

The Burden of Osteoarthritis in Older Adults



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KEYWORDS

• Osteoarthritis • Prevalence • Incidence • Risk factors • Economic burden

KEY POINTS

- OA is a serious, disabling condition that disproportionately affects older women and individuals with obesity.
- The coprevalence of symptomatic OA in older individuals with other common chronic conditions is high because of common risk factors, for example, aging and obesity.
- Untreated painful OA impacts sleep quality, causes fatigue, limits mobility and physical activity, and contributes to depressed mood, all of which reduce individuals' quality of life and the effective management of comorbid conditions.
- Enhanced efforts to diagnose and treat symptomatic OA among older adults are needed.

INTRODUCTION

Osteoarthritis (OA) is a serious disease. The most common form of arthritis,¹ OA typically affects the hips, knees, hands, feet, and spine, and multijoint involvement is common.² OA affects 1 in 3 older adults and women more so than men.^{1,3} Risk factors for OA include aging, obesity, prior joint injury, genetics, sex, and anatomic factors related to joint shape and alignment.^{4,5} As longevity and obesity increase, so, too, has the prevalence of OA.^{4,6,7}

OA is both a disease, with pathologic changes in the joint tissues (articular cartilage, subchondral bone, menisci, ligaments, etc.)⁸ and an illness (ie, symptomatic OA), characterized by joint pain and functional limitations.^{9–12} There is imperfect concordance between the disease and the illness; many people with structural changes on imaging will not develop symptoms, whereas the illness may occur before

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radiographic changes are evident. It is the illness that drives affected individuals to seek care. OA-related joint pain causes functional limitations, fatigue, depressed mood, and loss of independence, and is the primary indication for joint replacement surgery.^{9,10,12} Addressing the illness of OA is crucial to reduce the enormous individual and societal burden of OA.¹³

Although effective evidence-based treatments exist for OA,¹⁴ competing health care demands,¹⁵ due to comorbidities and widespread societal beliefs that OA is an inevitable part of aging for which nothing can be done, often lead to underdiagnosis and undertreatment of OA. A new narrative that reflects current evidence is needed.

INCIDENCE AND PREVALENCE OF SYMPTOMATIC OA

Estimates of the incidence and prevalence of OA vary depending on the definition (disease vs illness) and joints considered. Irrespective of the definition, the number of people living with symptomatic OA is on the rise. From the Global Burden of Diseases, Injuries, and Risk Factors Study, the age-standardized annual incidence rates for symptomatic hip and knee OA rose 8.2% between 1990 and 2017.¹⁶ In 2019, it was estimated that more than 500 million people or roughly 7% of the global population were living with OA (knee, hip, hand, and other sites).¹⁷ Of these, nearly 70% had knee OA, compared with 6% hip OA and 27% hand OA.¹⁷ From population-based studies, the prevalence of OA in persons over 40 years of age is about 22%.¹⁸ From prospective population-based studies, the rates of doctor-diagnosed hand, knee, and hip OA increase with age, peaking in the 70s overall, but somewhat earlier for hand OA, while prevalence continues to rise.¹⁹

The prevalence of multijoint OA is high. From the US Osteoarthritis Initiative and multicenter OA (MOST) studies, 80% of individuals with bilateral knee pain had remote site pain, including low back pain.²⁰ In a cohort of individuals undergoing primary, elective knee replacement for knee OA, 25.9% had concomitant low back pain; 23.95% had pain, aching, and stiffness in one or both hips; and 50.3% reported these symptoms in both knees.²¹

RISK FACTORS FOR OA

As noted earlier, there are many risk factors for OA. Of these, *aging* is the most prominent (Fig. 1).^{6,16,19} However, OA is not an inevitable consequence of aging. From the US National Health Interview Survey (NHIS), the prevalence of diagnosed knee OA among those aged 85 years and older ranged from ~13% in men without obesity to 32% in women with obesity.²²

The relationship between aging and OA is complex. As joints age, their ability to withstand insult lessens.²³ Increased cellular stresses in OA joint tissues, mitochondrial dysfunction, and dysfunction in energy metabolism associated with aging may contribute to cellular damage and disturbance of homeostatic physiologic cell signaling. Age-related changes in the extracellular matrix of cartilage reduce their ability to sense and respond to joint loading, increasing the risk for joint injury. A proinflammatory, catabolic state that, in the context of increased susceptibility to cell death and defective repair of the damaged matrix, leads to joint tissue destruction.²³

Irrespective of age, OA disproportionately affects *women* (see Fig. 1) and those with *obesity*.^{16,24} As for aging, the relationship between OA and sex/gender is complex. Systematic sex/gender differences in exposure to OA risk factors likely contribute to higher incidence and prevalence of OA in women than men. The incidence of OA rises among women around the time of menopause. Thus, many studies have investigated the potential impact of hormonal factors on risk for OA though findings remain

