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In the Clinic®

Knee Osteoarthritis

Knee osteoarthritis (OA) typically presents with joint pain that is exacerbated by use and alleviated with rest. There is relatively brief, self-limited morning stiffness and absence of constitutional symptoms. Overweight and obesity are the most important modifiable risk factors. Although pharmacologic and nonpharmacologic interventions are generally effective at alleviating pain and improving physical function, they do not fundamentally reverse the pathologic and radiographic process of knee OA. As the severity of disease increases, the magnitude of pain and functional impairment intensifies. Surgical intervention should be pursued to relieve pain and restore functionality only when nonpharmacologic approaches and pharmacologic agents fail to control pain.

Prevention

Diagnosis and Assessment

Treatment

CME/MOC activity available at Annals.org.

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Osteoarthritis (OA), the leading form of arthritis among aging adults, is a consequence of progressive structural compromise to articular components, particularly cartilage but also affecting adjoining bone, synovial lining, and periarticular muscle (1, 2). One may conceptualize OA development as a biomechanical process whereby joints respond pathologically to mechanical stress, resulting in cartilage degradation and remodeling of subchondral bone. Conceptually, an overt injury (such as an anterior cruciate ligament tear) or unseen repetitive injury (due to obesity or overuse) induces cartilaginous compromise, bone remodeling, periarticular muscle weakness, and abnormal joint mechanics that together result in OA.

Although OA may affect many joints of the appendicular and axial skeleton, some joint sites have a strong predilection for involvement, particularly the knee (3, 4). Knee OA is a major cause of joint pain, impaired function, and limitation of engagement in routine activities of daily living (ambulating on a level surface, ascending and descending stairs) and is a leading cause of disability in the aging population in the United States and worldwide. The global prevalence of all OA increased by about 100% between 1990 and 2019, from an estimated 250 million to 500 million (5). Notably, OA of the knee joint has contributed more to the global burden of OA than any other site (5). Substantial direct and indirect costs are associated with knee OA, such as impaired work-related productivity and quality-adjusted life-years lost (6). Direct costs attributable to direct medical care, therapeutic interventions, and comorbidity burden are approximately double compared with those among persons without knee OA (7, 8).

As humans age from early to middle adulthood and then to later adulthood, the incidence and prevalence of knee OA increase (9). With the aging of the U.S. population, the effect of knee OA on the health care system has grown substantially. The volume of total knee replacement surgeries is projected to increase substantially, to several million procedures annually across the United States by 2030 (10, 11). Understanding risk factors for the development and progression of knee OA and optimal nonpharmacologic and pharmacologic strategies to manage knee OA is critical. Achieving proficiency in the medical management of knee OA and confidence in when to refer patients for surgical intervention is a priority for this expanding public health problem.

Prevention

What are the major risk factors for knee OA?

Knee OA is not an inevitable consequence of aging; predisposing factors play a key role in its development. Disease susceptibility is influenced by genetic inheritance, age, and gender (3, 4), with age as the most important risk factor. With each advancing decade in adulthood, the incidence and prevalence of knee OA increase (9, 12). Studies of twins have shown that 39% of risk for knee OA results from genetic factors (13). Susceptibility loci for OA have been identified in genome-wide association studies (14).

Gender is strongly related to knee OA—prevalence in women is nearly twice that in men (5, 12). Although OA occurs worldwide, geographic and ethnic differences in population burden have been noted. The prevalence of knee OA is similar among Europeans and Americans; however, older Chinese women in Beijing have a higher prevalence of knee OA than White women in Framingham, Massachusetts (15). Notably, the worldwide prevalence of

1. Felson DT, Lawrence RC, Dieppe PA, et al. Osteoarthritis: new insights. Part 1: The disease and its risk factors. Ann Intern Med. 2000;133:635-646. [PMID: 11033593]
2. Felson DT, Lawrence RC, Hochberg MC, et al. Osteoarthritis: new insights. Part 2: Treatment approaches. Ann Intern Med. 2000;133:726-737. [PMID: 11074906]
3. Sharma L. Osteoarthritis of the knee. N Engl J Med. 2021;384:51-59. [PMID: 33406330]
4. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet. 2019;393:1745-1759. [PMID: 31034380]
5. Long H, Liu Q, Yin H, et al. Prevalence trends of site-specific osteoarthritis from 1990 to 2019: findings from the Global Burden of Disease Study 2019. Arthritis Rheumatol. 2022;74:1172-1183. [PMID: 35233975]
6. Menon J, Mishra P. Health care resource use, health care expenditures and absenteeism costs associated with osteoarthritis in US healthcare system. Osteoarthritis Cartilage. 2018;26:480-484. [PMID: 29269328]
7. Bedenbaugh AV, Bonafede M, Marchlewicz EH, et al. Real-world health care resource utilization and costs among US patients with knee osteoarthritis compared with controls. Clinicoecon Outcomes Res. 2021;13:421-435. [PMID: 34054301]
8. Jin X, Liang W, Zhang L, et al. Economic and humanistic burden of osteoarthritis: an updated systematic review of large sample studies. Pharmacoeconomics. 2023;41:1453-1467. [PMID: 37462839]
9. Nguyen U-SDT, Zhang Y, Zhu Y, et al. Increasing prevalence of knee pain and symptomatic knee osteoarthritis: survey and cohort data. Ann Intern Med. 2011;155:725-732. [PMID: 22147711]
10. Carr AJ, Robertsson O, Graves S, et al. Knee replacement. Lancet. 2012;379:1331-1340. [PMID: 22398175]
11. Shan L, Shan B, Suzuki A, et al. Intermediate and long-term quality of life after total knee replacement: a systematic review and meta-analysis. J Bone Joint Surg Am. 2015;97:156-168. [PMID: 25609443]

knee OA increased substantially between 1990 and 2019 (5, 16).

Joint trauma to the knee and repetitive occupational and leisure time joint stress are also associated with knee OA (17, 18). Local mechanical factors, including malalignment, muscle weakness, and prior joint injury, facilitate development and progression of knee OA (19, 20). Excessive joint loading can be affected by obesity, internal derangements, and occupations with repetitive bending (9, 12) and increases the likelihood of development or progression of OA. One study found that the presence of valgus knee alignment was related to a 50% increase in incidence, whereas varus alignment was associated with a 2-fold increase in incident knee OA (21). This association was present among adults with overweight and obesity and absent among those with normal body mass index (21). In addition, radiographic leg-length inequality has been found to be related to incidence and progression of knee OA (22).

As little as 5 degrees of genu varum (bowlegged) malalignment results in an estimated 70% to 90% increase in compressive loading of the medial knee compartment (19). This corresponds to a 4-fold increase in risk for worsening OA of the medial knee over 18 months of follow-up (19). Conversely, genu valgum (knock-kneed) malalignment markedly increases compressive load on the lateral compartment of the knee, elevating the risk for lateral OA progression by 5-fold.

Should weight and physical activity be modified to prevent knee OA or alter its progression?

Overweight and obesity are the most important modifiable risk factors for incidence and progression of knee OA (12, 17, 23). Mechanistically, higher body weight in young adulthood is predictive of development of knee OA decades later (24). As the prevalence of obesity has increased substantially across the United States in recent decades, a priority in the primary prevention of knee OA is to counsel patients with overweight and obesity to lose weight (12, 23).

Physical activity should be pursued in a manner that minimizes the potential for injury. Patients should be advised to use graduated training schedules, use appropriate conditioning programs, and avoid intense loading of previously injured joints. Contact sports may particularly increase risk for meniscus tears and cruciate ligament injury, which are known to predispose people to knee OA (20, 25).

