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Lifetime medical costs of knee osteoarthritis management in the United States: Impact of extending indications for total knee arthroplasty

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Abstract

Objective—The impact of increasing utilization of total knee arthroplasty (TKA) on lifetime costs in persons with knee OA is under-studied.

Methods—We used the Osteoarthritis Policy Model to estimate total lifetime costs and TKA utilization under a range of TKA eligibility criteria among US persons with symptomatic knee OA. Current TKA utilization was estimated from the Multicenter Osteoarthritis Study and calibrated to Health Care Utilization Project (HCUP) data. OA treatment efficacy and toxicity were drawn from published literature. Costs in 2013 USD were derived from Medicare

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reimbursement schedules and Red Book Online®. Time costs were derived from published literature and the US Bureau of Labor Statistics.

Results—Estimated average discounted (3%/year) lifetime costs for persons diagnosed with knee OA were $140,300. Direct medical costs were $129,600, with $12,400 (10%) attributable to knee OA over 28 years. OA patients spent, on average, 13 (SD 10) years waiting for TKA after failing non-surgical regimens. Under current TKA eligibility criteria, 54% of knee OA patients underwent TKA over their lifetimes. Estimated OA-related discounted lifetime direct medical costs ranged from $12,400 (54% TKA uptake) when TKA eligibility was limited to K-L 3 or 4 to $16,000 (70% TKA uptake) when eligibility was expanded to include symptomatic OA with a lesser degree of structural damage.

Conclusion—Due to low efficacy of non-surgical regimens, knee OA treatment-attributable costs are low, representing a small portion of all costs for OA patients. Expanding TKA eligibility increases OA-related costs substantially for a population, underscoring the need for more effective non-operative therapies.

Keywords

knee osteoarthritis; utilization of TKA; direct medical costs; lifetime costs

INTRODUCTION

Symptomatic knee osteoarthritis (OA) is a chronic, painful condition affecting an estimated 9.3 million adults 45 years and older in the US (1). In addition to lowering quality of life, knee OA is a major economic burden (2–6). The American College of Rheumatology (ACR) (7), Osteoarthritis Research Society International (OARSI) (8,9), and American Academy of Orthopaedic Surgeons (AAOS) (10,11) have published clinical practice guidelines for the management of knee OA. However, these guidelines do not consider costs and do not provide guidance on indications for TKA (7–11). Based upon the number of TKAs performed annually and the estimated number of individuals in the US with OA, we determined that surgery is currently performed in persons in pain and Kellgren-Lawrence (K-L) grades 3 or 4 (12,13).

Since OA often occurs with multiple concomitant comorbidities, it is important to understand what portion of total direct medical costs is attributable to OA. The majority of prior economic evaluations regarding knee OA have focused on individual treatments (14–23). However, knee OA management includes a combination of treatments over a long time horizon. To date, there have been no published studies estimating the *lifetime* costs incurred by persons affected by symptomatic knee OA in the US.

Furthermore, TKA utilization has doubled over the last decade, an increase that was not entirely explained by population growth and the obesity epidemic (24). The growth in utilization is partially due to expanding eligibility criteria and greater willingness of symptomatic OA patients to undergo TKA, regardless of radiographic severity (24). While patients below 65 years of age comprised just a quarter of TKA recipients in 1997 (25), almost 40% of TKAs are now done prior to age 65 (24).

In the absence of treatment guidelines linking clinical choices to data on the economic burden of disease, we sought to estimate the lifetime resource use (including direct, OA-specific costs; direct, non-OA costs; and time costs due to productivity losses) associated with alternative TKA eligibility criteria.

METHODS

Analytic overview

We used the Osteoarthritis Policy (OAPol) Model (26,27) and published data on costs, utilization, efficacy, and toxicity of OA treatments to project lifetime direct medical costs (costs due to OA as well as all other conditions), knee OA-related costs, and time costs due to productivity losses in persons with diagnosed symptomatic knee OA. For comparison, we also estimated lifetime costs for knee OA-free individuals with similar demographic and clinical characteristics. While guidelines are largely prescriptive for non-surgical OA treatments, those for TKA are less detailed. We therefore conducted analysis across five sets of TKA eligibility criteria based on pain that is not relieved by non-surgical treatment and: 1) 100% K-L grade 4 (most conservative, limited to end-stage disease), 2) 50% K-L 3 and 100% K-L 4; 3) 100% K-L 3 or greater (defined as the “current TKA eligibility” criterion); 4) 50% K-L 2, 100% K-L 3 or greater; and 5) 100% K-L 2 or greater (least conservative). Lifetime cost estimates in real (i.e. inflation-adjusted) 2013 USD are reported both undiscounted and discounted at an annual rate of 3%, as recommended by the Panel on Cost-Effectiveness in Health and Medicine (28). In additional analyses, we added estimates of time costs due to absenteeism among employees diagnosed with knee OA (29,30).

Under these ranging TKA eligibility criteria, we estimated the proportion of individuals with knee OA that received each treatment, the proportion that received TKA before age 65, the mean duration of each treatment, and the mean age of undergoing TKA.

OAPol Model structure

The OAPol Model is a validated, state-transition, computer simulation model of the natural history and management of knee OA (24,26,27,31,32). In the model, individuals transition among health states defined by structural severity of knee OA (K-L grades 0 to 4) and symptom status (33). Symptomatic knee OA is defined as radiographic knee OA (K-L grades 2 to 4) accompanied by pain on most days. In the beginning of each simulation, each hypothetical patient is assigned a K-L grade, age, sex, and BMI.

In addition to capturing the incidence and progression of knee OA, the OAPol Model tracks the development of other chronic conditions prevalent in persons with knee OA. Large cohorts are followed until death, which is determined in a probabilistic manner using US life tables adjusted with disease-specific relative risks of mortality (34–36). Additional descriptions of the OAPol Model structure have been published previously (26,32,37).

