Osteoarthritis: a story of close relationship between bone and cartilage
Osteoarthritis is the most common form of arthritis and results in pain and reduced quality of life. Although a structure-modifying treatment remains the greatest unmet need in osteoarthritis, several symptomatic treatments are available. This article will review the nonpharmacological approaches and pharmacological treatments currently available for osteoarthritis management, as well as the surgical treatments available for the condition. At present, a multimodal approach combining nonpharmacological and pharmacological treatments is still the best option for the management of osteoarthritis, as recommended in the guidelines of Osteoarthritis Research Society International and the American College of Rheumatology. Nonpharmacological management mainly relies on patient education, exercise, prevention of injuries, weight loss in overweight patients, and use of orthotic devices. Pharmacological symptomatic treatments include a number of analgesic options such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, duloxetine, topical NSAIDs, capsaicin, lidocaine patches, intra-articular corticosteroids and hyaluronic acid injections, and slow-acting drugs including glucosamine and chondroitin sulfate, diacerein, and avocado soybean unsaponifiables. When the combination of nonpharmacological and pharmacological approaches becomes unsuccessful at managing symptoms, surgical treatment may be considered.

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Nonpharmacological management

The combination of patient education, improved muscle strength, and reduced body mass index has been reported to be joint protective. Recent guidelines from the American College of Rheumatology (ACR) strongly recommend weight loss for overweight patients with knee or hip osteoarthritis, as well as cardiovascular and/or resistance land-based exercises and aquatic exercise.\(^1\) No preference is made regarding aquatic versus land-based exercise, as the choice will depend on individual ability. As to date there have been very few high-quality randomized controlled trials reported in the literature, the ACR conditionally recommends self-management programs, manual therapy in combination with supervised exercise, psychosocial interventions, use of thermal agents, walking aids if needed, tai chi, Chinese acupuncture, and transcutaneous electrical stimulation. For hand osteoarthritis, assistive devices, joint protection techniques, thermal modalities, and trapeziometacarpal joint splints are also conditionally recommended by the ACR guidelines.\(^1\)
Patient education
Patient education should form the cornerstone of nonpharmacological management for osteoarthritis, and patients should be involved in the management of their condition as much as possible. Indeed, as with other chronic diseases, patients should know about their condition's evolution over time as well as its management and any associated investigations, and this can be achieved through use of books, regular telephone calls, and education groups. It has been suggested that education contributes to pain reduction and optimization of health care resource usage.

Exercise programs
Physical activity involving aerobic and/or resistance land-based exercises and/or aquatic exercises, including local muscle strengthening and general fitness, is recommended for osteoarthritis patients. Strengthening exercises, especially for the quadriceps femoris muscle, may improve muscular balance, decrease impact loads, and support function, and they have also been reported to reduce pain and disability in hip and knee osteoarthritis. Water-based exercises have been shown to have short-term effects on pain relief for patients with hip and/or knee osteoarthritis. In addition, contrary to popular belief, running—even long distances—as part of normal nonprofessional conditioning does not accelerate the development of osteoarthritis of the knee. However, the risk of osteoarthritis development may be different for middle-intensity levels of running compared with high or competitive levels: moderate regular running may be safe, whereas professional runners may have an increased risk for osteoarthritis.

Prevention of injuries
Prevention of injuries is necessary in contact sports such as soccer. Increased joint traumatisms such as anterior cruciate ligament lesions or meniscal lesions increase the risk of developing osteoarthritis. Effective treatment such as postoperative rehabilitation should decrease this risk.

Weight loss
Does weight loss reduce osteoarthritis symptoms and prevent overall progression of structural damage? This is a most important and relevant question in the management of osteoarthritis. In obese patients, weight loss and maintenance of weight at a lower level seems to reduce osteoarthritis-related pain. Weight loss in obese people was reported to improve the content of the macromolecule proteoglycan in the cartilage, as well as the cartilage thickness in the medial, but not lateral, compartment of the knee. Interestingly, obesity increases the risk of progressive osteoarthritis in neutrally aligned knees or those in valgus alignment, but not in patients with varus alignment. Thus, overload alone across the joints does not seem to be sufficient to induce the development of osteoarthritis. As obese individuals also have a higher incidence of osteoarthritis in non-weight-bearing areas, including finger joints, it has been suggested that factors such as adipokines, one representative of this family being leptin, could promote cartilage damage, thus inducing osteoarthritis. Therefore, although mechanical factors may be one element favoring the development of osteoarthritis in obese patients, inflammatory mediators also appear to be important contributing factors. Thus, in addition to weight loss, additional treatments may eventually be required for optimal therapeutic intervention.