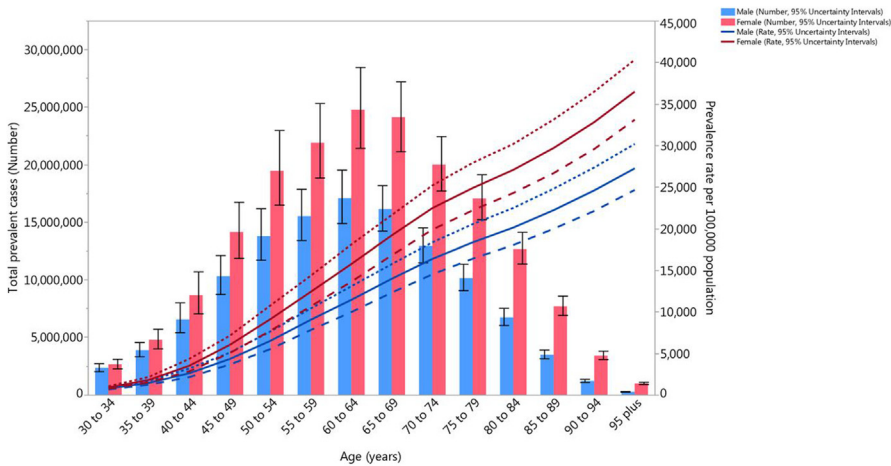


Fig. 1. Global prevalence rate of OA per 100,000 population by age and sex, 2017. Dotted and dashed lines indicate 95% upper and lower uncertainty intervals, respectively. Generated from data available from <http://ghdx.healthdata.org/gbd-results-tool>. (From Safiri S, Kolahi A, Smith E, et al. Global, regional and national burden of osteoarthritis 1990–2017: a systematic analysis of the Global Burden of Disease Study 2017 *Ann Rheum Dis*. 2020;79(6):819–28; with permission. (Figure 1 in original).)

inconclusive.²⁵ Systematic sex/gender differences in muscle strength, mechanical joint load, bone mass/bone turnover, metabolic factors, and nutritional differences may also contribute to higher incidence and prevalence of symptomatic OA in women than men.^{26,27} Gender differences in financial resources, social support, and gender biases in access to OA diagnosis and treatment may also contribute to these differences.^{28,29}

Obesity is the most important modifiable risk factor for the development and progression of OA, more so for knee OA than for OA in other joints. In a meta-analysis of 14 prospective studies, Zheng and colleagues found that overweight and obesity were associated with significantly higher knee OA risks (relative risk [RR] 2.45, 95% confidence interval [CI] 1.88–3.20, and RR 4.55, 95% CI 2.90–7.13, respectively); the risk of knee OA increased by 35% (95% CI 18%–53%) per 5 kg/m² increase in body mass index (BMI).³⁰ The lifetime risk of symptomatic knee OA has been estimated to be approximately 3 times higher among individuals with BMI ≥ 30 kg/m² and 5 times higher among individuals with BMI ≥ 35 kg/m² compared with individuals with BMI less than 25 kg/m² (Fig. 2).³¹ BMI is also strongly predictive of lifetime risk for hip or knee joint replacement surgery.^{32,33}

THE RELATIONSHIP BETWEEN SOCIAL DETERMINANTS OF HEALTH AND OA

Race/ethnicity, socioeconomic status, and geographic variations in the prevalence and severity of knee and hip OA are well established. This variation likely reflects person-level differences in risk for OA, for example, due to obesity, physical inactivity, and joint injury, and health system variability in access and outcomes of care. For example, OA prevalence is higher in high-income than lower-income countries (Fig. 3).^{16,18} Compared with other countries, the United States had the highest age-standardized prevalence of OA in 2017 (6128.1 per 100,000) and had experienced the greatest increase in prevalence (23.2%) over the period 1990 to 2017.¹⁶ Within