Treatment strategies

We considered two treatment strategies: 1) care limited to occasional analgesics (for comparison purposes); and 2) guideline-concordant care. Occasional analgesic use was

modeled as acetaminophen, over-the-counter NSAIDs (ibuprofen or naproxen), or one of three opioids (codeine, hydrocodone, or oxycodone) prescribed by a general practitioner.

Consistent with recommendations published by ACR, OARSI, and AAOS, guideline-concordant care was modeled as four regimens offered sequentially in order of increasing intensity, with analgesics used as needed between treatments (Table 1) (7–11,38). Under guideline-concordant care, all individuals with diagnosed symptomatic knee OA received Non-Surgical Regimen 1, comprised of physical therapy, knee braces, acetaminophen, and NSAIDs. Upon failure of Non-Surgical Regimen 1, individuals were offered Non-Surgical Regimen 2, consisting of corticosteroid injections. Failure of Non-Surgical Regimen 2 led to offering of TKA (Surgical Regimen 3) for all those whose pain was not relieved with non-surgical treatment and who had structural changes due to OA evident on plain radiographs. Acceptance of primary TKA varied by age and sex and was derived from data from two large cohort studies (39,40). Individuals with primary TKA failure received revision TKA (Surgical Regimen 4). Those with pain, including patients who were in pain despite undergoing TKA, were assumed to use analgesics and accrue time costs due to productivity loss. Subjects whose pain was relieved by TKA had lower OA-related healthcare costs. These patients were also assumed to have lower pain-driven time costs.

Input data

Demographics and clinical characteristics—The average age of diagnosis of symptomatic knee OA was assumed to be 54 (standard deviation (SD) 14) years (Table 1) (32). Data on sex, race, and obesity in persons with knee OA were derived from the 2012 National Health Interview Survey (41). Prevalence and incidence of comorbidities (cancer, coronary heart disease, chronic obstructive pulmonary disease, diabetes mellitus, and other musculoskeletal diseases) by sex and race/ethnicity were derived from the 2009–2010 National Health and Nutrition Examination Survey (NHANES) (42). Annual rates of knee OA progression, stratified by sex, obesity, and K-L grade, varied from 1.3% to 12.3% (26).

Knee OA treatment efficacy—The efficacy of non-surgical regimens in relieving pain was derived from published clinical trials, with Non-Surgical Regimen 1 efficacy weighted according to 2009 Medicare Current Beneficiary Survey (MCBS) data on NSAID utilization (43–45). Efficacy of pain relief in the first year for Non-Surgical Regimen 1 was 63% and for Non-Surgical Regimen 2 was 64% for individuals with early-stage knee OA. This efficacy was sustained in 76% of persons on Regimen 1 and in 81% on Regimen 2 in each subsequent year. For TKA, pain relief the first year after surgery was 86% (46). Mechanical failure of primary TKA leading to revision was stratified by age and ranged from 0.3% per year (for those 65 years and older) to 1.2% per year (for those younger than 65 years) (47) (see Technical Appendix for detailed data).

Knee OA treatment toxicity—Treatment toxicities were associated with specific costs, quality-of-life decrements, and risks of death. Estimated costs of toxicities were derived from 2011 HCUP data and converted to real (i.e. inflation-adjusted) 2013 USD (Table 1) (13,48).

Knee OA treatment costs

Occasional analgesic use: We included an annual cost of occasional analgesic use for knee OA subjects either in pain but not on any regular regimen or when TKA fails to relieve pain (Table 1). This cost ($102) was derived from the average annual cost of acetaminophen and opioids (49) weighted by the estimated utilization of each type of drug (21% - opioids; 79% - acetaminophen) (45). Additional details on cost derivation are presented in the Technical Appendix.

Non-Surgical Regimen 1: Overall, the cost of Non-Surgical Regimen 1 was estimated at $684 in the first year and $520 in each subsequent year. Costs of annual physician office visits, physical therapy, assistive devices, and laboratory tests were derived from 2012 Medicare reimbursement schedules (50,51). Costs of NSAIDs, acetaminophen, and gastro-protective agents were derived from Red Book Online® (49). Regimen component costs were weighted according to their utilization by OA patients, as derived from MCBS data. Further details are presented in the Technical Appendix.

Non-Surgical Regimen 2: Annual costs of Regimen 2 ($494) included the cost of one physician office visit ($99) (50,51) and an average of 2.5 corticosteroid knee injections per year (45). The estimated cost of each injection ($157) was derived from the 2012 Medicare reimbursement schedule (averaged for hospital and non-hospital settings) for joint injections of lidocaine (10 mg) and methylprednisolone (40 mg) (50,51).

Primary and revision TKA: Total costs in 2013 USD for primary ($20,293) and revision ($26,388) TKA included the costs of surgery and rehabilitation derived from 2012 Medicare reimbursement schedules (50), the 2011 Medicare Hospital Inpatient Prospective Payment System (52), and literature (53). Annual follow-up costs ($143) included a physician office visit and knee radiograph ($44) (50,51). From a national survey of physicians' recommendations regarding post-TKA follow-up care, we estimated the annual likelihood of having a post-TKA follow-up visit to be 67% (54). The product of these two quantities yielded an annual average cost for post-TKA follow-up of $95.

Direct medical costs unrelated to knee OA—We estimated average annual direct medical costs unrelated to knee OA, stratified by age and number of comorbidities, by weighting Centers for Medicare & Medicaid Services hierarchical condition categories (CMS-HCC) estimates according to aggregated data from NHANES 2009–10 (42). Costs were inflated to real (i.e., inflation-adjusted) 2013 USD using the Consumer Price Index (CPI) inflation calculator for Medical Care in the US (48). These costs varied from $1,414 to $8,202 per year for those with 0 to 1 comorbidities to $14,291 to $19,092 per year for those with greater than three comorbidities (Table 1).