Orthotic devices
Orthotic devices such as special footwear, insoles, knee bracing, and canes are recommended for patients with hip and/or knee osteoarthritis. The latest ACR guidelines recommend medially-directed patellar taping, as well as medially-wedge insoles for patients with lateral compartment knee osteoarthritis, and laterally-wedge subtalar strapped insoles for those with medial compartment knee osteoarthritis. Canes held in the contralateral hand as a walking aid can reduce pain in patients with hip and knee osteoarthritis. In knee osteoarthritis, use of braces and sleeves was shown to have beneficial effects compared with medical treatment alone (acetylaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs)), as assessed by the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and function tests. Moreover, braces seem to be more effective than sleeves, and laterally-wedge insoles may decrease NSAID intake compared with neutral insoles.

Alternative therapies
Acupuncture and transcutaneous electrical stimulation have been reported to show some short-term pain relief efficacy, and they are considered alternative strategies for the management of osteoarthritis. These strategies are conditionally recommended by the ACR guidelines for those patients with knee osteoarthritis who are candidates for total knee arthroplasty but are unwilling or unable to undergo surgery because of comorbidities or concomitant medications contraindicating such surgery.

Pharmaceutical treatment
The prescribing habits of physicians have changed over time. Because osteoarthritis is a chronic disease and is more common in people aged over 60 years, safety remains critical. Guidelines for the medical management of osteoarthritis fo-
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<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Adverse effect/safety profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Acetaminophen</td>
<td>GI discomfort, bleeding; renal failure; hypertension; hepatotoxicity</td>
</tr>
<tr>
<td>NSAIDs; coxibs</td>
<td>GI ulcer/bleeding; cardiovascular events; renal events</td>
</tr>
<tr>
<td>Opioids</td>
<td>Constipation; vomiting; somnolence; increased risk of fracture, morbidity, and mortality in elderly</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Constipation; nausea; hyperhidrosis</td>
</tr>
<tr>
<td>Topical Topical NSAIDs</td>
<td>Skin reactions; GI events</td>
</tr>
<tr>
<td>Capsaicin</td>
<td>Skin burning sensation; long-term skin desensitization?</td>
</tr>
<tr>
<td>Lidocaine patches</td>
<td></td>
</tr>
<tr>
<td>Injectable Intra-articular corticosteroids</td>
<td>Local infection, systemic effects</td>
</tr>
<tr>
<td>Intra-articular hyaluronic acid or viscosupplementation</td>
<td>Local reactions at the site of injection, swelling, flares of pain</td>
</tr>
<tr>
<td>Slow-acting symptomatic drugs Oral Glucosamine and chondroitin sulfate</td>
<td>„„</td>
</tr>
<tr>
<td>Diacerein</td>
<td>Lower GI effects</td>
</tr>
<tr>
<td>Avocado soybean unsaponifiables</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Adverse effects of different pharmacological options for the treatment of osteoarthritis. Abbreviations: GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug.

 succeeded on controlling pain and improving function and quality of life while minimizing therapeutic toxicity (see Table 1 for an overview of the adverse effects of the different pharmacological treatments available).[2,3,17] For hand osteoarthritis, the recent ACR guidelines recommend topical capsaicin, topical NSAIDs, oral NSAIDs including cyclooxygenase (COX)-2 inhibitors, and tramadol.[1] They also advise against the use of opioids or intra-articular treatments for this condition. For knee and hip osteoarthritis, acetaminophen, oral NSAIDs, topical NSAIDs (except for hip osteoarthritis), tramadol, and intra-articular steroid injections are recommended.[1]