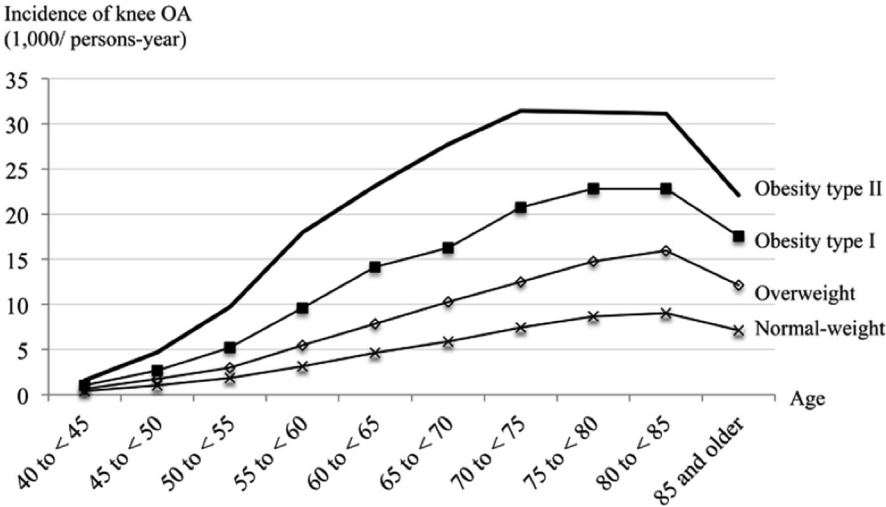


Fig. 2. Incidence of knee OA for each range of BMI^a per 1000/persons-year. ^aBMI based on WHO definitions: normal-weight (<25 kg/m²), overweight (25 to <30 kg/m²), obesity I (30 to <35 kg/m²), and obesity II (35 kg/m² and over). (From Reyes C, Leyland KM, Peat G, Cooper C, Arden NK, Prieto-Alhambra D. Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis: A Population-Based Cohort Study. *Arthritis Rheumatol* 2016;68:1869-75; with permission. (Figure 1 in original).)

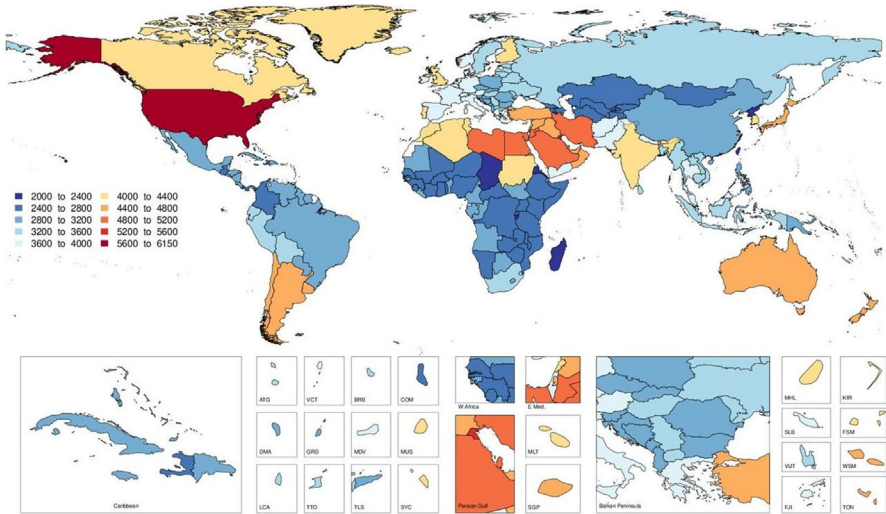


Fig. 3. Age-standardized prevalence estimates of OA per 100,000 population in 2017, by country. Generated from data available from <http://ghdx.healthdata.org/gbd-results-tool>. (From Safiri S, Kolahi A, Smith E, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis* 2020;79(6):819-28; with permission. (Figure 2 in original).)

the United States, both lower socioeconomic status and African Americans have been found to have higher incidence, prevalence, and severity of OA than US whites.³⁴

IMPACT OF OA ON OTHER CONDITIONS AND MORTALITY

Older age and obesity are risk factors for OA and many other chronic conditions. Thus, most older people living with symptomatic OA have at least one other chronic condition,³⁵ typically cardiometabolic conditions such as type 2 diabetes mellitus (T2DM) and cardiovascular (CV) diseases.³⁶ For example, in a meta-analysis of more than 1 million individuals, the risk of T2DM was 40% higher in individuals with versus without OA and 30% of individuals with T2DM had OA.³⁷

Symptomatic hip and knee OA have also been linked to higher risk for incident cardiometabolic conditions, such as diabetes and heart disease,^{7,38} and both CV-related and all-cause mortality.³⁹ Across multiple cohorts, and after controlling for potential confounders, a meta-analysis found that individuals with hip and knee OA were at 21% higher risk for CV-related death (hazard ratio [HR] 1.21, 95% CI 1.10–1.34) and 18% increased risk of all-cause death (HR 1.18, 95% CI 1.08–1.28) compared with those without.⁴⁰ These relationships appear to be due, at least in part to OA-related walking disability and resultant physical inactivity.^{40–42}

