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The Cost-Effectiveness of Weight Loss Interventions Prior to Total Knee Replacement for Patients with Class III Obesity

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Abstract

Background: Class III obesity (BMI>40kg/m^2) is associated with higher complications following total knee replacement (TKR), and weight loss is recommended. We aimed to establish the cost-effectiveness of Roux-En-Y Gastric Bypass (RYGB), Laparoscopic Sleeve Gastrectomy (LSG), and Lifestyle Non-surgical Weight Loss (LNSWL) interventions in knee osteoarthritis (OA) patients with Class III obesity considering TKR.

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Methods: Using the Osteoarthritis Policy Model (OAPol) and data from published literature to derive model inputs for RYGB, LSG, LNSWL, and TKR, we assessed the long-term clinical benefits, costs, and cost-effectiveness of weight loss interventions for patients with Class III obesity considering TKR. We assessed the following strategies with a healthcare sector perspective: 1)no weight loss/no TKR, 2)immediate TKR, 3)LNSWL, 4)LSG, and 5)RYGB. Each weight loss strategy was followed by annual TKR reevaluation. Primary outcomes were cost, quality-adjusted life-expectancy (QALE), and incremental cost-effectiveness ratios (ICERs), discounted 3%/year. We conducted deterministic and probabilistic sensitivity analyses to examine the robustness of conclusions to input uncertainty.

Results: LSG increased QALE by 1.64 quality-adjusted life-years (QALYs) and lifetime medical costs by $17,347 compared to no intervention, leading to an ICER of $10,600/QALY. RYGB increased QALE by 0.22 and costs by $4,607 beyond LSG, resulting in an ICER of $20,500/QALY. Relative to immediate TKR, LSG and RYGB delayed and decreased TKR utilization. In the probabilistic sensitivity analysis, RYGB was cost-effective in 67% of iterations at a willingness-to-pay (WTP) threshold of $50,000/QALY.

Conclusion: For patients with Class III obesity considering TKR, RYGB provides good value while immediate TKR without weight loss is not economically efficient.

Introduction

Patients with advanced knee osteoarthritis (OA) who undergo total knee replacement (TKR) with a body mass index (BMI)≥40kg/m^2 may experience a higher risk of post-operative complications and implant failure compared to patients with a lower BMI(1). They also incur higher costs, due to greater anesthesia costs and longer operative time or hospital stay(1). Despite these data, TKR is cost-effective in populations with BMI≥40kg/m^2(1, 2). The increased risk of complications in this patient group has led some institutions to consider BMI cutoffs for TKR eligibility(3). Weight loss prior to TKR may help patients meet BMI cut offs and lead to better TKR outcomes or defer the need for TKR altogether(4).

Weight loss options include lifestyle changes (diet and/or exercise), weight loss medications, and bariatric surgery(5). Currently, bariatric surgery results in the greatest excess weight loss in persons with Class III obesity, and can be accompanied by additional health benefits, including mortality reduction and type II diabetes (T2DM) remission(5, 6). For patients with chronic knee pain, weight loss can reduce knee pain and improve function, potentially reducing the need for TKR(7, 8). While the value of TKR has been established(1, 2), the value of weight loss interventions prior to TKR has received little study.

We aimed to investigate the long-term clinical and economic implications of surgical and non-surgical weight loss strategies for patients with Class III obesity who are considering TKR. For surgical strategies, we focused on Roux-En-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG), as these are the most frequently performed weight loss procedures(9). We also examined a Lifestyle Non-surgical Weight Loss (LNSWL) strategy that included diet, exercise, and the use of weight loss medication.