Quadriceps weakness decreases the ability of muscle to distribute load across the knee joint and maintain joint stability. Moreover, weakness of the quadriceps muscles may predate onset of knee OA and contribute to its development (26). Conceptually, quadriceps strengthening via exercise may diminish the risk for knee OA (27).

Prevention... Older persons and women are at greater risk for knee OA. Overweight and obesity are the most important modifiable risk factors for knee OA. Persons participating in sports should engage in proper training and conditioning to avoid musculoskeletal injury. Regular exercise is encouraged to maintain quadriceps strength.

CLINICAL BOTTOM LINE

12. Prieto-Alhambra D, Judge A, Javaid MK, et al. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. Ann Rheum Dis. 2014;73:1659-1664. [PMID: 23744977]
13. Spector TD, Cicuttini F, Baker J, et al. Genetic influences on osteoarthritis in women: a twin study. BMJ. 1996;312:940-943. [PMID: 8616305]
14. Zeggini E, Panoutsopoulou K, Southam L, et al; arcOGEN Collaborators. Identification of new susceptibility loci for osteoarthritis (arcOGEN): a genome-wide association study. Lancet. 2012;380:815-823. [PMID: 22763110]
15. Zhang Y, Xu L, Nevitt MC, et al. Comparison of the prevalence of knee osteoarthritis between the elderly Chinese population in Beijing and whites in the United States: the Beijing Osteoarthritis Study. Arthritis Rheum. 2001;44:2065-2071. [PMID: 11592368]
16. Yang G, Wang J, Liu Y, et al. Burden of knee osteoarthritis in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. Arthritis Care Res (Hoboken). 2023;75:2489-2500. [37221154]
17. Silverwood V, Blagojevic-Bucknall M, Jinks C, et al. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage. 2015;23:507-515. [25447976]
18. Lohmander LS, Ostenberg A, Englund M, et al. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. Arthritis Rheum. 2004;50:3145-3152. [PMID: 15476248]
19. Sharma L, Song J, Felson DT, et al. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. JAMA. 2001;286:188-195. [PMID: 11448282]
20. Gelber AC, Hochberg MC, Mead LA, et al. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. Ann Intern Med. 2000;133:321-328. [PMID: 10979876]

21. Brouwer GM, van Tol AW, Bergink AP, et al. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. Arthritis Rheum. 2007;56:1204-1211. [PMID: 17393449]
22. Harvey WF, Yang M, Cooke TDV, et al. Association of leg-length inequality with knee osteoarthritis: a cohort study. Ann Intern Med. 2010;152:287-295. [PMID: 20194234]
23. Zhou ZY, Liu YK, Chen HL, et al. Body mass index and knee osteoarthritis risk: a dose-response meta-analysis. Obesity (Silver Spring). 2014;22:2180-2185. [PMID: 24990315]
24. Gelber AC, Hochberg MC, Mead LA, et al. Body mass index in young men and the risk of subsequent knee and hip osteoarthritis. Am J Med. 1999;107:542-548. [PMID: 10625021]
25. Englund M, Roos EM, Lohmander LS. Impact of type of meniscal tear on radiographic and symptomatic knee osteoarthritis: a sixteen-year followup of meniscectomy with matched controls. Arthritis Rheum. 2003;48:2178-2187. [PMID: 12905471]
26. Slemenda C, Brandt KD, Heilman DK, et al. Quadriceps weakness and osteoarthritis of the knee. Ann Intern Med. 1997;127:97-104. [PMID: 9230035]
27. Slemenda C, Heilman DK, Brandt KD, et al. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? Arthritis Rheum. 1998;41:1951-1959. [PMID: 9811049]
28. Baker DG, Schumacher HR Jr. Acute monoarthritis. N Engl J Med. 1993;329:1013-1020. [PMID: 8366902]
29. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum. 1986;29:1039-1049. [PMID: 3741515]
30. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494-502. [PMID: 13498604]

Diagnosis and Assessment

What are the characteristic symptoms of knee OA?

The insidious onset of activity-related knee pain in middle and late adulthood heralds the onset of OA (see the **Box**: Common Symptoms and Treatment of Knee OA). A person with osteoarthritic knee involvement frequently experiences joint pain with weight bearing and ambulation, including stair walking and getting into and out of a chair (3, 4). Knee pain arising from OA is typically alleviated with rest. Stiffness and modest swelling of the knee joint may be observed, but the stiffness is usually brief (<30 minutes) and self-limited.

As the severity of osteoarthritic joint involvement progresses, so does the intensity of symptoms. As a result, persons with more advanced knee OA may develop restricted joint movement and increasingly severe pain during activities that were previously well tolerated (such as walking across a parking lot or stepping up into a home entryway); persistent pain, pain while at rest, and nocturnal pain may signal the presence of more advanced disease. However, nocturnal knee pain must be distinguished from pain due to other causes, including a microcrystalline arthropathy, occult cancer, osteonecrosis, or an evolving infection (28). Other sources of pain arising from sprains or strains that may inflame ligaments, tendons, muscles, and bursae in and around the knee joint, such as tendonitis (for example, iliotibial band syndrome) or pes anserine bursitis, may also contribute to knee pain.

What is the differential diagnosis?

Differentiating OA from other causes of knee pain requires a history focused on the pattern and timing of pain and on accompanying (vs. absent) constitutional symptoms. Alternative diagnoses for persons presenting with symptoms of knee OA are summarized in **Table 1**.

The brief duration of morning stiffness (<30 minutes) at the knee joints and the absence (vs. the presence) of constitutional symptoms (such as malaise, anorexia, fever, or unintentional weight loss) are key elements of the history that should alert the clinician to knee OA being the operative process. Notably, the onset of joint pain, including knee pain, may herald the onset of a systemic disorder arising from various disease mechanisms, including an underlying rheumatic (lupus, rheumatoid arthritis, spondyloarthropathy), infectious (parvovirus, hepatitis virus, septic arthritis), metabolic (hemochromatosis, ochronosis), microcrystalline (calcium pyrophosphate deposition disease, gout), endocrine (hypothyroidism), or neoplastic arthropathy. A primary bone disorder (osteonecrosis, infiltrative histiocytic disorder) or mechanical knee arthropathy (ligamentous injury, meniscus tear) must also be considered. When the knee is one of multiple symptomatic joint sites, the presence of a more generalized systemic rheumatic disorder (such as lupus or

Common Symptoms and Treatment of Knee OA

- Pain is activity-related or mechanical; is exacerbated by use, weight bearing, and ambulation; is alleviated by rest; usually is insidious in onset and commences in middle and late adulthood; and may be nocturnal in advanced disease
- Symptoms include morning stiffness of brief duration and reduced range of motion and crepitus in the absence of systemic features, such as fever, anorexia, or weight loss
- Management should always begin with nonpharmacologic and nonsurgical strategies and often involves a multidisciplinary approach, including physical and occupational therapy and weight management with a nutritionist
- Surgical intervention should be pursued to relieve suffering and restore functionality only when nonpharmacologic approaches and pharmacologic agents do not adequately control pain