LIVING WITH OA

Pain is the top concern for people living with OA. The pain associated with joint discomfort is highly variable and evolves over time. From qualitative studies, people describe early-stage OA pain as worse with joint use and improving with rest.^{8,43} As the disease progresses, the pain may become more constant, punctuated increasingly with short episodes of a more intense, often unpredictable, and emotionally draining pain, leading to avoidance of social and recreational activities.⁴³ Consistent with this, clinical studies suggest that early-stage OA pain is largely nociceptive in nature, emanating from richly innervated joint tissues, including the subchondral bone and periosteum.⁴⁴ As OA progresses, neuroplastic changes in the peripheral and central nervous systems may occur, resulting in pain sensitisation^{44,45} Pain in OA can be best considered using a biopsychosocial model (Fig. 4).⁴⁶

The downstream effects of OA-related joint pain are considerable. From a community-based longitudinal study of more than 500 people with hip and knee OA, OA pain is causally related to fatigue^{10,47} and functional limitations.⁴⁸ Fatigue and functional limitations, in turn, increase individuals' risk for depressed or anxious mood,^{9,12} which leads to worsening of OA pain and disability and increased risk for loss of independence (Fig. 5).^{9,48,49}

Fatigue and Sleep

From 35% to 41% of adults with OA report clinically significant fatigue, similar to that seen among adults with rheumatoid arthritis.^{50,51} The high prevalence of fatigue in OA may be due, at least in part, to OA pain-related sleep disturbances.^{52,53} OA pain is associated with delayed sleep onset, bedtime anxiety, and altered sleep architecture, resulting in sleep deprivation and disruption of slow-wave sleep.⁵⁴ These effects are exacerbated by a high prevalence of comorbid sleep disturbances, including restless legs syndrome and obstructive sleep apnea.^{52,53} Thus, among older people with symptomatic OA, there is a high prevalence of poor sleep. In a community cohort of more than 600 individuals with symptomatic hip/knee OA (mean age 78 years), 70% reported poor sleep (Pittsburgh Sleep Quality Index >5).¹⁰

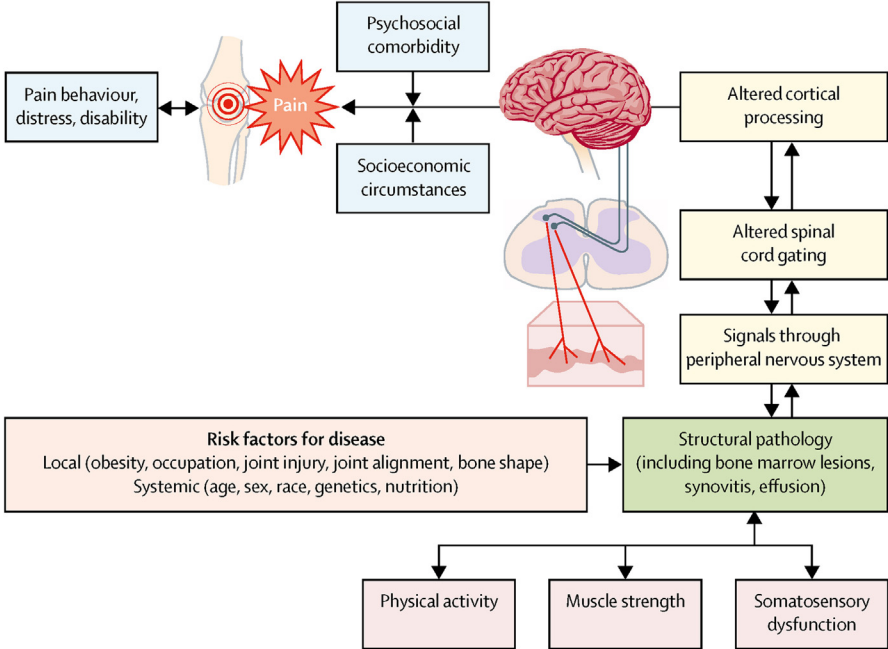


Fig. 4. The cause of pain in OA within a biopsychosocial model. (From Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019;393:1745–59; with permission. (Figure 3 in original). Reprinted with permission of Elsevier.)