Methods

Analytic Overview

We used the Osteoarthritis Policy (OAPol) Model to evaluate the cost-effectiveness of weight loss strategies among patients with Class III obesity and end stage knee OA considering TKR(10). The OAPol model and this study are approved by the Mass General Brigham IRB (Protocol #2006P001290). Primary outcomes were quality-adjusted life expectancy (QALE), lifetime medical costs, and incremental cost-effectiveness ratios (ICERs). QALE is life expectancy accounting for the quality of life (QoL) of each year lived, and is measured in quality-adjusted life-years (QALYs). QoL is expressed as a weight between 0 and 1, with value 0 representing a health-state equivalent to death and 1 representing a year of perfect health(11). We calculated ICERs as the ratio of the difference in lifetime costs to the difference in QALE between two strategies. Strategies are ordered by increasing cost and ICERs are calculated, after which some strategies may be excluded due to “strong dominance” or “extended dominance” and the remaining strategies’ ICERs are recalculated(12). A strategy is excluded from ICER calculations through “strong dominance” when it has a lower QALE and higher cost than any other intervention(12). A strategy is excluded through “extended dominance” when it has an ICER greater than that of an intervention with a higher QALE(12).

We modeled healthcare costs in 2020 USD, inflating costs reported in earlier years using the Personal Health Care and the Personal Consumption Expenditure price indices(13). We conducted analyses from the healthcare sector’s perspective, which includes payer-borne and patient out-of-pocket medical costs(14). As recommended by the 2nd Panel on Cost-Effectiveness in Health and Medicine, we discounted costs and benefits 3% annually(15). We evaluated uncertainty in input parameters in deterministic and probabilistic sensitivity analyses.

The OAPol Model

The OAPol Model is a widely published, validated Monte Carlo simulation of knee OA, used to portray the natural history and treatment of individuals with predefined demographic (age, sex, race/ethnicity) and clinical characteristics (BMI, pain, and comorbidities including cardiovascular disease, T2DM, cancer, chronic obstructive pulmonary disease, and non-OA musculoskeletal diseases)(1, 16, 17). In each annual model cycle, an individual passes through health states, accumulating OA-related and non-OA-related medical costs and quality-adjusted life years. Knee-OA specific health states are defined by Kellgren-Lawrence (KL) grades (0–4) and Western Ontario and McMaster Universities Osteoarthritis (WOMAC) pain (0–100, where 0 is no pain and 100 is worst). QoL utility weights and background medical costs are assigned each year based on BMI category, knee pain level, age, and number of comorbid conditions.

Weight loss regimens in OAPol can affect BMI, knee pain, and T2DM status. Upon entry into a weight loss regimen, a subject is assigned a weight loss trajectory detailing the percentage of weight they will lose, the speed of this weight loss, and the probability, magnitude, and speed of weight regain following weight loss. Each weight loss/regain trajectory can be accompanied by a pain reduction in the first year and a probability of returning to initial pain levels over the following years. Each weight trajectory can also be accompanied by a probability of T2DM remission in the first year, and a probability of T2DM recurrence in the following years for subjects who experienced remission. Weight loss regimens are associated with risk of complications, which reduce QoL and incur costs. Additional details on modeling weight loss interventions in OAPol have been published(18).

In OAPol, TKR can result in knee pain relief, which may lead to higher QoL, and is accompanied by a probability of complications that reduce QoL and incur costs. There is an annual probability of implant failure, which results in a subject's pain returning and subsequent revision TKR. Additional details describing modelling TKR with OAPol have been published(1).

We averaged lifetime costs and QALE over three million subjects for each strategy. Documentation for OAPol Model Version 4.8.0(01) is available upon request.

Treatment strategies

We modelled five strategies: 1) no weight loss intervention and no TKR, allowing for occasional pharmacologic pain management to control knee pain flares, 2) immediate TKR, 3) RYGB, 4) LSG, and 5) LNSWL. Subjects in the immediate TKR strategy were assessed for TKR in the year of model entry. Subjects in the RYGB, LSG, and NSWL strategies were assessed for TKR eligibility 1 year after weight loss intervention start and reassessed each year thereafter.

Assumptions

This analysis was based on several underlying assumptions:

1. Subjects could not exceed a maximum BMI of 60kg/m^2 in their lifetime.
2. TKR eligibility:
   a. Subjects with WOMAC pain score greater than 40 and BMI<40 kg/m2 or BMI between 40 kg/m^2 and 50 kg/m^2 without comorbid conditions were eligible to receive TKR(19).
   b. Subjects with BMI≥50kg/m^2 were not eligible for TKR(20) but became eligible if their BMI dropped below this threshold during annual re-evaluations.
   c. Subjects with BMI between 40kg/m^2 and 50kg/m^2 and WOMAC pain>40 with cardiovascular disease and/or T2DM had a 50% chance of being deemed ineligible(21).
   d. Subjects underwent TKR in the same year that they were deemed to be eligible.
3. Weight loss strategies:
   a. After a certain time period, informed by clinical study follow-up periods, subjects in a weight loss strategy can either revert to pre-

treatment BMI levels or continue to slowly regain weight while not reaching pre-treatment BMI. Further details are described in Supplementary Material Section 7.