Time costs due to productivity losses—We based time cost estimates (cost of lost productivity) on published data addressing work absenteeism among individuals with OA in the US work force (29). Our estimates are based entirely on the labor market and do not account for other types of productivity losses. The reported annual time costs for persons with OA who did not undergo TKA were estimated at $1,474 per year (in 2007 USD)

among those in the workforce. Time costs for OA patients who had TKA while being in the workforce were estimated at $7,104 (in 2007 USD) during the year of surgery. To properly account for differing levels of work absenteeism across age strata, we used employment data stratified by age provided by the US Bureau of Labor Statistics (30) (see the Technical Appendix for derivation details).

Sensitivity analyses—We conducted sensitivity analyses to address uncertainties in parameter estimates and to examine the effects of alternative assumptions. First, we varied the mean age of symptomatic knee OA diagnosis from 50 to 70 years. Second, we varied the distribution of background analgesics used from acetaminophen only to opioids only. Third, we varied K-L grade distribution at the time of diagnosis. Fourth, we evaluated the impact of using more effective and expensive analgesics in Regimens 1 and 2 on overall treatment utilization and cost. Lastly, we varied rates of knee OA progression based on obesity status.

RESULTS

Proportion of cohort receiving TKA and timing of treatments

Individuals spent several years on each non-surgical regimen before waiting an average of 13.3 (SD 10.4) years before receiving TKA, using analgesics as needed to manage pain prior to surgical treatment or death. Only about half the original cohort underwent primary TKA and a smaller percentage received revision TKA. Time spent on primary TKA was estimated at 16 years (Figure 1).

Utilization of primary TKA ranged from 19% of the total cohort when TKA eligibility was limited to K-L grade 4 to 70% with eligibility expanded to K-L grades 2 or above (Technical Appendix Figure 6-1). Under current TKA eligibility criteria, 38% of patients who underwent TKA received surgery prior to age 65. Overall, 21% of the knee OA population received primary TKA prior to age 65 (Technical Appendix Figure 6-1, third bar from the left, hatched black-and-white section). This estimate ranged from 6% with TKA eligibility limited to K-L 4 to 29% with eligibility set to K-L 2 or greater. Mean age at the time of primary TKA ranged from 65 (SD 12) years with TKA indications at K-L 2 or greater to 70 (SD 11) years with TKA indications limited to K-L 4 (Technical Appendix, Figure 6-1). The average time to revision or death for those TKA recipients under age 65 and for those ages 65 and over differed primarily due to competing mortality. When subjects were receiving TKA at age 65 or older, the time from primary to revision TKA or death was estimated at 13.0 years. For those receiving TKA before age 65, the average time from primary to revision TKA or death was estimated at 18.3 years.

Lifetime direct medical costs in persons with symptomatic knee OA

When followed from an average age of knee OA diagnosis of 54 (SD 14) years, persons without knee OA who had similar demographic and clinical characteristics had average estimated per-person discounted lifetime medical costs (total, for all conditions) of $117,500 ($209,800 undiscounted) (Table 2). Under Treatment Strategy 1 (occasional analgesics only), those with symptomatic knee OA incurred average lifetime direct medical costs of

$119,300 ($212,700 undiscounted) per person. Under Treatment Strategy 2 (guideline-concordant care), this estimate was $129,600 ($228,600 undiscounted) per person.

Direct medical costs attributable to knee OA

Under guideline-concordant care with current TKA eligibility criteria, direct lifetime medical costs attributable to knee OA were estimated at $12,400 ($19,600 undiscounted), 10% of the overall discounted lifetime direct medical costs for persons diagnosed with knee OA (Table 2). Knee OA-related direct medical costs ranged from $6,600 ($10,300 undiscounted) when only those with K-L grade 4 were eligible for TKA to $16,000 ($24,400 undiscounted) when those with K-L grades 2 or higher were eligible (Figure 2).

Distribution of knee OA-related costs by regimen

Under current TKA eligibility criteria, the largest proportion of knee OA-related direct medical costs was attributable to primary TKA, followed by Non-Surgical Regimen 1, which consisted of NSAIDs, annual physician visits, physical therapy, assistive devices, acetaminophen, and gastro-protective agents (Figure 2). As eligibility criteria for TKA expanded, costs associated with surgical treatments comprised a greater proportion of OA-related costs, while those associated with analgesic use and non-surgical treatment comprised a smaller proportion.

Sensitivity analyses

Under guideline-concordant care, knee OA-attributable per-person direct medical costs were greater when the mean age of symptomatic knee OA diagnosis was set to 50 years compared to 70 years. OA-related direct lifetime costs increased by about $2,000 when the annual cost of intermittent analgesics was varied from $71 (acetaminophen only) to $218 (opioids only). Lifetime direct medical costs and OA-related costs were higher as the radiographic severity of knee OA at the time of diagnosis increased. Increasing the efficacy of Non-Surgical Regimens 1 and 2 had minimal impact on the utilization of TKA. When efficacy and costs were increased by 50%, TKA utilization decreased from 54% to 51%. Costs were somewhat more affected with total direct medical costs increasing by 2% and direct medical costs attributable to OA increasing by 21%. Finally, altering knee OA progression rates by obesity had very little effect on lifetime direct medical costs (Table 3).

Discounted time costs due to lost productivity decreased with expanding eligibility criteria for TKA, ranging from $10,900 when TKA was restricted to symptomatic K-L grade 4 to $10,400 for symptomatic OA regardless of structural severity (Figure 3). However, combining time costs with non-OA and OA-related direct medical costs increased total discounted lifetime medical costs with expanding TKA indications, with $134,900 estimated for eligibility criteria of K-L grade 4 only to $143,400 for eligibility at all K-L grades 2 and higher (Figure 3).