Table 1. **Differential Diagnosis of Knee Osteoarthritis**

Disease Process	*Morning Stiffness*	*Constitutional Symptoms*	*Diagnostic Evaluation*	*Radiographic Findings*	*Synovial Fluid Analysis*
Osteoarthritis	Self-limited; <30 min	Absent	Normal CBC, CMP, ESR, CRP level	Heterogeneous JSN Osteophytes	Noninflammatory
Rheumatoid arthritis	Present*	Present†	Positive for RF, CCP	Joint margin erosion/ homogeneous JSN	Inflammatory
Lupus arthritis	Present*	Present†	Positive for ANA	Nonerosive	Inflammatory
Psoriatic arthritis	Present*	Present†	Cutaneous evidence of psoriasis Positive for HLA B27	Pencil-in-cup deformity Sacroiliitis	Inflammatory
Gout	Present*	Present†	Increased serum uric acid level Tophaceous deposit	Rat-bite erosion	Negatively birefringent uric acid crystals
Calcium pyrophosphate deposition arthritis	Present*	Present†	Hypercalcemia Hyperparathyroidism Hypophosphatasia Hypomagnesemia Hemochromatosis	Chondrocalcinosis	Positively birefringent calcium pyrophosphate crystals
Septic arthritis	Present	Present†	Gram stain Microbiology culture	Subchondral bone erosions (a late radiographic finding)	Markedly increased synovial fluid leukocyte count
Meniscus tear	Trauma-induced pain, buckling, locking	Absent	Positive result on McMurray test Joint line tenderness	MRI to identify meniscal injury	Bloody effusion
Osteonecrosis	Nocturnal pain Subacute daytime pain	Absent	Plain-film radiography MRI if early in duration	Bone marrow edema	Noninflammatory

ANA = antinuclear antibody; CBC = complete blood count; CCP = cyclic citrullinated peptide antibody; CMP = comprehensive metabolic panel; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; HLA = human leukocyte antigen; JSN = joint space narrowing; MRI = magnetic resonance imaging; RF = rheumatoid factor.
** Typically lasts ≥1 h among persons with inflammatory arthritis.*
† Symptoms include malaise, fever, anorexia, and unintentional weight loss.

rheumatoid arthritis) should be strongly considered, together with the possibility of generalized OA.

What should be assessed on the physical examination?

When OA affects the knee joint, it typically causes crepitus, an audible and palpable grating quality that is evident when the knee is flexed and extended during assessment of range of motion. Bony prominence is also a common finding. There may be tenderness at sites of bony enlargement, particularly at the knee medial or lateral joint line. Presence of these examination features (crepitus, bony enlargement, joint line tenderness) reinforces the diagnostic formulation of knee OA.

There may be periods of increased joint symptoms with evident joint swelling and palpable warmth. However, these signs are modest features in OA compared with their more overt presence in rampant inflammatory arthritis (for example, gout flare, exacerbation of psoriatic arthritis or rheumatoid arthritis, or septic arthritis) (Table 1).

A comprehensive examination should include measurement of weight and height for calculation of body mass index (defined as weight in kilograms divided by the square of height in meters). Overweight and obesity are key determinants associated with knee OA; their assessment provides a helpful baseline to establish weight loss goals among patients with newly diagnosed OA.

In this context, there are examination findings that may strengthen (vs. diminish) support for a diagnostic formulation of knee OA. For example, the presence of bony enlargement at the distal interphalangeal (Heberden nodes) and proximal interphalangeal (Bouchard nodes) joints provides evidence in support of OA. Alternatively, when soft tissue deposits over the extensor surface of the

31. Felson DT, McAlindon TE, Anderson JJ, et al. Defining radiographic osteoarthritis for the whole knee. Osteoarthritis Cartilage. 1997;5:241-250. [PMID: 9404469]
32. Chaisson CE, Gale DR, Gale E, et al. Detecting radiographic knee osteoarthritis: what combination of views is optimal? Rheumatology (Oxford). 2000;39:1218-1221. [PMID: 11085800]
33. Englund M, Guermazi A, Gale D, et al. Incidental meniscal findings on knee MRI in middle-aged and elderly persons. N Engl J Med. 2008;359:1108-1115. [PMID: 18784100]
34. Katz JN, Brophy RH, Chaisson CE, et al. Surgery versus physical therapy for a meniscal tear and osteoarthritis. N Engl J Med. 2013;368:1675-1684. [PMID: 23506518]
35. Goldenberg DL, Reed JI. Bacterial arthritis. N Engl J Med. 1985;312:764-771. [PMID: 3883171]

Table 2. **Criteria for Classification of Idiopathic Osteoarthritis of the Knee**

Clinical and Laboratory	*Clinical and Radiographic*	*Clinical**
Knee pain plus ≥5 of 9: • Age >50 y • Stiffness <30 min • Crepitus • Bony tenderness • Bony enlargement • No palpable warmth • ESR <40 mm/h • RF <1:40 • SF OA 92% sensitive 75% specific	Knee pain plus ≥1 of 3: • Age >50 y • Stiffness <30 min • Crepitus Plus osteophytes 91% sensitive 86% specific	Knee pain plus ≥3 of 6: • Age >50 y • Stiffness <30 min • Crepitus • Bony tenderness • Bony enlargement • No palpable warmth 95% sensitive 69% specific

ESR = erythrocyte sedimentation rate (Westergren); RF = rheumatoid factor; SF OA = synovial fluid signs of osteoarthritis (clear, viscous, or leukocyte count <2.0 × 10^9 cells/L).
** Alternative for the clinical category would be knee pain plus 4 of 6, which is 84% sensitive and 89% specific. Reproduced, with permission, from Altman R, Asch E, Bloch D, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the knee. Arthritis Rheum. 1986;29:1039-1049. ©2006 American College of Rheumatology.*

forearm suggest the presence of rheumatoid nodules or xanthomata, these findings tilt the diagnostic scale to consideration of rheumatoid arthritis and hyperlipidemia-associated arthritis, respectively, over OA. Tophaceous deposits at the ear pinna or over extensor surfaces of the forearms, hands, and feet strengthen support for a formulation of gouty arthritis. Similarly, a prominent malar rash should direct the evaluation of knee pain and stiffness to consideration of lupus arthritis.

It is important to note that back and hip disorders can refer pain distally to the knee. Both of these anatomic sites should be evaluated in a comprehensive approach to isolate the origin of knee pain. On occasion, pain arising from an ankle arthropathy may also refer proximally to the knee.

Are there formal diagnostic criteria for knee OA?

The American College of Rheumatology (ACR) has issued criteria for knee OA consisting of 3 classification schemas (**Table 2**) (29). The first set of diagnostic criteria used to invoke a diagnosis of knee OA is based on clinical and laboratory features, the second is based on clinical and radiographic features, and the third is based on clinical features alone (29). Each of these approaches has 91% to 95% sensitivity for a diagnosis of knee OA, and the clinical and radiographic schema has the greatest specificity (86%) (29).

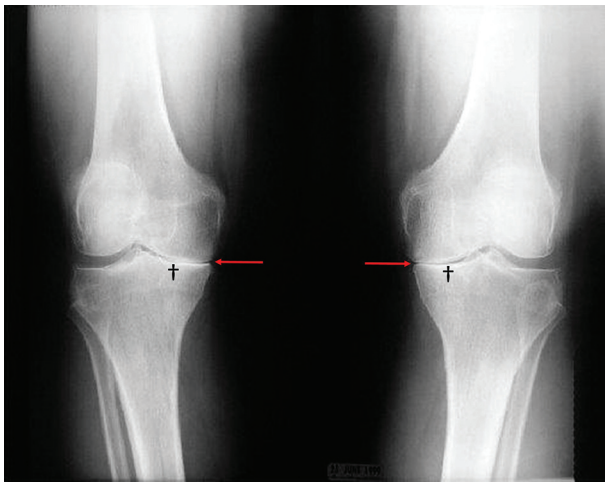
When should imaging studies be ordered?

Although plain-film radiography is not essential in the diagnostic evaluation of knee OA, it is frequently used and can improve specificity in diagnosis (**Table 2**) (29). More than 60 years ago, Kellgren and Lawrence described a radiologic approach to the assessment of OA (30). The key radiographic features they defined include joint space narrowing, osteophyte (or spur) formation at the joint margin, cortical bone thickening (or eburnation), and formation of subchondral cysts. These features are shown in **Figures 1** to **3**, in which prominent asymmetric, or heterogeneous, joint space narrowing is observed with osteophyte (spur) formation in each of the knee joint's 3 compartments.