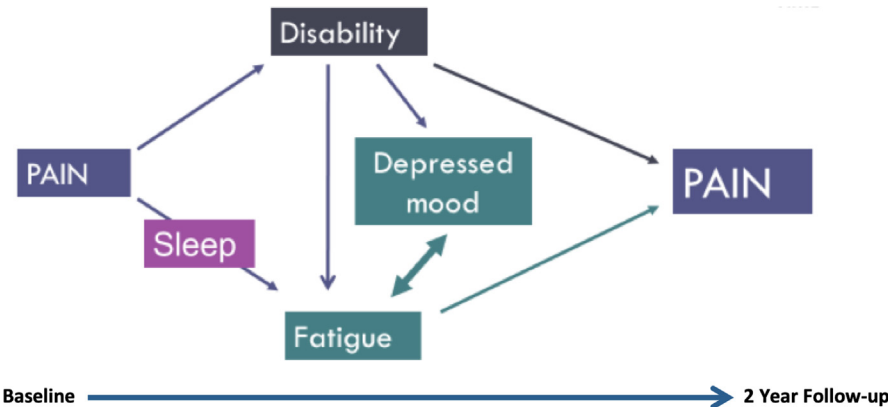


Fig. 5. Longitudinal relationships between OA-related pain, sleep, fatigue, mood, and disability, over time and adjusting for covariates^a. ^aA path analysis was performed to test interrelationships among pain, depression, fatigue, and disability for more than 500 community-cohort participants with symptomatic hip or knee OA. Controlling for psychosocial and demographic factors, it was found that female gender, older age, pain catastrophizing, poor coping behaviors, lower social support, worse general health status, and greater number of other chronic conditions negatively influenced these relationships over time. (Adapted from Hawker GA, Gignac MA, Badley E, et al. A longitudinal study to explain the pain-depression link in older adults with osteoarthritis. Arthritis Care Res (Hoboken). 2011;63(10):1382-1390; with permission. (Figure 2 in original).)

Mental Health

The prevalence of anxiety and depression is significantly higher in people with versus without OA. A systematic review reported a pooled prevalence of symptoms of depression of ~20% and symptoms of anxiety of ~21% among people with symptomatic OA.⁵⁵ Greater OA symptom severity increases the likelihood of developing depressed or anxious mood. Among individuals with painful OA, the presence of depressed or anxious mood is associated with greater health care use and worse outcomes.^{9,56,57}

Activity Limitations and Participation Restrictions

Hand OA is the most common disease affecting hand function in the elderly. Symptomatic hand OA is associated with reduced grip and pinch strength,⁵⁸ resulting in difficulty lifting, dressing, and eating.⁵⁹ Lower extremity OA is associated with activity limitations, contributing to physical inactivity, participation restrictions, and loss of independence.^{7,60,61} Inadequate treatment of OA pain also contributes, as people learn to manage their symptoms by avoiding physical activities, like walking, that exacerbate their pain.^{38,62,63} In a Canadian cohort of ~30,000 people aged 55 years or older,⁶⁰ the estimated probability of difficulty walking for an 80-year-old middle-income woman rose from 11% (no OA, no health conditions) to 52% with hypertension, heart disease, and a prior hip fracture, compared with 65% with 2 hips or knee affected by symptomatic OA (Fig. 6). If she had hypertension, heart disease, a prior hip fracture, and OA, the probability of difficulty walking was 99%.

CONTEXTUAL FACTORS INFLUENCING THE DOWNSTREAM IMPACT OF PAINFUL OA

Individuals' ability to cope with OA pain is influenced by their attitudes and tolerance of the pain (pain catastrophizing), efforts expended on coping, and level of social support. Greater pain catastrophizing, poor coping, and lower social support have consistently been found to negatively influence the impact of OA pain on sleep, fatigue, disability, and mood, and thus on OA-related quality of life over time.^{9,10,12}

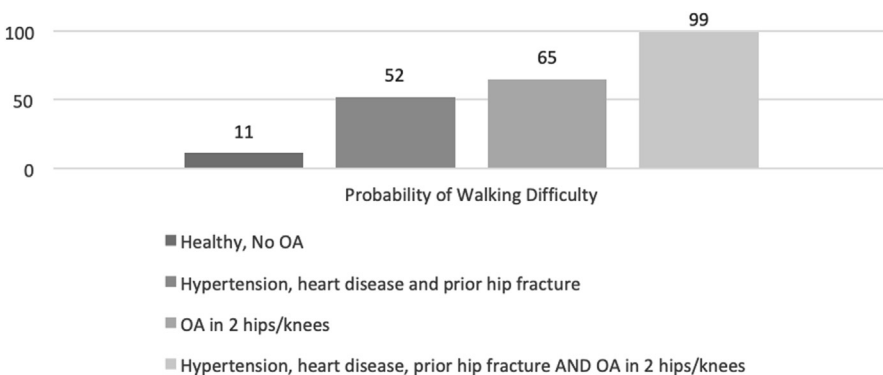


Fig. 6. Estimated probability of difficulty walking for an 80-year-old middle-income woman without obesity by the presence of comorbid conditions and hip/knee OA. (Adapted from King LK, Kendzerska T, Waugh EJ, Hawker GA. Impact of Osteoarthritis on Difficulty Walking: A Population-Based Study. *Arthritis Care Res (Hoboken)* 2018;70:71-9; with permission.)