### Symptomatic treatments

#### Oral analgesics
Acetaminophen remains the first-line therapeutic agent for mild-to-moderate pain[2,3,15] because of its low cost and its efficacy and safety profile for doses not exceeding 4 g per day (although a maximum of 3 g is more advisable, in line with US Food and Drug Administration recommendations). If found to be successful at alleviating pain, it is recommended that acetaminophen be the preferred long-term oral analgesic.2 It has been reported that acetaminophen is less effective at relieving osteoarthritis pain than NSAIDs[13] but more effective than placebo.26 However, this result was not confirmed by a study using WOMAC and the Lequesne index to assess efficacy.27

The use of analgesics in osteoarthritis should take into account the clinical context, however. Significant adverse effects have been reported with acetaminophen, including gastric ulcerations and bleeding, increased risk of mild loss of renal function with long-term consumption, and hypertension with doses of up to 3 g per day.25,29 Furthermore, even at therapeutic dos-

es, acetaminophen can cause asymptomatic elevation of liver enzymes in healthy people.24 The implications of this remain unclear, but it is recommended that acetaminophen should not be used in patients with existing liver dysfunction or related risk factors. On the basis of the aforementioned information, it is recommended that the lowest effective dose of acetaminophen be used for pain relief.

NSAIDs are generally recommended for patients who are unresponsive to appropriate dosages of acetaminophen. These should be prescribed at the lowest dose and for the shortest possible duration,17 and preferentially for inflammatory flares. According to the new ACR guidelines,1 NSAIDs should be used for the initial management of hand, hip, and knee osteoarthritis, as with acetaminophen and tramadol. Moreover, for patients aged over 75 years, rather than prescribing oral NSAIDs, guidelines recommend the use of topical NSAIDs, dicyclomine, tramadol, or intra-articular hyaluronan injections. In patients suffering from upper gastrointestinal ulcers without any gastrointestinal bleeding in the prior year, for cases where the physician chooses to prescribe an NSAID, the ACR and Osteoarthritis Research Society International (OARSI) guidelines recommend the use of either a COX-2 inhibitor rather than a nonselective NSAID, or a nonselective NSAID combined with a proton-pump inhibitor.11,17 For patients with reports of gastrointestinal bleeding within the past year, the use of a COX-2 inhibitor in association with a proton-pump inhibitor is recommended.1 Although NSAIDs are known to be superior to acetaminophen for pain relief,14 their use is limited by a number of adverse effects, including gastrointestinal, renal, and cardiovascular adverse effects, which increase with...
The risk level varies according to the drug and dosage. COX-2 inhibitors were shown to be as effective as convention-
al NSAIDs for pain relief, with fewer gastrointestinal compli-
cations, but with a potential cardiovascular risk—which is
also shared by conventional NSAIDs. Physicians should there-
fore take into account their patients’ comorbidities and as-
sess their individual global risk before prescribing NSAIDs.

In recent years, opioids have become a widely prescribed
class of drugs, especially for osteoarthritic patients who either
have contraindications or an intolerance to NSAIDs or who
have failed to respond to both acetaminophen and NSAID
treatment. Opioids are recommended by the new ACR
guidelines for patients with symptomatic knee osteoarthritis
who have not had an adequate response to nonpharma-
cological or pharmacological modalities and are either unwilling
to undergo or are not candidates for total joint arthroplasty. However, opioids are not recommended for the management
of hand osteoarthritis-related pain. It is common to start with
a weak opioid such as codeine or tramadol, often in combi-
nation with acetaminophen, and if ineffective or not tolerated,
to use a stronger opioid like hydrocodone, oxycodone, mor-
phine, or transdermal fentanyl. However, adverse events
are frequent and significant, and include sedation, constipation,
urinary retention, nausea and vomiting, respiratory depression,
and confusion. Impaired coordination and judgment can lead
to falls, particularly in older adults who are more susceptible
to opioid-related effects as a result of renal insufficiency and/or
lower lean body mass. In elderly people, opioids may cause
severe injuries from falls, such as hip fractures, or even death.
Fracture risk appears to be greater with opioids than with
NSAIDs in older people, and the risk increases with higher opi-
od dosage, especially during the first 2 weeks after initiating
short-term opioid therapy. Moreover, it seems that opioids
do not improve patient functioning or quality of life.