b. In the absence of available stratified data, we assumed reductions in knee pain due to bariatric surgery were similar across all weight loss trajectories.

c. Given select bariatric surgery complications may lead individuals to seek healthcare more frequently through their lifetime (e.g., elective procedures to remove excess skin), we modeled a probability of “healthcare re-engagement” over multiple years post bariatric surgery, incurring annual cost and risk of mortality. Greater detail is reported in Supplementary Material Section 8.

d. Weight loss due to LNSWL is similar among patients with and without T2DM.

e. Weight loss due to LNSWL does not result in sustainable knee pain reduction in people with Class III obesity. This assumption reflects evidence that weight loss <7.5% (typical weight loss in LNSWL programs) is not associated with decreased risk of TKR(22).

Model inputs

Cohort Characteristics

Demographic Characteristics: Table 1 depicts the baseline cohort characteristics. We modelled a population of patients with advanced knee OA and class III obesity, with an initial age of 58.8 (4.5) years and average BMI stratified by sex and race (42.9 to 46.5kg/m^2) (1).

OA pain: Patients started the simulation with a mean pain of 54 (15) on the WOMAC pain scale, with a minimum pain of 40(1). All subjects were eligible for TKR based on their OA severity; final TKR eligibility depended on BMI.

Background medical costs and quality of life: Background medical costs were derived from the 2020 CMS-HCC community model and 2017–2018 data on comorbidities(23, 24). Background QoL stratified by age, number of comorbidities, BMI category, and pain level was derived from Osteoarthritis Initiative (OAI) data(25). To account for the deleterious effects of obesity on non-OA-attributable medical costs and QoL, additional annual costs of Class II and Class III obesity were estimated at $2,114 and $3,695 respectively, and an annual QoL decrement of −0.0375 was applied for class III obesity compared to class II obesity(1).

Treatment Characteristics (TKR and revision TKR)—We stratified TKR and revision TKR efficacy, costs, and complications by BMI and by history of bariatric surgery. Model inputs are reported in Table 1 and Supplementary Tables 2 and 3.

TKR in *immediate TKR* and *Lifestyle weight loss* strategies: For the two strategies not including bariatric surgery, we derived complication rates and implant failure rates stratified by BMI (BMI<30kg/m^2, 30≤BMI<40kg/m^2, BMI≥40kg/m^2), with higher BMI leading to greater probability of complications and implant failure (Table 1)(26, 27). We accounted for differential risk of revision and prescription opioid overdose following surgery based on prior history of opioid use(1, 18). We also stratified the cost of primary and revision TKR by BMI using costs data reported by Chen et al (primary TKR cost: $19,711 for BMI≥40kg/m^2; $19,327 for BMI 30≤BMI<40kg/m^2; $19,038 for BMI<30kg/m^2)(1).

TKR in *RYGB* and *LSG* strategies: Patients who undergo TKR after bariatric surgery may have a higher risk of certain complications relative to both non-obese and obese TKR patients(28, 29). Odds and risk ratios were used to derive rates of complications and implant failure for TKR post-bariatric surgery in relation to TKR recipients with BMI>40kg/m^2 without a prior history of bariatric surgery(28, 30). Implant failure was 1.5 times more likely after bariatric surgery. We determined the average BMI at which TKR was performed in the RYGB and LSG strategies and applied the cost of undergoing TKR within that BMI category.

Treatment Characteristics (RYGB)

RYGB weight loss efficacy: Five weight loss and regain trajectories were derived using data from the Longitudinal Assessment of Bariatric Surgery (LABS) study, a large multicenter observational prospective cohort study with 7 years of follow-up following RYGB(6). Maximum BMI lost ranged from 23–47% of pre-RYGB BMI, and subsequent regain ranged from 0–30% of BMI lost (Supplementary Table 4, Supplementary Figure 1). After the 7-year post-surgical interval, 80% subjects experienced BMI fluctuations on trajectories described in Supplementary Material Section 7 and Supplementary Table 9, while 20% of subjects returned to pre-RYGB BMI levels.

