of antidepressants such as duloxetine. If difficulty coping or participating, consider referral to appropriate allied health practitioner (such as a psychologist, occupational therapist, social worker) or relevant self help groups for peer support</td>
</tr>
<tr>
<td>Patient’s knowledge, expectations, and goals</td>
<td>Facilitates a patient centred approach to management and communication that is tailored to patient’s needs and goals. Ensure that the patient understands the disease process, has realistic expectations, and participates in treatment decision making by providing education, information, and resources. Consider referral to a self management programme</td>
</tr>
<tr>
<td>Overweight or obesity (weight, body mass index, and waist girth)</td>
<td>If body mass index is &gt;25 or waist is &gt;80 cm (women) or &gt;94 cm (men), counsel about weight loss through both diet and exercise (aerobic and strengthening). If possible, refer to a dietitian for nutritional assessment and weight loss support. Weight loss programmes should aim for a 5-10% reduction</td>
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**Figure**

![Risk factors for osteoarthritis of the knee and related disability. Modified from Suri and colleagues, with permission from Elsevier and the American Academy of Physical Medicine and Rehabilitation.](image)

**Fig 1** Risk factors for osteoarthritis of the knee and related disability. Modified from Suri and colleagues, with permission from Elsevier and the American Academy of Physical Medicine and Rehabilitation.