Patients with osteoarthritis have been shown to have higher
mortality than the general population, particularly because of
vascular events in the knees. This appears to be strongly related to
walking disability and reduced physical activity. Thus, immo-
Bility resulting from osteoarthritis may shorten lifespan. One
may wonder if opioids, by reducing patient mobility, may re-
duce life expectancy by increasing cardiovascular risk. How-
ever, this relationship has not yet been established. The use
of opioids in a chronic and painful disease such as osteoarthri-
tis is still controversial for many reasons. It is recommended
that opioid treatment be started at a low dose and gradually
adjusted upwards, taking into account renal function, age, and
other relevant risk factors. Long-term opioid use should be
avoided or at least regularly reevaluated. The benefits of us-
ing opioids should be weighed as judiciously as possible.
For the past few years, antidepressants have been used in
chronic pain management because of their reported analgesic
action, which is independent of their antidepressive effect. In
recent years, the chronic pain often observed in osteoarthritis
has been shown to involve centrally-mediated pain pathway
dysfunction, which has led to the study of drugs that have a
centrally-mediated action. Duloxetine is a selective serotonin
and norepinephrine reuptake inhibitor with central nervous sys-
tem activity that is already used in three chronic pain condi-
tions: diabetic peripheral neuropathic pain, fibromyalgia, and
chronic low back pain. Recently, duloxetine was found to im-
prove pain as well as function in knee osteoarthritis, as evalu-
ated by clinically relevant outcomes in two 13-week trials.
The drug’s effect is related to a direct analgesic effect, inde-
dendent of improvement of depression and anxiety. The main
adverse events reported included nausea, constipation, and
hyperhidrosis. Duloxetine is recommended by the ACR guide-
lines as an alternative treatment for patients with symptomatic
knee osteoarthritis who have failed to respond to both phar-
macological and nonpharmacological options. Controlled
trials to compare duloxetine with other interventions in os-
teoarthritis and to evaluate its efficacy in combination with
other therapies may be useful to potentially enhance treat-
ment options.

Topical treatments
Adjuvant topical therapies are interesting treatments that can
be used to decrease the consumption of analgesics. Topical
NSAIDs, such as diclofenac and ketoprofen, seem to be as
effective as oral NSAIDs but with a lower risk of systemic
exposure and gastrointestinal complications. Their principal
reported adverse effect is local skin reactions. They are rec-
ommenced as alternative or adjuvant therapy, although ACR
guidelines recommend them for the initial management of knee
osteoarthritis and prefer them to oral NSAIDs for patients old-
er than 75 years of age.

Capsaicin, the active principle ingredient of hot chili peppers,
can cause depletion of substance P from sensory nerve end-
ings and reduce or abolish the transmission of painful stimuli.
However, its effectiveness and safety in pain relief remains con-
troversial. A burning sensation is the most common adverse
effect, particularly during the first week of application. It is
still unclear if long-term capsaicin treatment can cause per-
sistent desensitization of the skin that may not be totally re-
versible. Capsaicin is recommended by guidelines for the
initial management of hand osteoarthritis, but not knee os-
teoarthritis.

Lidocaine patches, which are approved for postherpetic neu-
ralgia, have also been reported to reduce neuropathic pain as-
associated with moderate to severe osteoarthritis of the knee,
without any reported treatment-related adverse effects.

Injectable therapies
Intra-articular injection of a long-acting corticosteroid is rec-
ommended for relief of pain from osteoarthritic flares, especial-
ly if accompanied by effusion and when NSAIDs are ineffec-
The ACR guidelines recommend intra-articular corticosteroid injections for the initial management of knee and hip osteoarthritis. Short-term pain reduction in knee osteoarthritis occurs after 2 to 3 weeks, but has no significant effect on function. The Cochrane Database of Systematic Reviews reported that after 4 weeks, there was no effect on pain, physical function, or stiffness. However, repeated injections of intra-articular corticosteroids every 3 months for 2 years showed pain relief efficacy after 1 year but not after 2 years. The long-term safety of repeated intra-articular steroid injections in symptomatic knee osteoarthritis has been demonstrated, with improvement of osteoarthritis symptoms for up to 2 years. Comparisons between corticosteroids have revealed that triamcinolone hexacetonide is superior to beta-methasone. Viscosupplementation could have a significant benefit for knee osteoarthritis, despite some reported local acute reactions such as transient pain and swelling at the injection site. Viscosupplementation is recommended by guidelines for knee osteoarthritis, and compared with intra-articular corticosteroids, it shows delayed but prolonged efficacy. The OARSI guidelines consider that intra-articular hyaluronic injections may be useful for the treatment of knee osteoarthritis and have a beneficial symptomatic effect. Moreover, the ACR guidelines conditionally recommend viscosupplementation for patients who have had an inadequate response to initial therapy. By contrast, a single injection of hyaluronic acid in hip osteoarthritis seems to be no more effective than placebo. More data are needed on the structural effect of viscosupplementation.