RYGB knee pain efficacy: We estimated a 31% reduction in knee pain from weight loss in the first year(31). We used the proportion of LABS participant who maintained clinically meaningful pain reduction between 1 and 3 years post-bariatric surgery to derive an annual probability of pain returning (3.7%)(31).

RYGB T2DM efficacy: We derived the probability of T2DM remission following RYGB (70%) from LABS data. Subjects without T2DM at baseline who underwent RYGB had a lower T2DM incidence rate than subjects of similar age and BMI not undergoing RYGB (relative risk ratio=0.162), derived from LABS and NHANES data(6, 24). T2DM incidence for subjects not undergoing RYGB is presented in Supplementary Table 1.

RYGB complications: We used data reported by Kapur et al. to derive probabilities of short-term surgical complications(32). We used LABS 5-year outcomes to derive probabilities of additional gastrointestinal procedures(33). The probability of any complication occurring in the year of surgery was 20.5% and in subsequent years 6.8% (Table 1). Supplementary Table 5 presents individual complication probabilities, costs, and QoL reductions.

RYGB cost: In the year of surgery, we included the cost of surgery ($22,774) (34), surgeon's fees ($1,963) (35), anesthesiologist fees ($1,351) (36), and seven post-operative visits ($158/visit) (37). In years following surgery, we included an annual cost of one physician visit ($158) and dietary supplements ($98) (37).

Treatment Characteristics (LSG)

LSG weight loss efficacy: We derived maximum weight loss sub-trajectories for LSG from published data and calibrated the overall cohort weight loss trajectory according to Arternburn et al(38). Maximum BMI lost ranged from 18–38% of pre-LSG BMI, and subsequent regain ranged from 0–60% of BMI lost (Supplementary Table 6, Supplementary Figure 2). After the 7-year post-surgical interval, 80% subjects experienced BMI fluctuations as described in Supplementary Material Section 7, while 20% of subjects returned to pre-LSG BMI levels.

LSG knee pain efficacy: We assumed LSG provided the same pain efficacy as RYGB, despite differences in the amount of weight loss conferred.

LSG T2DM efficacy: We estimated the probability of T2DM remission at 51% using a met-analysis by Borgeraas et al(39). We assumed the same reduction in T2DM incidence as RYGB.

LSG complications: We used Kapur et al. and 5-year LABS outcomes to derive probabilities of short-term complications of the LSG procedure and gastrointestinal reinterventions, leading to a complication probability of 8.1% in the year of LSG surgery and 3.3% in subsequent years (32, 33). Individual complication probabilities, costs, and QoL reductions are presented in Supplementary Table 5.

LSG cost: In the year of surgery, we included the cost of surgery ($20,291) (34), surgeon's fees ($1,222) (35), anesthesiologist fees ($1,081) (36), and six follow-up visits ($158/visit) (37). In years following surgery, we included an annual cost of one physician visit ($158) and dietary supplements ($98)(18).

Treatment Characteristics (LNSWL)—Our LNSWL intervention was based on the LookAHEAD (Action for Health in Diabetes) study, a randomized controlled trial comparing an Intensive Lifestyle Intervention (ILI) to a Diabetes Support and Education control in overweight and obese patients with T2DM(40, 41). Participants in the ILI group received group and individual coaching over 4 years, including behavioral intervention to reach diet and exercise goals, meal replacements, and potential use of the weight loss medication orlistat.

LNSWL weight loss efficacy: We used data reported from the sub cohort of LookAHEAD with BMI>40 kg/m^2 to derive probabilities and magnitudes of weight loss and regain. Maximum BMI lost ranged from 5–15% of BMI, and subsequent regain was 62% of BMI lost (Supplementary Table 7). The overall weight loss trajectory was calibrated to 4-year LookAHEAD follow-up data; validation is presented in Supplementary Figure 3(40). After the 4-year intervention period, 88% of subjects experienced BMI fluctuations described in Supplementary Section 7, and the remaining subjects returned to pre-intervention BMI levels.

