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Chapter 1: The Burden of OA-Health Services and Economics

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Abstract

Osteoarthritis (OA) is a highly prevalent and disabling condition that affects over 7% of people globally (528 million people). Prevalence levels are even higher in countries with established market economies, which have older demographic profiles and a higher prevalence of obesity, such as the US (14%). As the 15th highest cause of years lived with disability (YLDs) worldwide, the burden OA poses to individuals is substantial, characterized by pain, activity limitations, and reduced quality of life. The economic impact of OA, which includes direct and indirect (time) costs, is also substantial, ranging from 1 to 2.5% of gross national product (GNP) countries with established market economies. In regions around the world, the average annual cost of OA for an individual is estimated between $700-$15,600 (2019 USD). Though trends in OA prevalence vary by geography, the prevalence of OA is projected to rise in regions with established market economies such as North America and Europe, where populations are aging and the prevalence of obesity is rising.

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This chapter characterizes the clinical and economic burden that osteoarthritis poses to individuals and societies globally. The individual burden of osteoarthritis captures reductions in health-related quality of life, disability, loss of wages, and costs that result from osteoarthritis. The societal burden of osteoarthritis captures the aggregate consequences of osteoarthritis's impact on countries and regions around the world.

Epidemiological Observations

The prevalence of osteoarthritis (OA) is over 7% of people globally (528 million people), and even higher in countries with established market economies and older populations, such as the US (14%).[1, 2] OA is the 15th highest cause of years lived with disability (YLDs) worldwide, accounting for 2.2% of total global YLDs (18.9 million in 2019).[1] While OA can occur in any joint, it occurs most frequently in the knee, which accounts for 365 million cases worldwide and 61% of YLDs lost due to OA, followed by the hand (142 million cases and 24% of OA YLDs), then the hip (33 million and 5.5% of OA YLDs).[1, 3, 4]

Risk factors for OA include obesity, older age, female sex, prior traumatic joint injury, malalignment, genetic predisposition, and lower muscle mass.[5] Thus, the prevalence of OA rises with BMI, age, female sex, and likelihood of engaging in athletics or labor that carry a high risk of joint injury. Obesity in particular is a potent risk factor for developing OA.[6] For example, obesity increases the risk of knee OA three-fold.[7]

While the global prevalence of OA has been rising over time - from 1990 to 2019 it rose by 48% - trends in OA-prevalence vary by geography.[1, 3, 8] The age-standardized prevalence of knee and hip OA, for example, is highest in regions with established market economies, with North America (5,924 per 100,000 individuals) having the highest prevalence, followed by North Africa, then the Middle East (4,610 per 100,000), then Australasia (4,595 per 100,000).[9] By contrast, the prevalence of OA is much lower in Eastern Sub-Saharan Africa (2,568 per 100,000), Central Sub-Saharan Africa (2,633 per 100,000), and Western Sub-Saharan Africa (2,678 per 100,000).[9] Of any country, the US has the highest prevalence of knee and hip OA, at 6,128 per 100,000 individuals (approximately 32.5 million people, or 14% of US adults).[2, 9]

The prevalence of OA is projected to continue to rise countries with established market economies, such as North America and Europe, where populations are aging (median age rising) and the prevalence of obesity is increasing.[10–13]

Social Impact: Disparities in the prevalence, clinical characteristics, and treatment of OA around the world

Fransen et al. examined the prevalence of OA across different countries in Asia and found that OA disproportionately affects different communities based on geography and affluence.[10] In India, Bangladesh, and China, the prevalence of knee pain was significantly higher in rural communities than in urban settings. By contrast, in Pakistan, the prevalence of knee pain was higher among urban affluent individuals than among the urban poor, likely because the prevalence of obesity is higher among more those who are more affluent in Pakistan. Study authors also found that the prevalence of bilateral knee OA among Chinese

individuals was between 2 to 3 times higher than that of patients in the Framingham OA Study, one of the largest, longest, longitudinal population studies ever conducted in the US.[14] As both studies used the same symptomatic and radiographic diagnostic criteria these comparisons suggest that further research is needed to investigate disparities in the prevalence of OA between Chinese and Caucasian populations.

Safiri et al. examined trends in OA prevalence across the globe by Socio-demographic Index (SDI), a measure of a region's socio-demographic development based on average income per person, educational attainment, and total fertility rate.[16] Study authors found that OA prevalence rises with SDI score, leading to a high burden of OA in countries with established market economies such as the US. However, they also report a high burden of OA in countries with middle SDI levels where life expectancy is increasing, as Egypt and American Samoa.