Table 1 Economic costs of OA		
Direct Costs	Indirect Costs	Intangible Costs
Costs of surgery	Loss of productivity	Pain and suffering
Hospital resources	Absenteeism	Decreased quality of life
Caregiver time	Premature mortality	Potential depression/ anxiety
Pharmacologic and nonpharmacologic treatments	Disability payments/ benefits	
Costs of side effects from treatments		
Research		

From Chen A, Gupte C, Akhtar K, Smith P, Cobb J. The Global Economic Cost of Osteoarthritis: How the UK Compares. *Arthritis*. 2012;2012:698709; with permission. (Table 1 in original)

ECONOMIC IMPACT OF OA

Musculoskeletal conditions, including OA, have a substantial contribution to health care costs, accounting for an estimated 1.0% to 2.5% of the gross domestic product in the United States, Canada, the United Kingdom, France, and Australia.⁶⁴ Approximately 80% of the costs owing to musculoskeletal conditions are estimated to be related to symptomatic OA, including direct costs to the health care system, indirect costs to individuals living with OA, and the intangible costs of living with a chronic disabling condition (Table 1).⁶⁵ Greater health care use and associated costs are strongly related to OA pain severity.⁶⁶ The largest contributor to direct health care costs for OA is joint replacement surgery.⁶⁷ As the incidence and prevalence of symptomatic OA rises, so too do the societal costs. The aggregate expenses paid for the treatment of knee OA increased by \$1 billion from 2009 to 2014.

SUMMARY

Symptomatic OA is associated with substantial, persistent morbidity impacting day-to-day functioning. The pain, fatigue, depressed or anxious mood, and disability, including loss of mobility, that characterizes symptomatic OA present major barriers to healthy aging. The burden of symptomatic OA is increasing worldwide and disproportionately among women, those with lower education levels, and the socially disadvantaged. Although there is currently no cure for OA, many treatments exist to improve the OA-related quality of life of older adults. It is time to recognize that OA is a serious disease. It warrants far greater attention by health care providers and the health care system.

CLINICS CARE POINTS

- OA is a serious, disabling condition that disproportionately affects older women and individuals with obesity
- The coprevalence of symptomatic OA in older individuals with other common chronic conditions is high because of common risk factors, for example, aging and obesity
- Untreated painful OA impacts sleep quality, causes fatigue, limits mobility and physical activity, and contributes to depressed mood, all of which reduce individuals' quality of life and the effective management of comorbid conditions
- The burden and impact of OA is rising
- Enhanced efforts to diagnose and treat symptomatic OA among older adults are needed

REFERENCES

1. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;386:743–800.
2. Badley EM, Wilfong JM, Yip C, et al. The contribution of age and obesity to the number of painful joint sites in individuals reporting osteoarthritis: a population-based study. *Rheumatology (Oxford)* 2020;59:3350–7.
3. Murphy L, Schwartz TA, Helmick CG, et al. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Rheum* 2008;59:1207–13.
4. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: literature update. *Curr Opin Rheumatol* 2018;30:160–7.
5. Felson DT, Lawrence RC, Dieppe PA, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med* 2000;133:635–46.
6. 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. *Osteoarthr Cartil* 2015;23:507–15.
7. Herbolzheimer F, Schaap LA, Edwards MH, et al. Physical activity patterns among older adults with and without knee osteoarthritis in six European Countries. *Arthritis Care Res (Hoboken)* 2016;68:228–36.
8. Vincent TL. Peripheral pain mechanisms in osteoarthritis. *Pain* 2020;161(Suppl 1):S138–46.
9. Hawker GA, Gignac MA, Badley E, et al. A longitudinal study to explain the pain-depression link in older adults with osteoarthritis. *Arthritis Care Res (Hoboken)* 2011;63:1382–90.
10. Hawker GA, French MR, Waugh EJ, et al. The multidimensionality of sleep quality and its relationship to fatigue in older adults with painful osteoarthritis. *Osteoarthr Cartil* 2010;18:1365–71.
11. Hawker GA. Osteoarthritis is a serious disease. *Clin Exp Rheumatol* 2019;37(Suppl 120):3–6.
12. Sale JE, Gignac M, Hawker G. The relationship between disease symptoms, life events, coping and treatment, and depression among older adults with osteoarthritis. *J Rheumatol* 2008;35:335–42.
13. Whittaker JL, Runhaar J, Bierma-Zeinstra S, et al. A lifespan approach to osteoarthritis prevention: narrative review, part of the series. *Osteoarthr Cartil* 2021. <https://doi.org/10.1016/j.joca.2021.06.015>.
14. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthr Cartil* 2019;27:1578–89.
15. Christiansen MB, White DK, Christian J, et al. “It ... doesn’t always make it [to] the top of the list”: primary care physicians’ experiences with prescribing exercise for knee osteoarthritis. *Can Fam Phys* 2020;66:e14–20.
16. Safiri S, Kolahi AA, Smith E, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis* 2020;79:819–28.
17. Global burden of disease study 2019 results. Available at: <http://ghdx.healthdata.org/gbd-results-tool>.
18. Cui A, Li H, Wang D, et al. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine* 2020;29-30:100587.