LNSWL knee pain efficacy: LookAHEAD provided data for a cohort with less knee pain than typical TKR candidates (LookAHEAD baseline WOMAC=3.7 on 0–20 scale, which translates to approximately 18.5 on the 0–100 scale)(42). Given no difference in TKR utilization by arm in those who reported knee pain at baseline (hazard ratio of TKR risk, intervention vs education: 1.11, 95% confidence interval [0.92, 1.33])(43), We modeled no knee pain efficacy for the NSWL intervention.

LNSWL T2DM efficacy: We derived probability of T2DM remission during LNSWL intervention (8.8%) from data in a LookAHEAD sub-cohort with BMI>37kg/m^2(44). For those without T2DM at baseline, we derived a risk ratio for T2DM incidence (relative risk ratio=0.404) from a study on orlistat's effects on T2DM and 10-year follow-up of the Diabetes Prevention Program(45, 46).

LNSWL complications: We derived the probability of minor gastrointestinal complications due to orlistat(46) for the ~20% of LookAHEAD subjects with knee pain or BMI>40kg/m^2 who utilized orlistat(41, 42). We applied this probability to 21.8% of subjects participating in the LNSWL intervention. We did not model any complications attributable to diet or exercise. QoL utilities for LNSWL complications are reported in Supplementary Table 8.

LNSWL cost: We derived annual costs for the LNSWL from LookAHEAD staffing and non-staffing costs(47), excluding the cost of orlistat. For subjects taking orlistat, we derived costs of prescription orlistat from RedBook, estimating that subjects took orlistat for an average of 17 weeks of the year(48, 49). Further detail is provided in Supplementary Material Section 6.1.

Sensitivity Analyses

One-way deterministic sensitivity analyses: One-way sensitivity analyses permit us to understand how ICERs change as one key model input is varied across a plausible range while all other inputs are held constant at their base case values. The varied parameters and their ranges are described in Supplementary Table 10.

Two-way deterministic sensitivity analyses: We performed two-way sensitivity analyses of the most influential parameters from the one-way sensitivity analyses, using the same ranges. These analyses allow us to understand how ICERs change when two input parameters are varied simultaneously. Refer to Supplementary Material Section 9 for details.

Probabilistic sensitivity analysis (PSA): PSA is used to account for uncertainty of input parameters. We assigned distributions to and simultaneously varied the parameters that were influential in the deterministic sensitivity analyses: 1–4) the likelihood of RYGB and LSG complications in year of surgery and in subsequent years; 5–8) the probability and length of weight maintenance after RYGB and LSG; 9–10) the magnitude of knee pain reduction conferred by RYGB and LSG; 11–12) the annual probability of knee pain returning after RYGB and LSG; 13) the probability of healthcare re-engagement due to reintervention;

14) mortality due to healthcare re-engagement; 15) probability of T2DM remission after RYGB and LSG; and 16–17) the cost and QoL differentials between 35<BMI≤40kg/m^2 and BMI≥40kg/m^2. We ran 1,000 model simulations of 1 million subjects and drew parameters from distributions described in Appendix Section 9.3. For each simulation, we calculated ICERs for each strategy, then determined which strategy was cost-effective at a given willingness-to-pay (WTP) threshold, or the maximum cost a payer is willing to pay per QALY improvement. We constructed a cost-effectiveness acceptability curve for each strategy, displaying the probability of each strategy being cost-effective at a range of WTP thresholds.

Results

Base Case analysis

Table 2 presents QALEs, lifetime costs, and incremental cost-effectiveness ratios (ICERs) for the base case analysis. The no intervention strategy led to a QALE of 9.38 and lifetime medical costs of $241,262. LSG followed by TKR resulted in a lower ICER than both the immediate TKR and the LNSWL strategies, therefore eliminating immediate TKR and LNSWL by the principles of extended dominance; LSG was then compared to no intervention, resulting in an ICER of $10,600/QALY. Lastly, RYGB followed by TKR reevaluation led to an ICER of $20,500/QALY compared to the LSG strategy. Supplementary Figures 4 and 5 present additional visual representations of the base case QALE and cost data.