Treatment of OA also varies globally, particularly for total joint replacement (TJR), a treatment for end-stage OA, which is often performed after other, non-operative pain-management strategies have been exhausted, such as non-steroidal anti-inflammatory drugs and corticosteroid injections. While TJR is most frequently performed on the knee and hip joints, it is also performed on the ankle, wrist, shoulder, and elbow joints.[15] TJR is performed less frequently in countries without established market economies for a range of reasons, including the high cost of the surgery, the challenge of ensuring operating rooms are sterile, and lower availability of trained surgeons.[16, 17] In countries with established market economies, TJR utilization differs by race and ethnicity, a disparity that has been documented in the literature for decades. In 1995, for example, a study conducted at 17 hospitals in California found that white individuals were twice as likely to undergo total hip arthroplasty as Black patients, and that rates of TJR were even lower among Hispanic, Filipino, Japanese, and Chinese individuals.[18] More recently, in 2016, Zhang et al. report the following rates of total knee replacement utilization per 1,000 individuals per year in the US: whites (4.65), black (3.9), Hispanic (3.71), Asian (3.89), Native American (4.4), and mixed-race (3.69).[19] They also found that after controlling for patient- and health-system related factors, minority patients experienced worse outcomes (mortality and complications), and were more likely to undergo surgery at lower-volume, lower-quality care centers. Many complex factors may underlie these disparities, from patient preferences and expectations, to physician recommendations for surgery, to access to care and the quality of care received.

Clinical Characteristics and Implications of Osteoarthritis for Individuals:

The implications of pain on physical activity limitations, mental health, and overall health

Physical inactivity is not only a risk factor for developing OA, but also a symptom of the disease, brought on by pain and stiffness in the affected joint(s). Thus, among OA patients, many of whom are inactive to begin with, OA pain can perpetuate inactivity.[20]

The 2017 Burden of Musculoskeletal Disease reported that approximately 65% of OA patients experience movement limitations, such as difficulty performing daily tasks and household activities.[21] In the US, in a study of 566 adults with OA, only 9.6% engaged in the minimum amount of exercise (150 minutes of moderate to vigorous physical activity

per week) as recommended by the Centers for Disease Control, in contrast to the 53.5% of the general US population who meets these guidelines.[22, 23] As inactivity increases an individual's risk of all-cause mortality, doubles the risk of cardiovascular diseases, diabetes, and increases the risks of colon cancer, high blood pressure, osteoporosis, lipid disorders, depression and anxiety, it poses serious health risks to OA patients.[24]

Physical activity is also a recommended treatment for OA. The American College of Rheumatology recommends exercise and physical therapy as "mainstays" of OA treatment, explaining that "people with arthritis who exercise regularly have less pain, more energy, improved sleep, and better day-to-day function."[25] Indeed, exercise programs may reduce OA patients' pain.[26, 27] A recent randomized control trial conducted in Denmark investigated the effect of a 12-week exercise program on knee OA patients' pain.[28] Relative to the control group, patients in the exercise therapy group experienced a 6.8-point improvement in pain on a 100-point scale known as the Knee Injury and Osteoarthritis Outcome Score (KOOS). The KOOS is a questionnaire which patients complete that is designed to assess five outcomes: pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life.[29] While this improvement was statistically significant, it is important to note that changes in pain of 8–10 points on a 100-point scale are generally considered clinically meaningful.[30]

Nonetheless, there is substantial evidence that physical activity improves mental health, which is relevant to OA, as OA patients have demonstrated worse mental health than healthy controls.[31–33] A recent study using data from the Korea National Health and Nutrition Examination Survey compared mental health in cohorts of patients with and without OA.[34] The OA cohort exhibited higher rates of 2-week long depressive mood, psychological distress, and suicidal ideations when compared with the control group, and worse quality of life scores. Indeed, physical activity has been shown to reduce symptoms of depression and anxiety, and improve individuals' overall quality of life.[35, 36] Hurley et al. use the biopsychosocial model of health to argue that the psychosocial benefits of exercise for OA patients are as important as physiological benefits, such as reducing pain and increasing activity.[37] They argue that exercise not only helps patients by challenging their beliefs that physical activity causes pain and joint damage, but also helps them control their OA symptoms by providing them with a coping strategy, which can in turn enhance their self-efficacy and reduce feelings of helplessness, disability, and social isolation.