Although definitive osteophyte (spur) formation or joint space narrowing is only observed among approximately half of persons with OA (31), the specificity of having either of these radiographic features for a clinical diagnosis of knee OA is higher (about 80%) (31). Furthermore, 3 distinct radiographic views of the knee joint—the anteroposterior, lateral, and skyline views—are available to detect radiographic features of OA. Among these, the skyline view is recommended for assessment of the patellofemoral compartment (32).

36. Knowlton RG, Katzenstein PL, Moskowitz RW, et al. Genetic linkage of a polymorphism in the type II procollagen gene (COL2A1) to primary osteoarthritis associated with mild chondrodysplasia. N Engl J Med. 1990;322:526-530. [PMID: 2300123]
37. 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;72:149-162. [PMID: 31908149]
38. Fernandes L, Hagen KB, Bijlsma JWJ, et al; European League Against Rheumatism (EULAR). EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis. 2013;72:1125-1135. [PMID: 23595142]
39. Moseng T, Vliet Vlieland TPM, Battista S, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis: 2023 update. Ann Rheum Dis. 2024;83:730-740. [PMID: 38212040]
40. McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis Cartilage. 2014;22:363-388. [PMID: 24462672]
41. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 2019;27:1578-1589. [PMID: 31278997]
42. Brophy RH, Fillingham YA. AAOS clinical practice guideline summary: management of osteoarthritis of the knee (nonarthroplasty), third edition. J Am Acad Orthop Surg. 2022;30:e721-e729. [PMID: 35383651]
43. American Academy of Orthopaedic Surgeons. Management of Osteoarthritis of the Knee (Non-Arthroplasty): Appropriate Use Criteria. 11 September 2022. Accessed at www.aaos.org/oakauc on 15 July 2024.
44. Conley B, Bunzli S, Bullen J, et al. Core recommendations for osteoarthritis care: a systematic review of clinical practice guidelines. Arthritis Care Res (Hoboken). 2023;75:1897-1907. [PMID: 36762545]

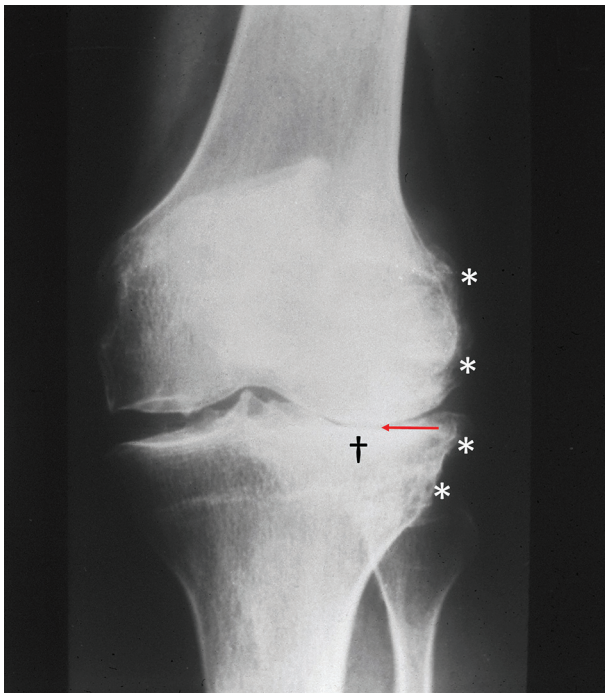
Figure 1. **Radiographic evidence of osteoarthritis in the medial compartment.**



There is prominent narrowing at the medial joint space at the femorotibial compartment (*arrows*) of the knee bilaterally. The width between the femoral condyle and tibial plateau is preserved at the lateral knee compartment. The daggers indicate bony sclerosis (eburnation). A bowlegged or varus knee deformity is shown.

Although radiographic features of OA are informative, they do not correlate perfectly with clinical symptoms of disease (31). A person with radiographic evidence of moderate knee OA may have few if any symptoms; conversely, some patients with prominent symptoms have only mild radiographic changes. Furthermore, plain-film radiography may inform exclusion of other disorders in

Figure 2. **Advanced osteoarthritis in the lateral compartment of the left knee.**

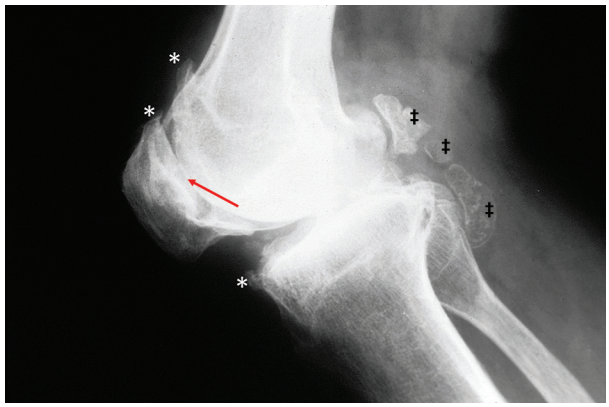


Advanced narrowing of the lateral joint space (*arrow*) is evident, together with bony sclerosis (eburnation) (*dagger*) and osteophyte (spur) formation (*asterisks*) at the opposing lateral femoral condyle and tibial plateau.

45. Allen KD, Oddone EZ, Coffman CJ, et al. Telephone-based self-management of osteoarthritis: a randomized trial. Ann Intern Med. 2010;153:570-579. [PMID: 21041576]
46. Warsi A, LaValley MP, Wang PS, et al. Arthritis self-management education programs: a meta-analysis of the effect on pain and disability. Arthritis Rheum. 2003;48:2207-2213. [PMID: 12905474]
47. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA. 2013;310:1263-1273. [PMID: 24065013]
48. Messier SP, Beavers DP, Queen K, et al. Effect of diet and exercise on knee pain in patients with osteoarthritis and overweight or obesity: a randomized clinical trial. JAMA. 2022;328:2242-2251. [PMID: 36511925]
49. Fransen M, McConnell S, Harmer AR, et al. Exercise for osteoarthritis of the knee: a Cochrane systematic review. Br J Sports Med. 2015;49:1554-1557. [PMID: 26405113]
50. Messier SP, Resnik AE, Beavers DP, et al. Intentional weight loss in overweight and obese patients with knee osteoarthritis: is more better? Arthritis Care Res (Hoboken). 2018;70:1569-1575. [PMID: 29911741]
51. Juhl C, Christensen R, Roos EM, et al. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. Arthritis Rheumatol. 2014;66:622-636. [PMID: 24574223]
52. Uthman OA, van der Windt DA, Jordan JL, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. BMJ. 2013;347:f5555. [PMID: 24055922]
53. Bartels EM, Juhl CB, Christensen R, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. Cochrane Database Syst Rev. 2016;3:CD005523. [PMID: 27007113]