**Symptomatic slow-acting drugs for osteoarthritis**

Disease-modifying agents that not only reduce joint pain but also slow progression of the disease are of interest for alleviation of the manifestations of osteoarthritis over the long term. For the past 10 years, chondroitin sulfate and glucosamine sulfate have been widely prescribed and used by osteoarthritis patients for symptom relief. They are safe, and have possible structure-modifying effects. Glucosamine is a naturally occurring amino monosaccharide, and chondroitin sulfate belongs to the group of glycosaminoglycans and is a major component of the articular cartilage.

In osteoarthritis clinical trials, the symptomatic effect size of glucosamine varies and is considered controversial. However, the results of studies have greatly depended on the different products used, the study population, and study design and quality. Formulations of glucosamine that result in lower plasma concentrations and potential low bioavailability, as well as study populations with a low baseline level of pain, may have contributed to the controversy. Glucosamine sulfate and chondroitin sulfate have been approved as drugs for the treatment of osteoarthritis in Europe, but not in North America, where they are regulated not as drugs but as nutraceuticals. As a consequence, substantial variation in their content is possible. This explains why in the latest ACR guidelines, these agents were not recommended for treatment of osteoarthritis. Glucosamine sulfate was found to be effective as an osteoarthritis pain relief treatment and for improvement of function. Recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system concluded that glucosamine sulfate demonstrated pain reduction and improvement in physical function with very low toxicity and with moderate-to-high-quality evidence. The latest OARSI guidelines recommend the use of glucosamine sulfate and chondroitin sulfate for osteoarthritis treatment, as they demonstrated pain relief with a moderate to large effect size (0.58 and 0.75, respectively). When a purified preparation of glucosamine sulfate is used, it appears to be safe—in particular, with no induction of glucose intolerance in healthy adults.

The protective effect of glucosamine sulfate on structural progression of knee osteoarthritis was reported in two studies exploring the radiological progression of knee osteoarthritis after daily administration of glucosamine sulfate for 3 years. Chondroitin sulfate has been shown to improve knee joint swelling and delay radiographic progression in patients with knee osteoarthritis evaluated by x-rays, and more recently a magnetic resonance imaging study reported that chondroitin decreases cartilage loss and the progression of bone marrow lesions. A recent post-hoc analysis of an osteoarthritis clinical trial reported a trend favoring chondroitin sulfate versus placebo for delayed occurrence of total knee replacement at 4 years. However, the structural effects of glucosamine and chondroitin sulfate remain under debate, and these treatments are not registered as structure-modifying agents.

Diacepin, an inhibitor of interleukin-1β, is a slow-acting agent with pain-relieving symptomatic effects in patients with knee osteoarthritis, and which also reduces the progression of hip osteoarthritis. Diacepin provides sustained pain relief for several weeks after discontinuation, suggesting a long carry-over effect, and an analgesic-sparing effect. Moreover, the effect of diacepin has been found to be additive to that of NSAIDs. Interestingly, it does not inhibit cyclooxygenase or prostaglandin E2. Loose stools and diarrhea are the most frequent adverse events. It is safer for the upper gastrointestinal system than NSAIDs and has a good overall safety profile, and it is therefore an alternative option to NSAIDs for the treatment of osteoarthritis.

Avocado soybean unsaponifiables (ASU) are fractions of unsaponifiable avocado and soybean oils. The symptomatic efficacy of ASU has been assessed in patients with hip and knee osteoarthritis. ASU seems to be effective at pain reduction and has shown some beneficial effects on clinical symptoms of knee and hip osteoarthritis, with a carry-over effect that persists after treatment discontinuation. A recent study reported that in hip osteoarthritis, a 3-year treatment with ASU reduced the percentage of joint space width progressors, indicating a potential structure-modifying effect.
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**Figure 1.** Multimodal management of osteoarthritis.