DISCUSSION

Using a validated, published computer simulation model (26,27), we projected the lifetime direct medical and time costs for patients with symptomatic knee OA from disease onset

until death. The small proportion of lifetime direct medical costs (10%) attributable to knee OA treatment can be explained by the limited treatment options available for persons diagnosed with this debilitating condition. We found that persons with knee OA spend nearly 50% of their post-diagnosis life expectancy 'in between' treatments while waiting for TKA after exhausting available non-surgical options. We estimated that under current TKA eligibility criteria (pain unrelieved by non-surgical regimens and K-L grades 3 and 4), primary TKA is utilized by 54% of those with symptomatic knee OA and accounts for 61% of OA-related direct medical costs.

We found previously that the recent increase in TKA utilization is not explained entirely by population growth and the obesity epidemic (24), and is likely due, in part, to expanding indications and an increased willingness among patients to undergo surgery. Extending current eligibility criteria for TKA to any symptomatic disease, regardless of structural severity, led to an earlier average age of TKA, greater uptake of primary and revision TKA, and a 29% increase in lifetime direct medical costs attributable to knee OA. This finding – coupled with recent data suggesting greater failure rates and lower satisfaction rates among persons who underwent TKA in less advanced stages of OA – could prompt a stricter definition of TKA appropriateness. It also underscores the importance of finding alternative treatments for knee OA.

Our results extend the literature regarding the cost of OA management (29,55,56). Previous estimates of the annual direct medical costs of OA in the US vary widely (29,55,56), partly owing to heterogeneity in the methods used to distinguish OA-related care from all-cause health care utilization (2–6,55,57). Prior studies in this area have focused on the *annual* cost of medical care for persons with OA and report costs ranging from $989 to $10,313 in the US (56). Similar to other studies (58), our paper demonstrates that individuals with knee OA spend substantial financial resources on managing comorbidities.

Several findings from our study deserve special emphasis. First, guideline-concordant treatment represents a low but non-trivial cost burden for individuals with diagnosed symptomatic knee OA. Per-person lifetime costs of knee OA-related care ($12,400) account for 10% of lifetime direct medical costs. Second, TKA is the only treatment for symptomatic knee OA with any substantial duration of sustained efficacy and represents the largest source of costs. While only half of those diagnosed with symptomatic knee OA ultimately underwent TKA in our model, costs related to primary and revision TKA constituted 69% of total direct medical costs attributable to OA. As eligibility criteria for TKA expanded, OA-related costs increased.

Third, our findings draw attention to the question of who is paying for these costly surgeries. We estimated that 38% of persons receiving primary TKA under current eligibility criteria underwent surgery prior to age 65, when most healthcare costs falls to private insurers. If eligibility criteria for TKA expand, OA-related costs will increase and a higher percentage of TKAs will occur prior to age 65. As a result, the number of revision surgeries after age 65 (when payment is likely to fall to Medicare) will increase (13). These findings highlight the dramatic shifts in cost burden among payers that could result from changes in TKA timing. Preventive measures focused, for example, on reducing obesity and knee injury could delay

knee OA onset, reducing the likelihood of eventual TKA. Although this has the potential to reduce the lifetime costs of the disease dramatically, attention must be paid to potential repercussions of shifting costs to Medicare.

Our study has certain limitations. First, we assumed that patients underwent treatments sequentially, failing prior treatments before undergoing new ones. While this sequence was based on multiple published treatment guidelines (7–11,38), some physicians may tailor treatments for individual patients, leading to variations in the time a patient spends on each regimen. Second, our lifetime cost estimates do not account for the high cost of nursing home care, suggesting a conservative estimate of costs. However, nursing home care is utilized only by a relatively small segment of the elderly population. Third, our projections of lifetime direct medical costs in patients affected by knee OA incorporate only currently available treatments and do not factor in the benefits of drugs and surgeries under development. Fourth, our estimates of time costs are likely to be conservative as other activities affected by pain or suffering (reduced work and home productivity, loss of leisure time) were not considered. Further examination of health-related utility – as a function of both K-L stages and age – might provide a more balanced perspective on the costs and benefits of changing TKA eligibility criteria. And finally, the data for background morbidity in persons with OA were derived from national data sources. These parameters do not change rapidly from year to year. To maintain data consistency, we occasionally use the previous release of the national data source. These restrictions do not affect any OA-related estimates we report.

This is the first study to report lifetime costs of knee OA and the first one to consider the effects of expanding eligibility criteria for TKA. TKA is the only long-term effective treatment for symptomatic knee OA, but it is also the most costly. Expanding eligibility criteria for TKA may contribute to patients receiving TKA earlier in life and thus increase knee OA-related costs for both private insurers and Medicare. Implementation of combined exercise and weight loss programs (shown to be efficacious in persons with knee OA (59)), efforts to prevent injuries, and the development of disease modifying osteoarthritis drugs (DMOADs) that reduce the progression of knee OA may delay or prevent the need for and use of TKA and later revision. On the other hand, DMOAD therapy may be very costly. Therefore it could potentially be more cost-effective to offer TKA earlier in OA progression. Some studies have shown that patients with worse pain and function prior to surgery have worse outcomes following TKA (60–62), suggesting that there may be some benefit to offering TKA to patients with less severe OA. However, studies have also indicated that patients with more severe OA tend to be more satisfied with the results of surgery (63–65). Many studies have also suggested that undergoing primary TKA at a younger age is associated with an increased risk of failure and revision surgery (66,67). Additionally, several other variables, such as mental health, patient expectations, obesity and other comorbidities, affect outcomes of TKA (68–70), making it difficult to distill the effects that expanding indications would have on outcomes. Taken together with these considerations, our findings may have major policy implications for the cost and treatment of knee OA and the budgetary impact on payers, including Medicare. Additional research is needed to fully explain the costs and/or benefits of earlier surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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SIGNIFICANCE AND INNOVATIONS

- This is the first study to report lifetime costs of knee OA. Our estimates suggest that the cost of symptomatic knee OA in the US is relatively low ($12,400 per-person), accounting for 10% of total direct medical costs for persons diagnosed with symptomatic knee osteoarthritis.
- Expanding TKA eligibility criteria may contribute to patients receiving TKA earlier in life and thus could increase knee OA-related costs by 29%.