54. Quicke JG, Foster NE, Thomas MJ, et al. Is long-term physical activity safe for older adults with knee pain? A systematic review. Osteoarthritis Cartilage. 2015;23:1445-1456. [PMID: 26003947]
55. Chen P-Y, Song C-Y, Yen H-Y, et al. Impacts of tai chi exercise on functional fitness in community-dwelling older adults with mild degenerative knee osteoarthritis: a randomized controlled clinical trial. BMC Geriatr. 2021;21:449. [PMID: 34332537]
56. Bennell KL, Schwartz S, Teo PL, et al. Effectiveness of an unsupervised online yoga program on pain and function in people with knee osteoarthritis: a randomized clinical trial. Ann Intern Med. 2022;175:1345-1355. [PMID: 36122378]
57. Wang C, Schmid CH, Iversen MD, et al. Comparative effectiveness of tai chi versus physical therapy for knee osteoarthritis: a randomized trial. Ann Intern Med. 2016;165:77-86. [PMID: 27183035]
58. Allen KD, Woolson S, Hoenig HM, et al. Stepped exercise program for patients with knee osteoarthritis: a randomized controlled trial. Ann Intern Med. 2021;174:298-307. [PMID: 33370174]
59. Derry S, Wiffen PJ, Kalso EA, et al. Topical analgesics for acute and chronic pain in adults - an overview of Cochrane reviews. Cochrane Database Syst Rev. 2017;5:CD008609. [PMID: 28497473]
60. Bannuru RR, Schmid CH, Kent DM, et al. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. Ann Intern Med. 2015;162:46-54. [PMID: 25560713]
61. da Costa BR, Reichenbach S, Keller N, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. Lancet. 2017;390:e21-e33. [PMID: 28699595]
62. Puljak L, Marin A, Vrdoljak D, et al. Celecoxib for osteoarthritis. Cochrane Database Syst Rev. 2017;5:CD009865. [PMID: 28530031]
63. Bally M, Dendukuri N, Rich B, et al. Risk of acute myocardial infarction with NSAIDs in real world use: Bayesian meta-analysis of individual patient data. BMJ. 2017;357:j1909. [PMID: 28487435]

Figure 3. **Knee osteoarthritis with osteophyte formation in the patellofemoral compartment.**



Joint space narrowing (*arrow*) and osteophyte formation (*asterisks*) are prominently featured at the patellofemoral articulation, the third compartment of the knee joint. Calcified loose bodies (*double daggers*) are present at the posterior (popliteal fossa) aspect of the affected knee joint.

the differential diagnosis (Table 1). As such, there are key radiographic findings in rheumatoid arthritis (juxta-articular osteopenia, homogeneous compartmental narrowing) that are distinct from those observed with OA.

Magnetic resonance imaging (MRI) is rarely indicated when the diagnostic suspicion for OA is already high. However, MRI may be useful to evaluate for internal derangement of the knee when clinically indicated (in the setting of knee locking, instability, or catching) or to detect early osteonecrosis. An unfortunate consequence of frequent use of MRI in clinical practice is excessive detection of meniscus tears. Meniscal pathology is nearly universal among persons with knee OA and does not necessarily cause increased knee pain (33). A torn meniscus should not be surgically removed unless it is contributing to joint locking or buckling (34).

When should clinicians perform diagnostic arthrocentesis?

In the event of overtly hot, red, or swollen joints, diagnostic aspiration to evaluate for possible septic arthritis, gout, and pseudogout should be strongly considered. Synovial fluid from osteoarthritic joints is relatively clear, viscous, and noninflammatory. Analysis of the aspirated joint fluid shows a modestly elevated but noninflammatory leukocyte count in the range of 0.200 to 2.0 $\times$ 10^9 cells/L (28). If arthrocentesis yields a higher leukocyte count (>2.0 $\times$ 10^9 cells/L), there is a strong possibility that the knee symptoms are better explained by an inflammatory arthritis rather than by OA. Aspirated synovial fluid should be examined via polarized microscopy for the presence of monosodium urate and calcium pyrophosphate crystals.

In the setting of diagnostic uncertainty, synovial fluid should be sent for a leukocyte count and also for Gram stain and culture. Viral, fungal, and mycobacterial culture should be considered beyond routine bacteriologic culture in the immunocompromised host or when exposure to these pathogens is suspected. Even with multiple imaging methods (such as plain-film radiography, ultrasonography, bone scintigraphy, computed tomography, and MRI), microbiologic culture of the synovial fluid aspirate is the gold standard to confirm a diagnosis of septic arthritis (35).

Should other diagnostic studies be done in suspected cases?

Laboratory testing beyond arthrocentesis is not essential to establish a diagnosis of knee OA. Because OA is a relatively noninflammatory process, the

complete blood count and acute-phase reactant levels should be normal. When there is diagnostic uncertainty about the cause of knee pain, and particularly when a systemic or autoimmune rheumatic disorder is suspected, several diagnostic studies can be considered, such as erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, cyclic citrullinated peptide antibody, and antinuclear antibody (**Table 1**). Notably, a low sedimentation rate, a negative rheumatoid factor test result, and noninflammatory synovial fluid findings were integrated into the ACR criteria for classification of knee OA, based on clinical and laboratory parameters (**Table 2**) (29).

Obtaining a creatinine level and performing liver function tests before initiating nonsteroidal anti-inflammatory drug (NSAID) and acetaminophen therapy, especially in elderly persons or those with comorbid conditions, should be considered to establish a baseline and to assess for relative versus absolute contraindication to these pharmacologic agents. This baseline quantification of blood counts and renal and hepatic function can be helpful if iatrogenic injury develops later.

Are there distinct subsets of knee OA?

OA can be categorized as primary or secondary. Secondary OA results from a well-defined cause, including a known injury (torn meniscus), metabolic disorder (hemochromatosis, Wilson disease, ochronosis), hypermobility syndrome, or endocrinopathy (acromegaly). It can also develop as a consequence of an underlying inflammatory arthropathy (rheumatoid arthritis, psoriatic arthritis) or in joints previously damaged by infection (septic arthritis).

Persons with primary knee OA may harbor degenerative arthritis limited to one or both knee joints. Alternatively, OA may occur in the knee within the framework of broader osteoarthritic involvement in other areas of the body. Specifically, a construct of generalized OA is invoked when OA simultaneously affects multiple joint groups in the appendicular skeleton (knees, hips, first carpometacarpal joint, proximal and distal interphalangeal joints) and the axial skeleton (cervical and lumbar spine).

When should clinicians consult a rheumatologist or an orthopedist?

Referral for diagnostic consultation is advisable when the pattern of joint involvement or the quality of the joint pain is atypical, when the presenting symptoms suggest an inflammatory arthropathy, or with severe manifestations. Similarly, it is unusual for knee OA to present in young adults. Consequently, for adults aged 18 to 30 years with prominent knee pain, stiffness, or swelling, consultation with a rheumatologist is advisable. Such patients may not have primary OA but may harbor another type of arthritis (juvenile idiopathic arthritis) or may have secondary OA. Alternatively, they may have a genetic susceptibility to early-onset OA with high familial penetrance (36).

Similarly, if a patient presents with features more consistent with a periarticular source of pain, such as pes anserine bursitis or iliotibial band syndrome, referral to an orthopedist or a rheumatologist should be considered if guidance is needed. As noted, a red, hot, and swollen joint requires prompt aspiration. Consequently, if arthrocentesis cannot be obtained, immediate specialist consultation should be sought. When the treating clinician is contemplating surgical intervention, referral to an orthopedist is the key next step.

64. Jüni P, Hari R, Rutjes AWS, et al. Intra-articular corticosteroid for knee osteoarthritis. Cochrane Database Syst Rev. 2015;2015:CD005328. [PMID: 26490760]
65. Kirkley A, Birmingham TB, Litchfield RB, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med. 2008;359:1097-1107. [PMID: 18784099]
66. Hannon CP, Goodman SM, Austin MS, et al. 2023 American College of Rheumatology and American Association of Hip and Knee Surgeons clinical practice guideline for the optimal timing of elective hip or knee arthroplasty for patients with symptomatic moderate-to-severe osteoarthritis or advanced symptomatic osteonecrosis with secondary arthritis for whom nonoperative therapy is ineffective. Arthritis Rheumatol. 2023;75:1877-1888. [PMID: 37746897]

Diagnosis and Assessment... Knee OA is characterized by self-limited morning stiffness lasting less than 30 minutes, joint pain that is exacerbated with weight bearing and ambulation, and an absence of constitutional symptoms. Evidence of knee OA on examination includes crepitus on range-of-motion testing and bony prominence at the articular margin. Plain-film radiography may provide diagnostic support, with evidence of joint space narrowing and spur (osteophyte) formation, but it is not mandatory in the diagnostic evaluation. For a swollen knee with demonstrable effusion, diagnostic joint aspiration should be pursued to exclude other causes. MRI should be reserved for evaluation for internal derangement of the knee joint that manifests with joint instability (locking, giving way).