OA poses serious implications to individuals' health via inactivity. Given the potential benefits of physical activity for OA patients for OA and their broader physical and mental health, developing interventions to help promote physical activity among knee OA patients is extremely important. A number of contemporaneous clinical trials are conducted to determine the means of increasing physical activity in persons affected by low extremity OA.[38, 39]

The impact of OA on mortality:

While a growing body of evidence suggests that OA leads to increased mortality, a consensus has not been reached in the literature.[40–44] Nüesch et al. report that relative to the general population, knee and hip OA patients exhibit an increased risk of all-cause

mortality with a standardized mortality ratio of 1.55 (95% confidence interval: 1.41 to 1.70).[45] Study authors further note that while subjects exhibited excess mortality for all disease specific causes of death, excess mortality as a result of cardiovascular disease and dementia was particularly pronounced, with standardized mortality ratios of 1.71 (95% CI: 1.49 to 1.98) and 1.99 (95%: 1.22 to 3.25), respectively. Two potential mechanisms by which OA may increase mortality are: (1) physical inactivity, which is associated with increased mortality and risks of chronic conditions, such as cardiovascular disease, (2) treatment with non-steroidal anti-inflammatory drugs (NSAIDs), as NSAIDs carry the risk of adverse events, including mortality.[46, 47] Yet, in a recent literature review, Cleveland et al. explain that a consensus has not yet been reached. Several studies conducted in the UK, European countries, and the US, did not find a noteworthy increase in all-cause mortality due to knee OA, while several studies conducted in Asian populations did report increases in mortality for OA patients, and for OA concurrent with cardiovascular disease specific mortality.[44]

The Economic Burden of Osteoarthritis

The economic costs of OA -- definitions and concepts:

Direct costs refer to resources expended on the management of a health problem, including health-related resources and related expenditures.[48] Direct *medical* costs are those relating directly to care, such as hospitalization, outpatient visits, medications, physical therapy, assistive devices, diagnostic tests, and alternative therapies. Non-medical direct costs include childcare and transportation costs incurred in the process of receiving care. By contrast, “indirect” costs refer to costs that do not relate to the medical management of a health problem, but which otherwise would not be incurred, such as lost wages and productivity.[49] Costs of either kind (direct or indirect) may be incurred by individuals, healthcare systems, and/or societies, and are often reported in public health studies from different “perspectives.”[50] Generally, a “societal” perspective captures all costs (both direct and indirect) associated with a disease, regardless of who pays those costs (e.g. patients, healthcare systems, or insurers).[50] By contrast, a “patient” perspective only captures costs directly incurred by the patient, and a payer perspective only captures costs that an insurer (e.g. Medicare) would pay.[50] In this section, we describe the substantial costs, both direct and indirect, that patients and societies across the globe experience due to OA. All costs have been converted to USD and inflated to 2019 values using the Personal Health Care Price Index and Personal Consumption Expenditure Price Index.[51–54] Years in which costs were originally reported are noted.

The economic cost of OA for populations:

The direct costs of OA amount to 1–2.5% of Gross National Product in countries with established market economies such as the US, UK, Canada, and Australia.[55] In 2013 in the US, OA was the second most costly medical condition treated in US hospitals, accounting for 4.3% ($18.4 billion) of all hospitalization costs ($415 billion).[56] The direct medical cost of OA in the US is estimated at $72 billion (using average cost data from 2008–2011).[21] However, healthcare costs are much greater in the US than in other high-income countries, where OA costs are lower, though still substantial.[57] In Australia, for example, the direct

medical costs of OA were estimated to be $1.7 billion in 2015, roughly 2.4% of the cost of OA the US, despite having a population that is roughly 7.3% that of the population in the US (in other words, there are 7,300 individuals in Australia per 100,000 individuals in the US).[58–60] The indirect costs of OA are also substantial. Published estimates of the indirect cost of OA in different established market economies countries include: Spain ($1.2 billion, originally 2010£), UK ($6.5 billion, originally 2010£), and US ($12.7 billion, originally 2007 USD).[61, 62]

Data on the economic burden that OA poses on individual and population levels are lacking in countries where market economies are less well established, suggesting the need for further research to understand the financial impact OA has on healthcare systems and economies in these regions.