*Abbreviations: COX, cyclooxygenase; NSAID, nonsteroidal anti-inflammatory drug; SYSADOA, symptomatic slow-acting drugs for osteoarthritis.*

**Surgical treatment**

Initial treatment of osteoarthritis should be conservative. However, when pain and loss of function persist after the use of appropriate nonpharmacological and pharmacological treatments, surgery should be considered to reduce disease morbidity. Surgical options for knee osteoarthritis are arthroscopy, including lavage and debridement (the efficacy of which is controversial), cartilage repair surgery (bone marrow stimulating techniques, transplantation of osteochondral grafts), osteotomy with axis correction, and arthroplasty (unicondylar knee arthroplasty [UKA] and total joint replacement). Arthroscopy is a minimally invasive surgical technique used for chondral surface debride ment, lavage of joints, removal of torn meniscal fragments, and repair of menisci and cruciate ligament injuries. It remains controversial because it usually provides a short-term benefit and does not seem to delay progression to joint replacement. Arthroscopy should be of interest for selected patients such as those with symptomatic meniscal

**Figure 2.** Multimodal management of osteoarthritis: initiate with nonpharmacological approaches (blue), follow with pharmacological treatments (pink), and if ineffective, culminate in surgery (green).

*Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; SYSADOA, symptomatic slow-acting drugs for osteoarthritis.*

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonpharmacological</strong></td>
<td>Education; exercise; injury prevention; weight loss; orthotic devices</td>
</tr>
<tr>
<td>Pharmacological</td>
<td>Acetaminophen</td>
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<td>NSAIDs and COX-2 inhibitors</td>
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<td></td>
<td>Opioids</td>
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<td></td>
<td>Duloxetine</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>Topical NSAIDs</td>
</tr>
<tr>
<td>drugs</td>
<td>Capsaicin</td>
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<td></td>
<td>Lidocaine patches</td>
</tr>
<tr>
<td>Injectable</td>
<td>Intra-articular corticosteroids</td>
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<td></td>
<td>Intra-articular hyaluronic acid or visco supplementation</td>
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<tr>
<td>Slow-acting</td>
<td>Glucosamine and chondroitin sulfate</td>
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<tr>
<td>symptomatic</td>
<td>Diacerein</td>
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<tr>
<td>drugs</td>
<td>Avocado soybean unsaponifiables</td>
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<tr>
<td>Surgical</td>
<td>Arthroscopic: lavage and debridement; cartilage repair; osteotomy with</td>
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<tr>
<td></td>
<td>axis correction; arthroplasty (UKA, TKR, THR)</td>
</tr>
</tbody>
</table>

**Table II.** Multimodal approach to osteoarthritis management involving nonpharmacological, pharmacological, and surgical treatment options.

*Abbreviations: COX, cyclooxygenase; NSAID, nonsteroidal anti-inflammatory drug; THR, total hip replacement; TKR, total knee replacement; UKA, unicondylar knee arthroplasty.*
<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Intervention</th>
<th>OARSI effect size* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td></td>
<td>0.06 (0.03, 0.10)</td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td>0.32 (0.23, 0.42)</td>
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<tr>
<td>Nonpharmacological</td>
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<td>0.52 (0.34, 0.70)</td>
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<tr>
<td>Strengthening for knee</td>
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<td>0.38 (0.08, 0.68)</td>
</tr>
<tr>
<td>Aerobic for knee</td>
<td></td>
<td>0.19 (0.04, 0.35)</td>
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<tr>
<td>Exercises for hip</td>
<td></td>
<td>0.20 (0.00, 0.39)</td>
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<td>In water for hip and knee</td>
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<tr>
<td>Prevention of injuries</td>
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<td></td>
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<tr>
<td>Weight loss</td>
<td>Acetaminophen</td>
<td>0.14 (0.05, 0.22)</td>
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<tr>
<td>Orthotic devices</td>
<td>NSAIDs and COX-2 inhibitors</td>
<td>0.29 (0.22, 0.35)</td>
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<tr>
<td>Pharmacological</td>
<td>Opioids</td>
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<td>Oral</td>
<td>Duloxetine</td>
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<tr>
<td>Symptomatic drugs</td>
<td>Topical NSAIDs</td>
<td>0.44 (0.27, 0.62)</td>
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<td>Topical</td>
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<tr>
<td>Injectable</td>
<td>Lidocaine patches</td>
<td>0.58 (0.34, 0.75)</td>
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<tr>
<td>Symptomatic slow-acting osteoarthritis drugs</td>
<td>Intra-articular corticosteroids</td>
<td>0.60 (0.37, 0.83)</td>
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<tr>
<td>Injectable</td>
<td>Glucosamine sulfate</td>
<td>0.58 (0.30, 0.87)</td>
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<tr>
<td>Oral</td>
<td>Glucosamine hydrochloride</td>
<td>-0.02 (-0.15, 0.11)</td>
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<tr>
<td>Arthroscopic lavage and debridement</td>
<td>Chondroitin sulfate</td>
<td>0.75 (0.50, 1.01)</td>
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<td>Osteotomy with axis correction</td>
<td>Diacerein</td>
<td>0.24 (0.08, 0.39)</td>
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<tr>
<td>Arthroplasty (UKA, TKR, THR)</td>
<td>Avocado soybean unsaponifiables</td>
<td>0.38 (0.01, 0.76)</td>
</tr>
<tr>
<td>Surgical</td>
<td>21 (0.12, 0.54)</td>
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</tbody>
</table>