CLINICAL BOTTOM LINE

Treatment

What is the overall therapeutic approach to knee OA?

Therapeutic methods to treat knee OA may be subdivided into nonpharmacologic, pharmacologic, and surgical approaches. It is important for the management of knee OA to be tailored to the individual patient. Treatment should begin with a comprehensive initial evaluation that includes assessment of the patient's pain level, functional status in activities of daily living, engagement, mood, health education needs, health beliefs, and motivation to self-manage (37–41). Notably, the presence of overweight and obesity during an evaluation for knee OA warrants inclusion of weight loss goals in the therapeutic plan (37–43).

A comprehensive approach necessitates discussion of various treatment options and often integrates family members into the care plan, the primary goals of which are to diminish joint pain and enhance functional capacity of the patient. Of note, treatment plans should not be defined rigidly by radiographic findings because the degree of joint space narrowing and the number of osteophytes may not correlate perfectly with pain and functional capacity. Therefore, treatment should remain flexible and should be modified according to functional and symptomatic responses to a therapeutic trial. The intensity of knee pain and the ability of the patient to navigate activities of daily living are key parameters in formulating the treatment plan (37–43).

Educating patients on self-management

Education is an integral part of treatment for any chronic disease and can favorably affect disease outcomes. Patients with knee OA should be encouraged to participate in self-management programs, to take advantage of available resources about the natural history of disease, and to access resources for social support and instructions on coping skills, such as those from the Arthritis Foundation (AF) (www.arthritis.org) (44). Such OA self-management educational materials are designed to provide fundamental information on the diagnosis of OA; principles of, instructions for, and benefits of exercise; healthy eating; the importance of weight management; optimal use of analgesic and anti-inflammatory drugs; descriptions of joint injections and surgeries; recommendations for communicating with health care providers; relaxation exercises; and strategies for improving sleep (45). Self-management educational programs focused on arthritis have been shown to diminish pain and disability (46).

A trial randomly assigned 461 participants in equal numbers to receive OA self-management educational materials and 12 monthly telephone calls, non-OA

educational materials and 12 monthly telephone calls (attention control), or usual care (control group). Self-management was designed to support individualized goals and action plans related to OA management. The telephone-based OA self-management program produced moderate improvements in pain, particularly compared with the health education group (45).

Nonpharmacologic strategies often involve a multidisciplinary approach, with input from physical therapists, occupational therapists, nutritionists, nurses, and physicians.

Knee OA management guidelines

Evidence-based guidelines from professional organizations addressing the management of knee OA are a valuable resource (37–43). An overview of the recommendations from ACR/AF, the American Academy of Orthopaedic Surgeons (AAOS), the European Alliance of Associations for Rheumatology (formerly the European League Against Rheumatism), and the Osteoarthritis Research Society International (OARSI) is provided in the **Appendix Figure** (available at Annals.org).

Is weight loss part of the treatment plan for knee OA?

All clinical practice guidelines recommend that patients with overweight or obesity who have OA of the knee joint should be encouraged to lose weight through a combination of dietary and exercise interventions. Several randomized controlled trials have demonstrated the efficacy of this approach at achieving improvement in pain control, physical function, and weight reduction (47, 48). In fact, a dose–response association has been noted in the degree of weight loss achieved and the benefits that accrue (49, 50). Furthermore, greater improvement in physical function and pain is evident among persons engaged in both exercise and a calorie-restricted diet than those participating in either of these approaches alone (47, 48). Consequently, weight management in the treatment of knee OA is endorsed in several evidence-based guidelines (37–43).

Among 454 community-dwelling adults aged 55 years or older who had overweight or obesity and were enrolled in the IDEA (Intensive Diet and Exercise for Arthritis) trial, over an 18-month intervention, those assigned to the diet-plus-exercise group and those assigned to the diet-only group had greater weight loss than those in the exercise-only group (47). Mean weight loss was greater in the diet-plus-exercise group (10.6 kg [11.4%]) than in the diet-only group (8.9 kg [9.5%]) or the exercise-only group (1.8 kg [2.0%]). The diet-plus-exercise group also experienced less pain and better function than the diet-only and exercise-only groups.

What is the role of exercise in the management of knee OA?

An exercise program that matches the patient's ability, whether conducted in a group setting or at home, is a critical component of knee OA management. Exercise increases aerobic capacity, muscle strength, and endurance while facilitating weight loss (47–52). Patients with knee OA who can exercise should be encouraged to participate in a low-impact aerobic exercise program, such as walking, biking, or swimming (49). Aerobic walking and quadriceps-strengthening exercises reduce pain and increase function (50). The buoyant nature of water makes aquatic exercise an attractive option for those with poor tolerance of exercise on an unyielding firm surface, with observed clinical benefits on pain, disability, and quality of life among persons with knee OA (53).

Strength-training programs that integrate resistance-based leg exercise and quadriceps-strengthening exercise have been shown to reduce pain and improve function among persons with knee OA (47–50). Long-term therapeutic exercise among older persons with knee pain has also been shown to be safe, lending further support to current

clinical guideline recommendations (54).

Exercise programs should be individualized. Strategies to improve adherence (such as periodic monitoring), a key predictor of long-term outcomes, should be adopted. Exercise that is enjoyed is more likely to be sustained. Of note, some forms of exercise, particularly high-velocity and high-impact exercise, can be harmful to an already compromised osteoarthritic knee joint. For this reason, activities such as running and step aerobics should be discouraged in symptomatic patients with knee OA who tolerate vigorous exercise poorly. Affordability and access are fundamentally important attributes in broad dissemination of exercise programs and key predictors of adherence to this intervention strategy.

Although patients with knee OA and their providers may seek out evidence to support the optimal form of exercise to adopt and the optimal regimen in terms of duration, intensity, and frequency, evidence is not currently available to recommend a specific exercise program. Evidence-based guidelines do not recommend one form of exercise over another (37–43).

What is the role of tai chi and yoga?

As the patient and health care team seek to identify an optimal program that can be effectively and safely integrated into a regular routine, there is an appropriate gravitation toward an exercise of modest force and without high loading impact to osteoarthritic joints. In this context, evidence has accrued in recent years to support tai chi and yoga as viable and attractive options (55, 56).

The effectiveness of an unsupervised 12-week online yoga program was evaluated among 212 community residents with symptomatic knee OA. All participants received online OA information, and the active intervention group also received access to an unsupervised yoga program delivered online via prerecorded videos (56). At 12 weeks of follow-up, differences in knee pain during walking were not observed between groups. However, some secondary outcomes, including improvements in overall knee pain, stiffness, quality of life, and self-efficacy, were greater among those in the yoga intervention group.

This approach of delivering yoga via online instructional materials was broadly accessible and had a relatively low cost. The effect of tai chi has also recently been studied, including in a head-to-head comparison with physical therapy (57).

Among 204 persons with symptomatic knee OA, tai chi was implemented twice weekly for 12 weeks and compared with physical therapy undertaken twice weekly for 6 weeks then followed by 6 weeks of monitored home exercise. Both interventions produced clinically significant improvement in knee pain (57). Although between-group differences were not observed, improvement in depression and the physical component of quality of life was greater in the tai chi group.

When should clinicians prescribe physical and occupational therapy?