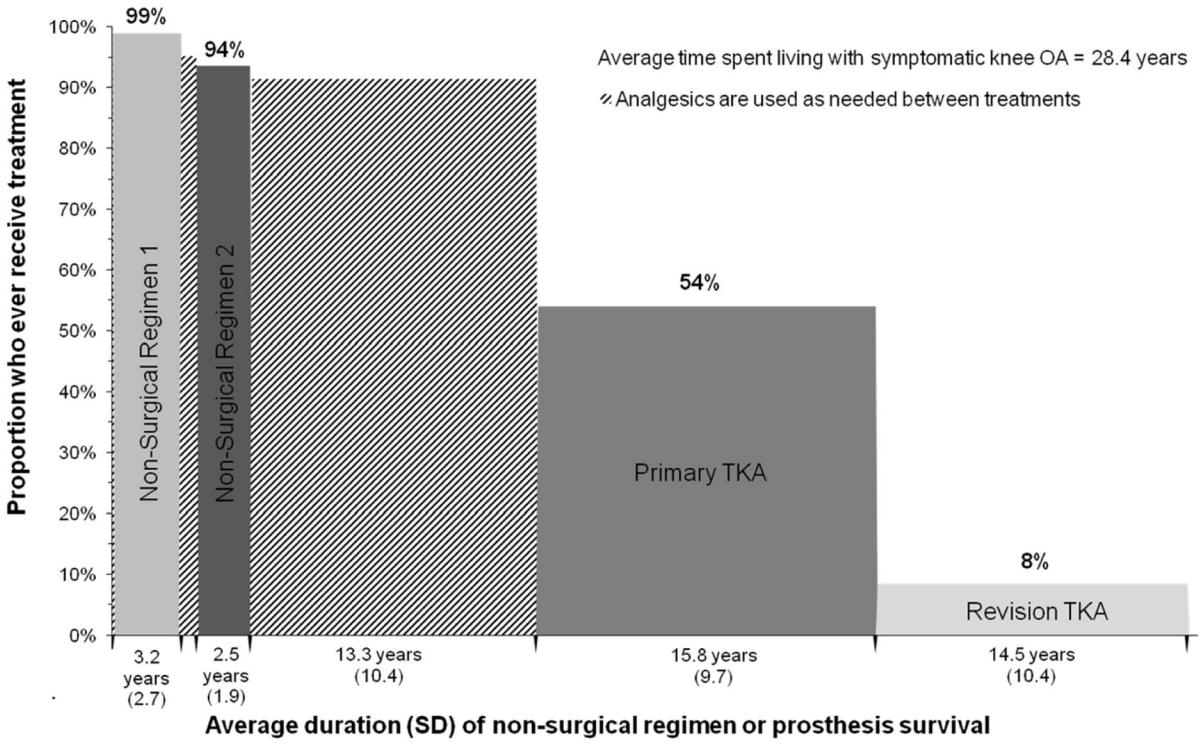

Figure 1. Utilization and duration of Knee OA treatments under guideline-concordant care, assuming TKA eligibility criteria is defined by persistent pain, unrelieved by non-surgical regimens and evidence of advanced knee OA (K-L grades 3 or 4)

Treatments under Treatment Strategy 2 (guideline-concordant care) are organized chronologically in order of increasing intensity along the x-axis. Intervening periods of occasional analgesic use are depicted with the hatched portions, with the longest duration of analgesic use occurring after Non-Surgical Regimen 2 and prior to primary TKA. The vertical height of each segment represents the proportion of those with symptomatic knee OA who ever received the treatment. The horizontal width of each segment represents the average duration (in years) of non-surgical regimens or prosthesis survival for those who ever received the treatment. The average time spent within each time period is written under each segment with the standard deviation, reported in years, in parenthesis. The average time spent living with symptomatic knee OA was 28.4 years. Primary and revision TKA were offered to patients with K-L grades 3 or 4.