Trends in the direct costs of OA management:

While the direct costs of OA depend on an individual's affected joint, disease severity, treatment choices, the healthcare system/country in which care is received, in addition to his or her overall health status, certain factors are associated with higher costs. For example, surgical management of the disease (e.g. total joint replacement) is often costlier than non-surgical alternatives (e.g. pain medication or physical therapy). In a model-based evaluation, Losina et al. report that total knee replacement (TKR) is the largest driver of knee OA costs at $21,930 (originally 2013 USD), followed by those of pain management, such as non-steroidal anti-inflammatory drugs (NSAIDs), annual physician visits, physical therapy, and intra-articular injections, which range from $560–740 per year (originally 2013 USD).[63]

Obesity is also associated with a higher cost of disease management. Using data from over 8,000 patients at a large US medical center from 2000 to 2008, Kremers et al. report that for every 5-point increase in BMI beyond 30 kg/m^2, hospitalization costs for primary and revision TKR increased by $440 and $740 (originally 2010 USD), respectively, even after adjusting for comorbidities and complications. Increases in costs were driven largely by longer hospital stays and higher operating room costs.[64] Thus, in countries experiencing aging populations and rises in the prevalence of obesity, utilization of total joint replacement (TJR) is projected to rise too, which suggests that the average cost of OA management will likely rise too.[10, 65–68]

Trends in the indirect costs of OA: absenteeism and presenteeism

Indirect costs associated with OA are caused by lost workplace productivity, early retirement, and disability, and are often categorized as resulting from absenteeism or presenteeism. Absenteeism refers to time lost at work because of problems resulting from a medical condition and the time spent seeking treatment to mitigate its symptoms.[69] Presenteeism refers to disease-specific losses that may occur even when a person is at work.[69] The association between absenteeism and knee OA in particular is well documented in countries around the world. In a 2013 systematic review of studies conducted in countries with established market economies across the globe, Agaliotis et al. report that the 12-month

prevalence of absenteeism among individuals with chronic knee pain ranged from 5% to 22%.[70]

In 2009 in the US, DiBonaventura et al. report that individuals with OA pain of any kind, relative to those without it, incur nearly two-fold higher annual indirect costs resulting from lost workplace productivity.[71] They also report that individuals with physician-diagnosed OA and OA-related pain in the past month were less likely to report full-time employment than those without OA (57% vs. 71%). In terms of time lost due to absenteeism vs. presenteeism, those with OA pain lost 31% of productive time at work due to presenteeism and 8% due to absenteeism, compared to 16% and 4%, respectively, for those who did not report OA pain. For those with OA pain, these percentages translate to 2.7 hours lost due to absenteeism and 9.7 hours lost due to presenteeism, compared to 1.4 and 5.2 hours lost by those without OA pain.

The fact that indirect costs due to presenteeism are higher than those due to absenteeism means that OA costs patients more lost productivity at work than it causes them to miss days of work entirely.

The economic cost of OA for individuals across the globe:

In a 2016 systematic literature review, Salmon et al. examined the economic impact of lower limb-OA (knee and hip), both in terms of direct medical and indirect costs, in different countries around the world from payer and societal perspectives.[72] Study authors report average annual direct medical per-patient costs of OA across countries in Asia, Europe, North America, and Oceania (which includes Australasia, Melanesia, Micronesia, and Polynesia). Across the world, these costs ranged from $700-$15,600, with a global mean of $13,600 (originally 2013€). Countries in North America exhibited the highest average annual direct costs ($14,000), while costs were lower in Asia ($8,900), Europe ($1,400), and Australia (Oceania) ($900). Average annual indirect costs per patient ranged from $300–17,700, with a global mean of $6,300. Similar to trends observed for direct costs, countries in North America exhibited the highest average annual indirect costs ($6,500), while they were lower in Europe ($5,500) and Asia ($2,300/year). Indirect costs in Oceania were not reported.

Salmon et al. note that significant heterogeneity exists in the methodologies used in different papers to estimate OA costs. To estimate direct costs, different studies included different combinations of costs from categories such as physician visits, emergency room, hospital, non-traditional healthcare, physiotherapy, drugs, transportation, biology, radiology, and surgery. The most commonly included costs were physician visits, drugs, and hospital costs, and the least frequently included were non-traditional healthcare and physiotherapy. Similar heterogeneity was present in the methodologies used to estimate the indirect costs of OA, with some articles reporting costs due to both absenteeism and presenteeism, and others only reporting those due to absenteeism. The key take-away is that despite this methodological heterogeneity, and variations in cost by geography, lower limb OA imposes a substantial economic burden to individuals around the world.