Physical and occupational therapy is an excellent option for improving joint biomechanics in patients with knee OA. Instruction in active and passive range-of-motion exercise, muscle strengthening, and joint-protection principles is helpful (38, 39). Physical therapy can help strengthen periarticular muscles and improve alignment, thereby reducing stress borne by the osteoarthritic knee and diminishing joint pain (58).

Is there a role for assistive devices?

In the management of knee OA, improvement in stability and diminished pain on ambulation can frequently be achieved with use of a cane. Canes and other assistive devices (such as a walker) work by unloading the osteoarthritic knee joint, resulting in improved gait and mobility and diminished pain.

Instruction in proper use of a cane is important. Patients should be counseled to place the cane in the hand contralateral to the predominantly affected knee joint. As the affected limb is brought forward on a level surface, the cane should be concomitantly brought forward, thereby shifting the body's weight to the cane. This maneuver enables the body's weight to be transferred away from the structurally compromised osteoarthritic limb. When navigating stairs, the patient should be advised to ascend each stair 1 at a time while advancing with the unaffected limb first; in contrast, when descending a flight of stairs 1 step at a time, the affected limb should descend ahead of the unaffected one. During both the ascent and the descent, the cane (and the body's weight on it) advances when the affected osteoarthritic limb is brought forward.

When are topical analgesics useful?

Topical NSAIDs are effective at relieving pain compared with placebo for OA of the knee (59), although the therapeutic upside

is most evident in the initial 1 to 2 weeks after therapy starts. A systematic review indicated that although use of topical diclofenac and ketoprofen, in particular, had limited efficacy over 6 to 12 weeks of follow-up assessment, a small proportion of participants experienced good pain relief from these agents (59). Their use is recommended by ACR/AF, AAOS, and OARSI guidelines (37, 40–43).

An attractive feature of the topical approach is a reduction in adverse gastrointestinal reactions associated with this mode of administration, achieved by maximizing local delivery and minimizing systemic toxicity. Although these topical agents may cause local adverse effects, such as rash, itching, and burning, these are usually minimal and acceptably tolerated. Notably, among the noncore interventions, the 2019 OARSI guideline recommended topical NSAIDs more strongly than oral NSAIDs (41), based on consistent therapeutic efficacy with a relatively modest toxicity profile.

Topical capsaicin, an active ingredient of chili peppers that modulates nociceptive fibers, can be used as an alternative to systematic pharmacologic therapy (37). Capsaicin is applied over the affected knee joint. The hands must be promptly washed after this agent is applied to avoid potential ocular irritation. Although capsaicin is conditionally recommended by ACR/AF (37), the 2019 OARSI guideline recommends against its use due to poor quality of the supportive evidence (41).

Which oral analgesics should clinicians prescribe first?

There are several recommended pharmacologic agents for the management of knee OA depending on the comorbidity profile, age, and level of pain of the patient. Acetaminophen is often an early choice for mild-to-moderate pain associated with knee OA (37) given its relatively safe gastrointestinal toxicity profile. However, its therapeutic benefit is increasingly recognized to be modest, and it also carries the potential to increase liver aminotransferase levels (41, 60). Currently, the ACR/AF guidelines provide conditional support, whereas use of acetaminophen/paracetamol was not recommended in the 2019 OARSI guideline for any OA phenotype or comorbidity subgroup (41).

The ACR/AF, AAOS, and OARSI guidelines strongly recommend use of oral NSAIDs in the management of knee OA (37, 40–43). However, the appropriateness of the recommendation to treat knee OA with NSAID therapy varies depending on the patient's comorbidity profile (40, 41); the greater the comorbidity profile, the less applicable is the recommendation. This is because all NSAIDs, both nonselective and cyclooxygenase (COX)-2–selective agents, are associated with significant potential toxicity, particularly to the gastrointestinal, renal, and central nervous systems (61, 62). Caution is needed in their prescription, particularly among elderly patients, where the burden of knee OA is highest. In addition, COX-2–selective and nonselective NSAIDs carry a heightened risk for incident cardiovascular events (63). The OARSI guideline conditionally recommends nonselective NSAIDs for persons with OA in the absence of comorbidity, whereas COX-2 inhibitors are advocated for persons with gastrointestinal comorbidity and COX-2 inhibitors or a nonselective NSAID plus a proton-pump inhibitor are recommended for those with widespread pain and depression (40, 41).

Other medications, such as tramadol and duloxetine, can also be considered. Duloxetine is conditionally recommended by ACR/AF and OARSI (37, 40, 41). Opiates have limited applicability for the management of knee OA and are not endorsed by evidence-based guidelines (37, 41–43).

When are intra-articular injections indicated?

Intra-articular glucocorticoids have shown moderate benefits for pain and small improvements in physical function in the context of knee OA (64). Their use is recommended by ACR/AF and conditionally recommended by OARSI to achieve short-term (<1 month) diminution in pain (37, 40, 41). Intra-articular steroids should not be used more than once every 4 months because repeated use and related instrumentation may induce joint damage. At the same time, systematic reviews have found that most trials of intra-articular therapy are small and have low methodologic quality. Consequently, whether therapeutic benefit remains demonstrable after 1 to 6 weeks after an injection remains unclear (64).

Notably, the OARSI guideline conditionally recommends intra-articular hyaluronic injection therapy for long-term treatment of knee OA, given its association with symptom improvement beyond 12 weeks after an injection and given a more favorable long-term safety profile than repeated intra-articular steroid injections (40, 41). However, the ACR/AF guidelines only recommend intra-articular hyaluronic acid injection therapy as an option in patients with inadequate pain relief with first-line therapies. AAOS recommends against its use for all persons with knee OA due to a lack of generalizable results; a specific subset of patients might benefit (42, 43).

When should clinicians consider joint lavage, debridement, or joint replacement?

Joint lavage and arthroscopic debridement are not recommended by AAOS in the treatment of knee OA (65). Several large, randomized, methodologically rigorous studies have examined the role of these methods in knee OA (65). Across these reports, neither intervention offered therapeutic benefit at 6 months or 1 or 2 years postoperatively in relation to a sham surgical procedure or an exercise control.

Joint replacement surgery should be reserved for patients whose symptoms are refractory to medical therapy (66). Typical indications for knee arthroplasty (total knee replacement) are debilitating pain and major limitations in fundamental activities of daily living, such as walking, working, and sleeping. The most common indication for knee replacement surgery in the United States is advanced knee OA.

Treatment... The overarching goal of treatment is to alleviate pain and improve functional capacity. Primary care for knee OA should emphasize nonpharmacologic treatments, including weight loss, exercise, and physical therapy. Only when more conservative efforts fail to improve function should pharmaceutical options be implemented. Topical NSAIDs are more strongly recommended than oral NSAIDs in the management of knee OA, given a more favorable risk–benefit profile regardless of comorbidity profile. Oral NSAIDs should be used with caution with due attention to potential gastrointestinal adverse effects, particularly in elderly patients and those with substantial comorbidity. Intra-articular corticosteroids may provide some acute pain relief but should not be used frequently. Knee replacement surgery should be reserved for advanced osteoarthritic disease that is refractory to medical therapy, with the goal of restoring functionality in activities of daily living.

CLINICAL BOTTOM LINE

In the Clinic
Tool Kit

Knee Osteoarthritis

Patient Information

https://medlineplus.gov/osteoarthritis.html
https://medlineplus.gov/languages/osteoarthritis.html
Information on osteoarthritis in English and other languages from the National Institutes of Health's MedlinePlus.

www.niams.nih.gov/health-topics/osteoarthritis
Overview of osteoarthritis and what steps patients should take from the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

www.nia.nih.gov/health/osteoarthritis/osteoarthritis
Information on osteoarthritis from the National Institute on Aging.

https://rheumatology.org/patients/osteoarthritis
https://rheumatology.org/patients/osteoartritis
Information on osteoarthritis in English and other languages from the American College of Rheumatology.

https://familydoctor.org/condition/osteoarthritis/?adfree=true
Information on osteoarthritis from the American Academy of Family Physicians.

www.arthritis.org/osteoarthritis-patient-education
Information on osteoarthritis from the Arthritis Foundation.