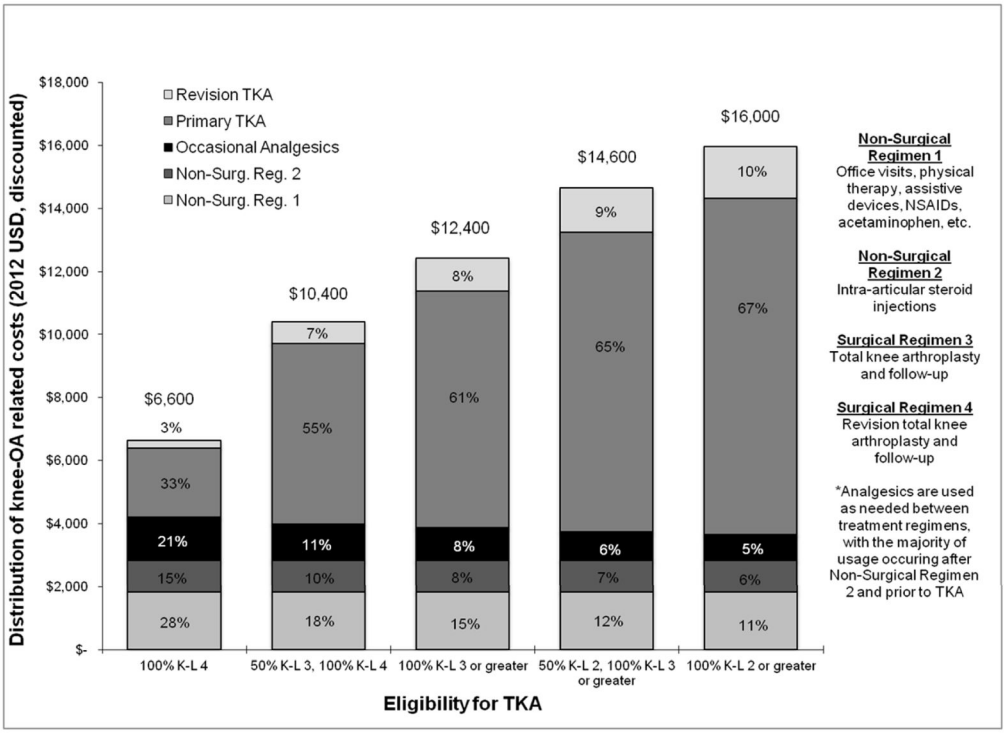

Figure 2. Varying eligibility criteria for TKA: Effects on distribution of OA-related, lifetime direct medical costs in patients with knee OA under guideline-concordant care

The series of stacked columns compares the percent and dollar distribution of lifetime direct medical costs (discounted) attributable to the four treatments for knee OA as well as occasional analgesic use under Treatment Strategy 2 (guideline-concordant care). Columns are presented across expanding eligibility criteria for TKA (left to right). The total direct medical costs attributable to knee OA under guideline-concordant care are listed above the columns. The cost of occasional analgesic use is shown in black and positioned between regimens 2 and 3 because use of analgesics is greatest during this treatment phase. Non-surgical Regimen 1 consists of office visits, physical therapy, assistive devices, and typical pain relief medications such as NSAIDs, acetaminophen, etc. Non-surgical Regimen 2 consists of intra-articular steroid injections. Surgical Regimen 3 is total knee arthroplasty and follow-up appointments, and Regimen 4 is revision total knee arthroplasty and follow-up appointments. Analgesics are used as needed between treatment regimens, with the majority of usage occurring after Non-surgical Regimen 2 and prior to TKA.

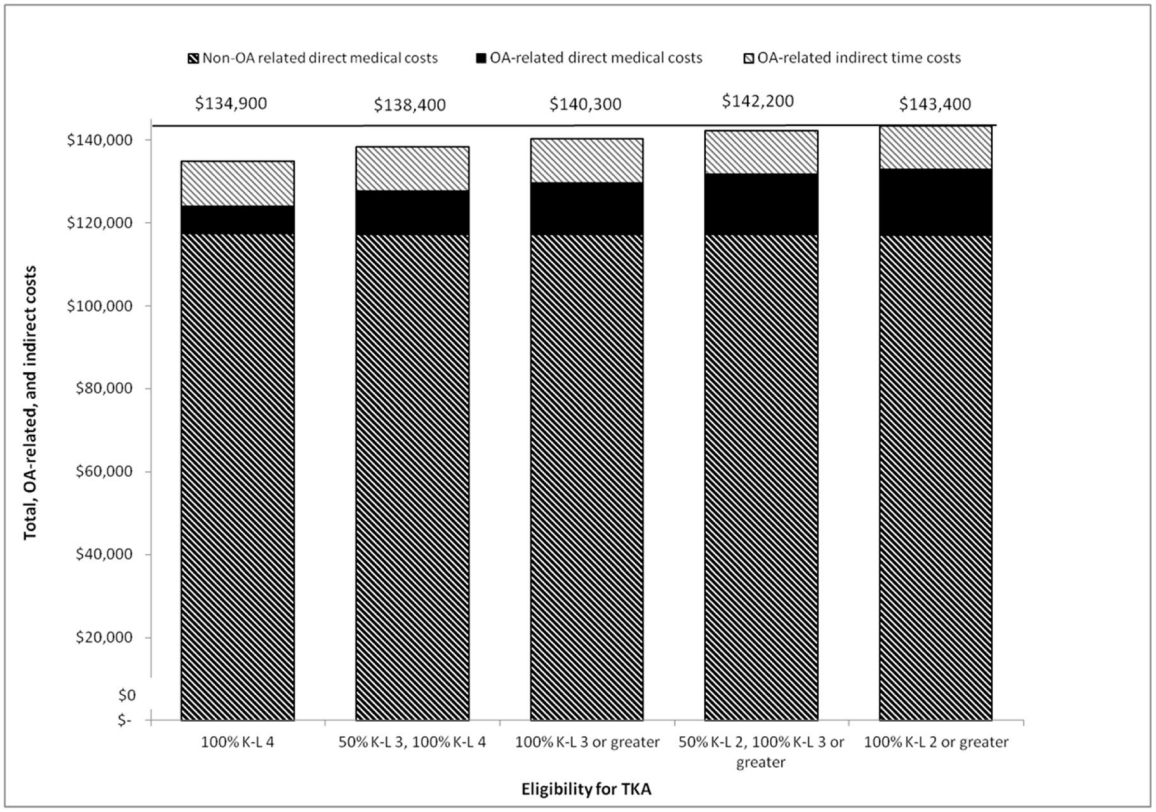

Figure 3. Varying eligibility criteria for TKA: Effects on lifetime direct and indirect medical costs for patients with knee OA

The series of stacked columns compares the distribution of lifetime total medical costs in knee OA patients receiving guideline-concordant care across expanding eligibility criteria for TKA (left to right). The total costs for each TKA eligibility criterion are listed above the columns. OA-related direct medical costs are shown in between total indirect medical costs attributable to knee OA (above) and non-OA related direct medical costs (below). For comparison, the horizontal line represents the total cost under TKA eligibility K-L grade 2 or greater.