Table 2 also depicts TKR utilization for each strategy. In the immediate TKR strategy, 79.4% of subjects underwent TKR; 17% of subjects were ineligible for TKR due to BMI over 50kg/m^2 and the remaining 3.6% of subjects were ineligible due to BMI between 40 and 50kg/m^2 with concomitant T2DM and/or cardiovascular disease throughout their lifetime. Adding LSG or RYGB prior to reassessment of TKR indications reduced TKR utilization as subjects no longer met knee pain thresholds for TKR. Adding the LNSWL intervention prior to TKR reevaluation increased TKR utilization to 81.4%, because knee pain persisted and more subjects met the TKR BMI threshold.

One-way deterministic sensitivity analyses

Table 2 also presents the results with a starting BMI of 42kg/m^2. The LSG ICER decreased slightly from the base case ($9,918/QALY) while the ICER for RYGB increased from the base case ($35,104/QALY).

Figure 1A displays ICER ranges of the RYGB strategy for all other one-way sensitivity analyses. The cost-effectiveness of RYGB was most sensitive to the following four parameters: 1) the probability of RYGB complications (varied −50 to +50% of base case, with ICERs ranging from $5,200/QALY to dominated); 2) the probability that BMI returns to pre-surgical levels 7-years post-RYGB (varied 0–100%; ICERs: $8,700/QALY to dominated); 3) the probability that reinterventions lead to healthcare re-engagement (varied 0–3 times base case; ICERs: $10,000/QALY to dominated); 4) years of weight loss durability after RYGB (varied lifetime-7 years; ICERs: $20,100/QALY to dominated). In these scenarios, as RYGB becomes less favorable, it is dominated by the LSG strategy.

The cost-effectiveness of RYGB was also sensitive to the probability that BMI returns to pre-surgical levels 7 years after LSG (varied 0–100%; ICERs: $5,300-$101,900/QALY), the probability of LSG complications (varied −50 to +50% of base case, ICERs: $11,800-$88,900/QALY), and the probability of T2DM remission after LSG (varied 0–200%; ICERs: $11,800-$82,500/QALY). The RYGB ICER remained under $50,000/QALY while varying all other parameters in one-way sensitivity analyses (Figure 1A).

Figure 1B displays ICER ranges for the LSG strategy, which ceases to be attractive when varying 10 out of the 23 parameters evaluated.

Two-way deterministic sensitivity analyses

Figure 2 and Supplementary Figures 6–9 present the results of varying parameters in two-way sensitivity analyses. When varying weight durability (probability and duration) and RYGB and LSG complication probability, as RYGB's durability decreases and LSG's increases, RYGB becomes dominated by LSG (Figure 2, Supplementary Figures 6–7). LSG's attractiveness, compared to RYGB, decreases as its relative durability decreases. As RYGB's complication probability decreases, LSG quickly goes into extended dominance (Supplementary Figure 8). When varying the probability of T2DM remission, RYGB reaches ICERs of $230,000/QALY, but is not dominated by LSG (Supplementary Figure 9).

Probabilistic sensitivity analysis

Figure 3 displays the probability of each strategy being cost-effective through a range of WTP thresholds. At very low WTP (<$10,000/QALY), no intervention appears to have the highest likelihood of being cost-effective. Between WTP of $10,000 and $20,000/QALY, it is less clear which strategy is most likely to be cost-effective. At more plausible WTP (greater than ~$40,000/QALY), RYGB emerges as the most likely to be cost-effective. Using the distribution of model outcomes from the PSA (Supplementary Figure 10), we calculated 90% credible intervals for QALE and cost of each strategy (Supplementary Table 12).

Discussion

We used the OAPol model to estimate cost and quality of life differences between five different treatment strategies for patients with Class III obesity considering TKR. Our base case results suggest that undergoing RYGB prior to reevaluation for TKR is cost-effective at any WTP threshold greater than $21,000/QALY. Undergoing LSG prior to TKR reevaluation is cost-effective between WTP thresholds of $11,000 and $20,000/QALY. The strategies of undergoing TKR without any weight loss and LNSWL prior to TKR reevaluation are not cost-effective because they result in a higher ICER than LSG for less QALE benefit.