Information for Health Professionals

https://rheumatology.org/osteoarthritis-guideline#2019-osteoarthritis-guideline
American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee.

https://ard.bmj.com/content/early/2024/01/11/ard-2023-225041
Recommendations for nonpharmacologic core management of hip and knee osteoarthritis from the European Alliance of Associations for Rheumatology.

www.sciencedirect.com/science/article/pii/S1063458419311161
Guidelines for nonsurgical management of knee, hip, and polyarticular osteoarthritis from the Osteoarthritis Research Society International.

www.aaos.org/quality/quality-programs/lower-extremity-programs/osteoarthritis-of-the-knee
Clinical practice guideline on management of osteoarthritis of the knee from the American Academy of Orthopaedic Surgeons.

WHAT YOU SHOULD KNOW ABOUT KNEE OSTEOARTHRITIS

What Is Knee Osteoarthritis?

- Knee osteoarthritis is a degenerative joint disease that causes cartilage to break down.
- Without cartilage, your bones start to rub together. Over time, this can permanently damage the joint.
- Osteoarthritis causes pain, swelling, and reduced motion in your joints.
- It can occur in other joints besides the knee, such as your hands, hips, or spine.

What Are Risk Factors?

- Getting older
- Being a woman
- Bone deformities, such as malformed joints or defective cartilage
- Joint injuries, such as from playing sports or from an accident
- Being overweight, which puts added stress on your weight-bearing joints
- Working in an occupation that places repetitive stress on a particular joint

How Is It Treated?

- Keep as active as you can.
- Do low-impact exercises you and your doctor agree are right for you. Go to physical therapy if you need to.
- If you are too heavy, try to lose weight. Ask your doctor for help.
- Use canes, braces, and other aids to make it easier to get around if needed.

- To reduce pain, your doctor may recommend topical or oral pain relievers or cortisone injections.
- Surgery may be used to replace joints.
- Call your doctor if you have fever; red, hot, or swollen joints; more pain than usual; or falls.

What Questions Should You Ask Your Doctor?

- Which medicines are best to treat my pain?
- Are there side effects? If so, what are they?
- What should I do if my medicines stop working?
- Will shots into my joints help?
- Will I need surgery on my joints?

For More Information

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Information on exercise from the National Institute on Aging, including a video on the benefits of exercise, tips to stay motivated, and resources for a self-managed exercise plan.
www.nia.nih.gov/health/exercise-and-physical-activity/how-older-adults-can-get-started-exercise

Handout on osteoarthritis from the National Institute of Arthritis and Musculoskeletal and Skin Diseases.
www.niams.nih.gov/Health_Info/Osteoarthritis/default.asp

Instructions on mobility devices and using assistive devices from the National Institutes of Health's MedlinePlus.
https://medlineplus.gov/mobilityaids.html
https://medlineplus.gov/ency/patientinstructions/000343.htm

Patient Information

Appendix Figure. **Guideline recommendations for medical management of knee osteoarthritis.**

Intervention	ACR/AF (37)	AAOS (42, 43)	EULAR (38, 39)	OARSI (40, 41)
Patient education		Strong recommendation	Level 1a or 1b evidence	Strong recommendation (level 1A)
Exercise	Strongly recommended	Strong recommendation	Level 1a or 1b evidence	Strong recommendation (level 1A)
Strength training	Strongly recommended		Level 1a or 1b evidence	Strong recommendation (level 1A)
Balance training	Conditionally recommended	Moderate recommendation	Level 1a or 1b evidence	
Weight loss	Strongly recommended	Moderate recommendation	Level 1a or 1b evidence	Strong recommendation (level 1A)
Self-efficacy/self-management programs	Strongly recommended	Strong recommendation	Level 1a or 1b evidence	Conditional recommendation (level 1B)
Physical therapy			Level 1a or 1b evidence	
Tai chi	Strongly recommended		Level 1a or 1b evidence	Strong recommendation (level 1A)
Yoga	Conditionally recommended		Level 1a or 1b evidence	Strong recommendation (level 1A)
Balneotherapy	Conditionally recommended			Recommendation against
Cognitive behavioral therapy	Conditionally recommended			Conditional recommendation (level 1B)
Cane	Strongly recommended	Moderate recommendation	Level 1a or 1b evidence	Strong recommendation (level 1A)
Tibiofemoral knee brace	Strongly recommended	Moderate recommendation		Strong recommendation (level 1A)
Walking aids, assistive technology			Level 1a or 1b evidence	Strong recommendation (level 1A)
Kinesiotaping	Conditionally recommended			
Modified shoes	Conditionally against		Level 1a or 1b evidence	
Wedged insoles	Conditionally against	Strong recommendation	Recommendation rejected	Conditional recommendation (level 2)
Acupuncture	Conditionally recommended	Limited recommendation		Recommendation against
Thermal interventions	Conditionally recommended			
Radiofrequency ablation	Conditionally recommended			
Massage therapy	Conditionally against	Limited recommendation		Conditional recommendation (level 2)
Manual therapy	Conditionally against	Limited recommendation		
Pulsed vibration therapy	Conditionally against			
Transcutaneous electrical nerve stimulation	Strongly against	Limited recommendation		
Laser		Limited recommendation		Recommendation against
Pulsed electromagnetic field therapy		Limited recommendation		Recommendation against
Extracorporeal shockwave therapy		Limited recommendation		

Continued on the following page

Appendix Figure–**Continued.**

Intervention	ACR/AF (37)	AAOS (42, 43)	EULAR (38, 39)	OARSI (40, 41)
Acetaminophen	Conditionally recommended	Strong recommendation		Recommendation against
Topical NSAIDs	Strongly recommended	Strong recommendation		Strong recommendation (level 1A)
Capsaicin	Conditionally recommended	Strong recommendation		Recommendation against
Oral NSAIDs	Strongly recommended	Strong recommendation		Conditional recommendation (level 1B)
Topical capsaicin	Conditionally recommended			Recommendation against
Intra-articular corticosteroid injection	Strongly recommended	Moderate recommendation		Conditional recommendation (level 1B)
Duloxetine	Conditionally recommended			Conditional recommendation (level 2)
Tramadol	Conditionally recommended	Strong recommendation against		
Nontramadol opioids	Conditionally against	Strong recommendation against		Recommendation against
Colchicine	Conditionally against			
Fish oil	Conditionally against			
Vitamin D	Conditionally against	Limited recommendation		Recommendation against
Bisphosphonates	Strongly against			
Diacerein				Recommendation against
Glucosamine	Strongly against	Limited recommendation		Recommendation against
Chondroitin	Strongly against	Limited recommendation		Recommendation against
Hydroxychloroquine	Strongly against			
Methotrexate	Strongly against			
Intra-articular hyaluronic acid	Conditionally against	Moderate recommendation against		Conditional recommendation (level 1B)
Intra-articular botulinum toxin A	Conditionally against			
Prolotherapy	Conditionally against			
Platelet-rich plasma	Strongly against	Limited recommendation		Recommendation against
Stem cell injection	Strongly against			
Biologics	Strongly against			

AAOS = American Academy of Orthopaedic Surgeons; ACR/AF = American College of Rheumatology/Arthritis Foundation; EULAR = European Alliance of Associations for Rheumatology; NSAID = nonsteroidal anti-inflammatory drug; OARSI = Osteoarthritis Research Society International.