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Table 1

OAPol model input parameters, cohort characteristics, and treatment parameters

Parameter	Overall Estimates
Mean Age (St. Dev)	53.5 (14.4)
% Female	53.2
Mean Body Mass Index (SD)	30.4 (6.8)
Prevalence of Knee Osteoarthritis	100% of population has Kellgren-Lawrence (K-L) grade 2 100% of population has knee pain associated with osteoarthritis

Progression estimates (annual probability, %)	**Male**	**Female**
Progression from K-L 2 to K-L 3 (non-obese/obese)	5.6/12.3	4.0/8.9
Progression from K-L 3 to K-L 4 (non-obese/obese)	1.3/2.9	1.9/4.3

Direct Medical Costs/Year (42,71) (in real (i.e. inflation-adjusted) 2013 USD)

Age	0–1 comorbidities	2–3 comorbidities	>3 comorbidities
25–34	$1,414.26	$7,464.92	$14,290.62
35–44	$1,975.45	$8,026.10	$14,290.62
45–49	$2,673.83	$8,170.64	$14,290.62
50–54	$2,674.65	$8,171.46	$14,291.43
55–59	$3,502.56	$8,798.13	$14,702.03
60–64	$4,269.37	$9,564.95	$15,468.85
65–69	$4,582.21	$9,899.78	$15,472.25
70–74	$5,337.78	$10,655.35	$16,227.82
75–79	$6,240.09	$11,557.66	$17,130.13
80+	$8,201.93	$13,519.49	$19,091.96

Treatment description	Treatment parameters			Source
Occasional analgesics [a] (acetaminophen, over-the-counter NSAIDs, opioids)	**Regimen cost (annual, $)[b]**	102		Red Book Online®; IMS Report; Office of Inspector General (49,72,73)
Non-Surgical Regimen 1: office visits, devices, physical therapy, NSAIDs, acetaminophen	**Regimen cost (annual, $)[b]**	**Initial year**	**Subsequent years**	2012 Medicare reimbursement schedules;

Treatment description	Treatment parameters					Source
		684	520			Red Book Online®; MCBS 2009; Van Der Esch et al, 2003; Grindrod et al, 2010; IMS Report; Office of Inspector General (45,49–51,72–75)
	Toxicities	**Cost of toxicity ($)**[b]	**Risk of toxicity while on regimen (annual, %)**	**Risk of death due to toxicity (annual, %)** (13)	**Cost**	**Risk of toxicity**
	General[c]	51	2.76 (initial year) 2.11 (subsequent years)	0.00	Kamath et al, 2003(16)	Bensen et al, 1999; Scott et al, 2000 (44,76)
	Cardiovascular[d,e]	19,089	0.12	5.29	HCUP 2011(13)	Solomon et al, 2005(77)
	Gastrointestinal[d,f]	9,984	0.23	2.68	HCUP 2011(13)	Goldstein et al, 2000; Silverstein et al, 1995(78,79)
Non-Surgical Regimen 2: office visits, injections	**Regimen cost (annual, $)**[b]	**Initial year**	**Subsequent years**		**Source**	
		494	494		2012 Medicare reimbursement schedules, MCBS 2009(45,50,51)	
	Toxicities	**Cost of toxicity ($)**[b]	**Risk of toxicity while on regimen (annual, %)**	**Risk of death due to toxicity (annual, %)** (13)	**Cost**	**Risk of toxicity**
	Skin flare	0	24.00	0.00	Yen et al, 2004(80)	Ayral et al, 2001(81)
	Sepsis[d]	14,065	0.0013	8.35	HCUP 2011(13)	Ayral et al, 2001(81)
Treatment 3: primary TKA and follow-up	**Treatment cost (annual, $)**[b]	**Year of surgery**	**Years of follow-up**		**Year of surgery**	**Years of follow-up**
		20,293	95		2012 Medicare reimbursement schedules; Buntin et al, 2005; HCUP 2011(13,50,52,53)	Medicare reimbursement schedules; Teeny et al, 2003(50,51,54)
	Toxicities	**Cost of toxicity ($)**[b]	**Risk of toxicity during year of surgery (%)**(13) [g]		**Cost**	**Risk of toxicity**
	Myocardial infarction	19,089	0.80		HCUP 2011(13)	Katz et al, 2004(82)

Treatment description	Treatment parameters				Source
	Pulmonary embolus	11,440	0.79	HCUP 2011(13)	Katz et al, 2004(82)
	Pneumonia	10,684	1.36	HCUP 2011(13)	Katz et al, 2004(82)
	Prosthetic joint infection[d]	23,488	0.70	HCUP 2011(13)	Paxton et al, 2010(47)
	Death from toxicity	**Cost of death due to toxicity ($)**[b]	**Risk of death due to toxicity during year of surgery (%)**(13) [g]	**Cost**	**Risk of death**
		15,149	0.63	HCUP 2011(13)	Katz et al, 2004(82)
Treatment 4: revision TKA and follow-up	**Treatment cost (annual, $)**[b]	**Year of surgery**	**Years of follow-up**	**Year of surgery**	**Years of follow-up**
		26,388	95	2012 Medicare reimbursement schedules; Buntin et al, 2005; HCUP 2011(13,50,52,53)	Medicare reimbursement schedules; Teeny et al, 2003(50,51,54)
Treatment 4: revision TKA and follow-up	**Toxicities**	Same as primary TKA			
	Death from toxicity	**Cost of death due to toxicity ($)**[b]	**Risk of death due to toxicity during year of surgery (%)**(13)[g]	**Cost**	**Risk of death**
		15,149	0.96	HCUP 2011(13)	Katz et al, 2004 (82)

[a] We did not account for toxicities related to occasional use of analgesics for pain management.