19. 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;9:1659–64.
20. Suri P, Morgenroth DC, Kwoh CK, et al. Low back pain and other musculoskeletal pain comorbidities in individuals with symptomatic osteoarthritis of the knee: data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken)* 2010;62:1715–23.
21. Hawker GA, Conner-Spady BL, Bohm E, et al. Patients' preoperative expectations of total knee arthroplasty and satisfaction with outcomes at one year: a prospective cohort study. *Arthritis Rheumatol* 2021;73:223–31.
22. Losina E, Weinstein AM, Reichmann WM, et al. Lifetime risk and age at diagnosis of symptomatic knee osteoarthritis in the US. *Arthritis Care Res (Hoboken)* 2013; 65:703–11.
23. Loeser RF, Collins JA, Diekmann BO. Ageing and the pathogenesis of osteoarthritis. *Nat Rev Rheumatol* 2016;12:412–20.
24. Srikanth VK, Fryer JL, Zhai G, et al. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthr Cartil* 2005;13(9): 769–81.
25. Wluka AE, Cicuttini FM, Spector TD. Menopause, oestrogens and arthritis. *Maturitas* 2000;35:183–99.
26. Nicolella DP, O'Connor MI, Enoka RM, et al. Mechanical contributors to sex differences in idiopathic knee osteoarthritis. *Biol Sex Differ* 2012;3:28.
27. Ferre IM, Roof MA, Anoushiravani AA, et al. Understanding the observed sex discrepancy in the prevalence of osteoarthritis. *JBJS Rev* 2019;7:e8.
28. Hawker GA, Wright JG, Coyte PC, et al. Differences between men and women in the rate of use of hip and knee arthroplasty. *N Engl J Med* 2000;342:1016–22.
29. Borkhoff CM, Hawker GA, Kreder HJ, et al. Influence of patients' gender on informed decision making regarding total knee arthroplasty. *Arthritis Care Res (Hoboken)* 2013;65:1281–90.
30. Zheng H, Chen C. Body mass index and risk of knee osteoarthritis: systematic review and meta-analysis of prospective studies. *BMJ Open* 2015;5:e007568.
31. Reyes C, Leyland KM, Peat G, et al. Association between overweight and obesity and risk of clinically diagnosed knee, hip, and hand osteoarthritis: a population-based cohort study. *Arthritis Rheumatol* 2016;68:1869–75.
32. Lohmander LS, Gerhardsson de Verdier M, Rollof J, et al. Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass: a population-based prospective cohort study. *Ann Rheum Dis* 2009;68:490–6.
33. Wang Y, Simpson JA, Wluka AE, et al. Relationship between body adiposity measures and risk of primary knee and hip replacement for osteoarthritis: a prospective cohort study. *Arthritis Res Ther* 2009;11:R31.
34. Callahan LF, Cleveland RJ, Allen KD, et al. Racial/ethnic, socioeconomic, and geographic disparities in the epidemiology of knee and hip osteoarthritis. *Rheum Dis Clin North Am* 2021;47:1–20.
35. Muckelt PE, Roos EM, Stokes M, et al. Comorbidities and their link with individual health status: a cross-sectional analysis of 23,892 people with knee and hip osteoarthritis from primary care. *J Comorb* 2020;10. 2235042x20920456.
36. Swain S, Sarmanova A, Coupland C, et al. Comorbidities in osteoarthritis: a systematic review and meta-analysis of observational studies. *Arthritis Care Res (Hoboken)* 2020;72:991–1000.
37. Louati K, Vidal C, Berenbaum F, et al. Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. *RMD Open* 2015;1: e000077.