Just as OA imposes a substantial burden on patients' quality of life--a burden that is distributed differentially across demographic and clinical lines--it also exacts high economic costs on individuals around the world, which vary according to geographic, demographic, and clinical characteristics. Given that OA disproportionately affects women, the elderly, certain racial/ethnic minorities, and those with lower socioeconomic status, the direct and indirect costs of the disease are likely higher among these patient populations than the average estimates presented by Salmon et al. Likewise, the cost of OA may be lower among populations that are less severely impacted by the disease, such as those who are younger and male.

Metrics used to capture, understand, and compare the burden of disease:

Researchers and clinicians also use quality-adjusted life-years (QALYs) to capture the impact that OA pain and activity limitations have on patients' quality of life (QoL). QALYs are a standardized metric, not specific to knee OA, which allow clinicians and researchers to compare and contrast the burden of OA to that of other medical conditions.[73]

To determine the impact a medical condition has on a patient's quality of life (QoL), a patient's perceived QoL in a given year is rated on a 0 to 1 scale, where 0 represents a state equivalent to death and 1 represents perfect health.[74] For example, a patient living with advanced OA may have difficulty choosing between a year lived at their given pain level, or 0.7 years of perfect health.[75] Here, a year of advanced OA equates to 0.7 QALYs.

Losses in QALYs resulting from knee OA have been compared to those from conditions such as cancer, liver disease, and cardiovascular disease.[76–79] Using computer modeling, Losina et al. estimate that US adults aged 50–84 lose an average of 1.9 QALYs over the remainder of their lives due to knee OA, and that those with OA and obesity lose an average of 3.5 QALYs.[76]

Quantifying the value of OA treatments

Gains in QALYs may be used to capture the potential benefit of a treatment. Determining the cost per QALY gained due to incorporating a given treatment into a patient's care--a ratio known as the "incremental cost-effectiveness ratio" (ICER)--is the goal of many cost-effectiveness analyses. If a treatment's "ICER" falls below a predetermined setting or payer specific willingness to pay threshold (WTP), the treatment is considered cost-effective.[80]

Given different OA treatments' benefits, costs, and potential complications, different treatments produce substantially different ICERs. For example, Losina et al. report that total knee replacement (TKR) surgery is cost-effective with an ICER of $35,800/QALY (originally 2006 USD) at a WTP threshold of $50,000/QALY, but that generic celecoxib, a COX-2 selective NSAID, is not (ICER = $301,000/QALY, originally 2015 USD).[81, 82]

ICERs may also vary substantially for a single treatment, depending on parameters such as the demographic and clinical characteristics of the patient population under consideration (e.g. age, BMI, knee OA severity), the costs included, the setting considered (e.g. global region, or rural vs. urban) the cost-perspective (e.g. societal, payer) from which the analysis is conducted. For example, patients with greater pain levels and knee OA severity may stand

to benefit more (gain more QALYs) from surgery than those with less severe OA. The more QALYs gained, the lower the dollar cost per-QALY, and therefore the more favorable and lower the ICER. In this way, the more similar a patient's demographic and clinical profile is to that of the population used to obtain a published ICER, the more likely that ICER is to accurately capture the costs and benefits that patient can expect to receive for a given treatment.

TKR is an example of a procedure whose value and cost-effectiveness are well agreed upon in the literature. Compared to Losina et al.'s estimate ($35,800/QALY, 2019 USD), recently published ICERs for TKR in other countries (converted to 2019 USD) include $11,800/QALY in the UK (originally 2007–2008£), and $21,200/QALY in China (originally 2015¥).[83, 84] These ICERs all fall below $50,000 USD/QALY, a commonly used threshold for cost-effectiveness.[80] Indeed, in a recent systematic review, Lan et al. report that of ten studies conducted around the world comparing TKR to non-surgical strategies, all reported ICERs below $50,000 USD/QALY.[85]

Conclusion

OA imposes substantial pain and disability on patients, which reduce their quality of life and lead to high economic costs. Because OA is so prevalent, these decrements in quality of life and costs add up to enormous totals for populations across the globe. As the prevalence of OA is predicted to rise due to aging populations and the obesity epidemic, the economic costs of OA are likely to rise too. However, it is possible that the development of new treatments, such as disease-modifying drugs that slow or halt the progression of OA, or community-based interventions that increase access to care among disproportionately affected populations, could mitigate some of the losses of quality of life and productivity currently resulting from OA.

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