[b] All costs are reported in real (i.e. inflation-adjusted) 2013 USD.

[c] General toxicity includes the most common adverse events associated with the use of celecoxib for OA. These include headache, upper respiratory tract infection, dyspepsia, diarrhea, and abdominal pain.

[d] Occurrence of this toxicity in a given year causes the individual to be removed from the current regimen and evaluated for the subsequent regimen.

[e] Cardiovascular adverse events include myocardial infarction and thromboembolic events.

[f] Gastrointestinal adverse events include symptomatic upper gastrointestinal ulcer complications.

[g] For surgical regimens, we assume that any toxicity associated with the treatment will occur in the initial year. Thus, likelihood of toxicity or death due to toxicity in subsequent years is 0.

Table 2

Average per-person lifetime direct medical costs and costs attributable to symptomatic knee OA

Treatment Strategy(or Cohort Description)	Total direct medical costs* (SD)		Direct medical costs* attributable to symptomatic knee OA (SD)		Proportion (%) of lifetime costs attributable to symptomatic knee OA	
	Discounted	*Undiscounted*	*Discounted*	*Undiscounted*	*Discounted*	*Undiscounted*
Matched control group**	$117,500 ($63,300)	$209,800 ($136,300)	-	-	-	-
1. Occasional analgesic use only	$119,300 ($63,800)	$212,700 ($137,600)	$1,800 ($700)	$2,900 ($1,600)	1.5%	1.4%
2. Guideline-concordant care	$129,600 ($66,800)	$228,600 ($144,800)	$12,400 ($9,400)	$19,600 ($16,200)	9.6%	8.6%

* Costs are reported in real (i.e., inflation-adjusted) 2013 USD.

** The matched control group had zero prevalence or incidence of symptomatic knee OA. Treatment Strategies 1 and 2 refer to cohorts with symptomatic knee OA.

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Table 3

Sensitivity analyses, evaluating the effect on outcomes of varying natural history and intervention input parameters

Treatment strategy	Mean age of onset	Discounted lifetime direct medical costs	Undiscounted lifetime direct medical costs	Discounted OA-related costs	Undiscounted OA-related costs
Matched control group	50	$117,000	$217,900	-	-
	60	$115,900	$191,100	-	-
	70	$106,300	$156,400	-	-
1. Occasional analgesic use only	50	$119,000	$221,000	$1,900	$3,200
	60	$117,500	$193,600	$1,600	$2,400
	70	$107,600	$158,200	$1,300	$1,700
2. Guideline-concordant care	50	$129,900	$238,400	$13,100	$21,300
	60	$126,400	$206,700	$10,800	$16,100
	70	$114,200	$167,200	$8,100	$11,200

Treatment strategy	Percent of cohort using: opioids/ acetaminophen (average cost of analgesic use)	Discounted lifetime direct medical costs	Undiscounted lifetime direct medical costs	Discounted OA-related costs	Undiscounted OA-related costs
1. Occasional analgesic use only	100% use acetaminophen ($71)	$118,800	$211,900	$1,300	$2,000
	50% use opioids, 50% use acetaminophen ($144)	$120,100	$214,000	$2,600	$4,100
	100% use opioids ($218)	$121,400	$216,000	$3,900	$6,200
2. Guideline-concordant care	100% use acetaminophen ($71)	$129,200	$228,000	$12,000	$19,000
	50% use opioids, 50% use acetaminophen ($144)	$130,200	$229,500	$12,900	$20,400
	100% use opioids ($218)	$131,000	$230,800	$13,800	$21,800

Treatment strategy	OA severity at time of diagnosis (K-L grade)	Discounted lifetime direct medical costs	Undiscounted lifetime direct medical costs	Discounted OA-related costs	Undiscounted OA-related costs
2. Guideline-concordant care	85% K-L 2, 10% K-L 3, 5% K-L 4	$130,400	$229,600	$13,200	$20,500
	60% K-L 2, 30% K-L 3, 10% K-L 4	$131,700	$231,200	$14,500	$22,100

Treatment Strategy	OA Progression Rate Used	Discounted Lifetime Direct Medical Costs*	Undiscounted Lifetime Direct Medical Costs*	Discounted OA-related costs*	Undiscounted OA-related Costs*
Matched control group	Current	$117,500	$209,800	-	-

Treatment Strategy	OA Progression Rate Used	Discounted Lifetime Direct Medical Costs*	Undiscounted Lifetime Direct Medical Costs*	Discounted OA-related costs*	Undiscounted OA-related Costs*
	Non-obese	$117,500	$209,800	-	-
	Weighted	$117,600	$210,000	-	-
	Obese	$117,500	$209,800	-	-
1. Occasional analgesic use only	Current	$119,400	$212,900	$1,800	$2,900
	Non-obese	$119,400	$212,900	$1,800	$2,900
	Weighted	$119,300	$212,700	$1,800	$2,900
	Obese	$119,300	$212,700	$1,800	$2,900
2. Guideline-concordant care	Current	$258,100	$455,500	$12,400	$19,600
	Non-obese	$255,200	$451,100	$11,000	$17,400
	Weighted	$258,500	$456,200	$12,700	$20,100
	Obese	$261,000	$459,600	$13,900	$21,800

* The matched control group had zero prevalence or incidence of symptomatic knee OA. Treatment Strategies 1 and 2 refer to cohorts with symptomatic knee OA.

** Costs are reported in real (i.e., inflation-adjusted) 2013 USD.