*An effect size of 0.2 is considered small, while 0.5 is considered moderate, and >0.8 is considered large.

**Table III.** Multimodal management of osteoarthritis and effect size of the different components of the 2010 guidelines from Osteoarthritis Research Society International (OARSI).

Abbreviations: CI, confidence interval; COX, cyclooxygenase; NSAID, nonsteroidal anti-inflammatory drug; THR, total hip replacement; TKR, total knee replacement; UKA, unicompartmental knee arthroplasty.


Tears, in whom it can be used to remove the degenerative fragments and alleviate mechanical symptoms. Bone marrow stimulation through the use of a microfracture technique induces subchondral injury and bleeding that may promote chondrogenesis by mesenchymal stem cells in the defective area. Its efficacy is uncertain, however, because of variability in the volume of cartilage repair that has been achieved, as well as possible functional deterioration.32

Patients with unicompartmental osteoarthritis of the knee can be treated with a correction osteotomy17 or unicompartmental or total knee arthroplasty (TKA). Osteotomy can be considered when knee osteoarthritis is associated with valgus or varus deformations. It transfers load-bearing from the pathological compartment of the knee to the normal compartment in order to reduce pain and delay joint replacement. Nevertheless, its longevity is limited, and conversion to total knee replacement often occurs within the following few years. UKA seems to be as safe and effective for pain relief and functional improvement as TKA, as well as high tibial osteotomy in patients with unicompartmental knee osteoarthritis.31 Long-term survival rates with UKA are variable but are reported to be around 90% at 10 years, which is less than for TKA (up to 98% at 15 years), except in younger patients.31 TKA remains a success-
ful treatment for end-stage symptomatic knee osteoarthritis, especially in elderly patients. The main complications are per-
sistent postoperative pain (especially in the femoropatellar compartment), infections, and stiffness of the knee. In order to improve outcomes with TKA, computer-assisted navigation and minimally invasive techniques are being developed.

The choice of surgical treatment may be based on level of pain and physical function, disease stage, patient age, and comor-
bidities. No specific cut-off point defining the requirement for joint replacement currently exists.64 However, the aim of a surgical intervention for osteoarthritis such as joint replace-
ment should be to restore patient mobility and give the pa-
tient enough capacity to perform the level of activity required to help prevent cardiovascular diseases.

Conclusion

Clinicians managing osteoarthritis are able to draw upon a wide spectrum of therapeutic options, combining nonphar-
macological approaches and pharmacological treatments both to relieve pain and to attempt to delay disease progress-
ion (Figures 1 and 2; Table II, page 177), as recommended by the OARSI (Table III) and ACR guidelines. The trade-off be-
tween benefits and adverse effects should always be considered when choosing an appropriate treatment from among the
available agents. The current therapeutic options, how-
ever, are neither exclusive nor sufficient. Thus, the focus is moving toward developing disease-modifying osteoarthritis
drugs that can be taken in association with conventional therapeutic strategies to provide more effective treatment of
osteoarthritis.

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