38. van Dijk GM, Veenhof C, Schellevis F, et al. Comorbidity, limitations in activities and pain in patients with osteoarthritis of the hip or knee. *BMC Musculoskelet Disord* 2008;9:95.
39. Hawker GA, Croxford R, Bierman AS, et al. All-cause mortality and serious cardiovascular events in people with hip and knee osteoarthritis: a population based cohort study. *PLoS One* 2014;9:e91286.
40. Veronese N, Cereda E, Maggi S, et al. Osteoarthritis and mortality: a prospective cohort study and systematic review with meta-analysis. *Semin Arthritis Rheum* 2016;46:160–7.
41. Wang H, Bai J, He B, et al. Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies. *Sci Rep* 2016;6:39672.
42. Nuesch E, Dieppe P, Reichenbach S, et al. All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ* 2011;342:d1165.
43. Hawker GA, Stewart L, French MR, et al. Understanding the pain experience in hip and knee osteoarthritis—an OARSI/OMERACT initiative. *Osteoarthr Cartil* 2008;16:415–22.
44. Neogi T. Structural correlates of pain in osteoarthritis. *Clin Exp Rheumatol* 2017; 35(Suppl 107):75–8.
45. Arendt-Nielsen L. Pain sensitisation in osteoarthritis. *Clin Exp Rheumatol* 2017; 35(Suppl 107):68–74.
46. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet* 2019;393:1745–59.
47. Power JD, Badley EM, French MR, et al. Fatigue in osteoarthritis: a qualitative study. *BMC Musculoskelet Disord* 2008;9:63.
48. Gignac MA, Cott C, Badley EM. Adaptation to chronic illness and disability and its relationship to perceptions of independence and dependence. *J Gerontol B Psychol Sci Soc Sci* 2000;55:P362–72.
49. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthr Cartil* 2013;21:1145–53.
50. Hackney AJ, Klinedinst NJ, Resnick B, et al. A review and synthesis of correlates of fatigue in osteoarthritis. *Int J Orthop Trauma Nurs* 2019;33:4–10.
51. Cross M, Lapsley H, Barcenilla A, et al. Association between measures of fatigue and health-related quality of life in rheumatoid arthritis and osteoarthritis. *Patient* 2008;1:97–104.
52. Wilcox S, Brenes GA, Levine D, et al. Factors related to sleep disturbance in older adults experiencing knee pain or knee pain with radiographic evidence of knee osteoarthritis. *J Am Geriatr Soc* 2000;48:1241–51.
53. Moldofsky H. Sleep and pain. *Sleep Med Rev* 2001;5:385–96.
54. Lavigne GJ, Nashed A, Manzini C, et al. Does sleep differ among patients with common musculoskeletal pain disorders? *Curr Rheumatol Rep* 2011;13:535–42.
55. Stubbs B, Aluko Y, Myint PK, et al. Prevalence of depressive symptoms and anxiety in osteoarthritis: a systematic review and meta-analysis. *Age Ageing* 2016; 45:228–35.
56. Gleicher Y, Croxford R, Hochman J, et al. A prospective study of mental health care for comorbid depressed mood in older adults with painful osteoarthritis. *BMC Psychiatry* 2011;11:147.
57. Sharma A, Kudesia P, Shi Q, et al. Anxiety and depression in patients with osteoarthritis: impact and management challenges. *Open Access Rheumatol* 2016;8: 103–13.

58. Bagis S, Sahin G, Yapici Y, et al. The effect of hand osteoarthritis on grip and pinch strength and hand function in postmenopausal women. *Clin Rheumatol* 2003;22:420–4.
59. Dillon CF, Hirsch R, Rasch EK, et al. Symptomatic hand osteoarthritis in the United States: prevalence and functional impairment estimates from the third U.S. National Health and Nutrition Examination Survey, 1991-1994. *Am J Phys Med Rehabil* 2007;86:12–21.
60. King LK, Kendzerska T, Waugh EJ, et al. Impact of osteoarthritis on difficulty walking: a population-based study. *Arthritis Care Res (Hoboken)* 2018;70:71–9.
61. Petursdottir U, Arnadottir SA, Halldorsdottir S. Facilitators and barriers to exercising among people with osteoarthritis: a phenomenological study. *Phys Ther* 2010;90:1014–25.
62. Hawker GA, Croxford R, Bierman AS, et al. Osteoarthritis-related difficulty walking and risk for diabetes complications. *Osteoarthr Cartil* 2017;25:67–75.
63. Reeuwijk KG, de Rooij M, van Dijk GM, et al. Osteoarthritis of the hip or knee: which coexisting disorders are disabling? *Clin Rheumatol* 2010;29:739–47.
64. March LM, Bachmeier CJ. Economics of osteoarthritis: a global perspective. *Baillieres Clin Rheumatol* 1997;11:817–34.
65. Chen A, Gupte C, Akhtar K, et al. The global Economic cost of osteoarthritis: How the UK Compares. *Arthritis* 2012;2012:698709.
66. Rejas-Gutierrez J, Llopart-Carles N, García-López S, et al. Disease burden on health care by pain severity and usual analgesic treatment in patients with symptomatic osteoarthritis: a Spanish nationwide health survey. *Expert Rev Pharmacoecon Outcomes Res* 2021;21:711–9.
67. Ackerman IN, Bohensky MA, Zomer E, et al. The projected burden of primary total knee and hip replacement for osteoarthritis in Australia to the year 2030. *BMC Musculoskelet Disord* 2019;20:90.