One prior study has shown that bariatric surgery followed by TKR has an ICER of $13,910, compared to immediate TKR(50). This study did not distinguish among different bariatric procedures, did not consider non-surgical weight loss treatment options, such as diet, exercise, or weight loss medications, and did not evaluate the possibility of weight loss delaying or reducing need for TKR. In this cost-effectiveness analysis, we incorporated TKR complication risks and efficacy stratified by both BMI and history of bariatric surgery, as well as the potential to delay or prevent TKR based on knee pain outcomes following weight loss. Although undergoing immediate TKR without attempts at weight loss was eliminated from consideration, as it was not as favorable as LSG, it did confer benefit, which aligns with prior studies of TKR in populations with Class III obesity(1, 2).

In our analysis, both LSG and RYGB strategies confer substantial benefits for reasonable costs; RYGB is likely to be the preferred option at WTP thresholds exceeding $20,000/QALY. Our lifestyle non-surgical intervention approach is not cost-effective, likely because it employs extensive supervision to be effective and durable, leading to a high cost for a small magnitude of weight loss compared to bariatric surgery. The bariatric surgery strategies that we considered both delayed and reduced TKR utilization, which aligns with recent research that ~30% of people decline TKR after bariatric surgery due to symptom improvement(51). However, the non-surgical weight loss strategy we modeled increased TKR utilization, as subjects did not experience knee pain relief and became eligible for TKR due to lower BMI. ICERs were not sensitive to changes in the knee pain benefits of weight loss, suggesting that weight-associated quality of life and potential T2DM remission are more influential than TKR utilization on quality of life in this population.

This analysis has several limitations. We derived data from multiple sources. RYGB and LSG were modeled using data from cohort studies with a younger age than that of the typical TKR patient, and we derived weight loss strategy parameters from studies with no more than 7 years of follow-up data. Since studies that have shown dose-response relationships between weight loss and knee pain have been focused on non-surgical interventions in populations with substantially lower starting BMI, we assumed knee pain reduction to be similar for RYGB and LSG(52, 53). We also assumed that knee pain reduction was not sustainable for our modeled LNSWL intervention. In the absence of primary sources reporting TKR BMI eligibility, we assumed that patients with BMI≥50kg/m^2 would be ineligible for TKR until their BMI dropped below this threshold – this may not model current practice, as orthopaedic surgeons may perform TKR on patients after unsuccessful weight loss attempts(54). We assessed these assumptions in extensive sensitivity analyses and found that several inputs influence whether RYGB or LSG is cost-effective at a given WTP threshold: bariatric surgery complications, long-term weight durability, and T2DM remission. We also found that reductions in knee pain and TKR BMI threshold criteria do not have a substantial effect on ICERs. Our LNSWL intervention was based on a diet/exercise study including potential for orlistat use; a newly approved indication (long-term weight management) for the weight loss medication semaglutide results in greater weight reduction and study of its cost-effectiveness as a non-surgical option for this population is warranted.

If RYGB was not available, LSG would offer good value to patients with Class III obesity considering TKR. LSG is the most commonly performed bariatric surgery in the US, as it is associated with very good weight loss outcomes with lower risks of post-operative complications compared to RYGB. This may inform patient and surgeon decisions between bariatric surgeries.

Our results have important implications for clinical care and policy. Many patients with knee OA fail to lose weight before TKR using lifestyle weight loss interventions, despite surgeon recommendations(55). Bariatric surgery, which is highly effective in reducing weight and has also been shown to reduce knee OA pain and improve function, is not presently included in current knee OA treatment guidelines(56). Our analysis suggests that RYGB is a valuable strategy for patients with Class III obesity who are considering TKR and willing to undergo weight loss surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovation

- Both LSG and RYGB strategies confer substantial benefits for reasonable costs; RYGB is likely to be the preferred option at WTP thresholds exceeding $20,000/QALY.
- RYGB may be a cost-effective option for patients with Class III obesity considering TKR and may reduce the need for TKR.
- Bariatric surgery is likely to offer good value for patients with advanced knee OA considering total knee replacement and should be considered as a management strategy for these patients.

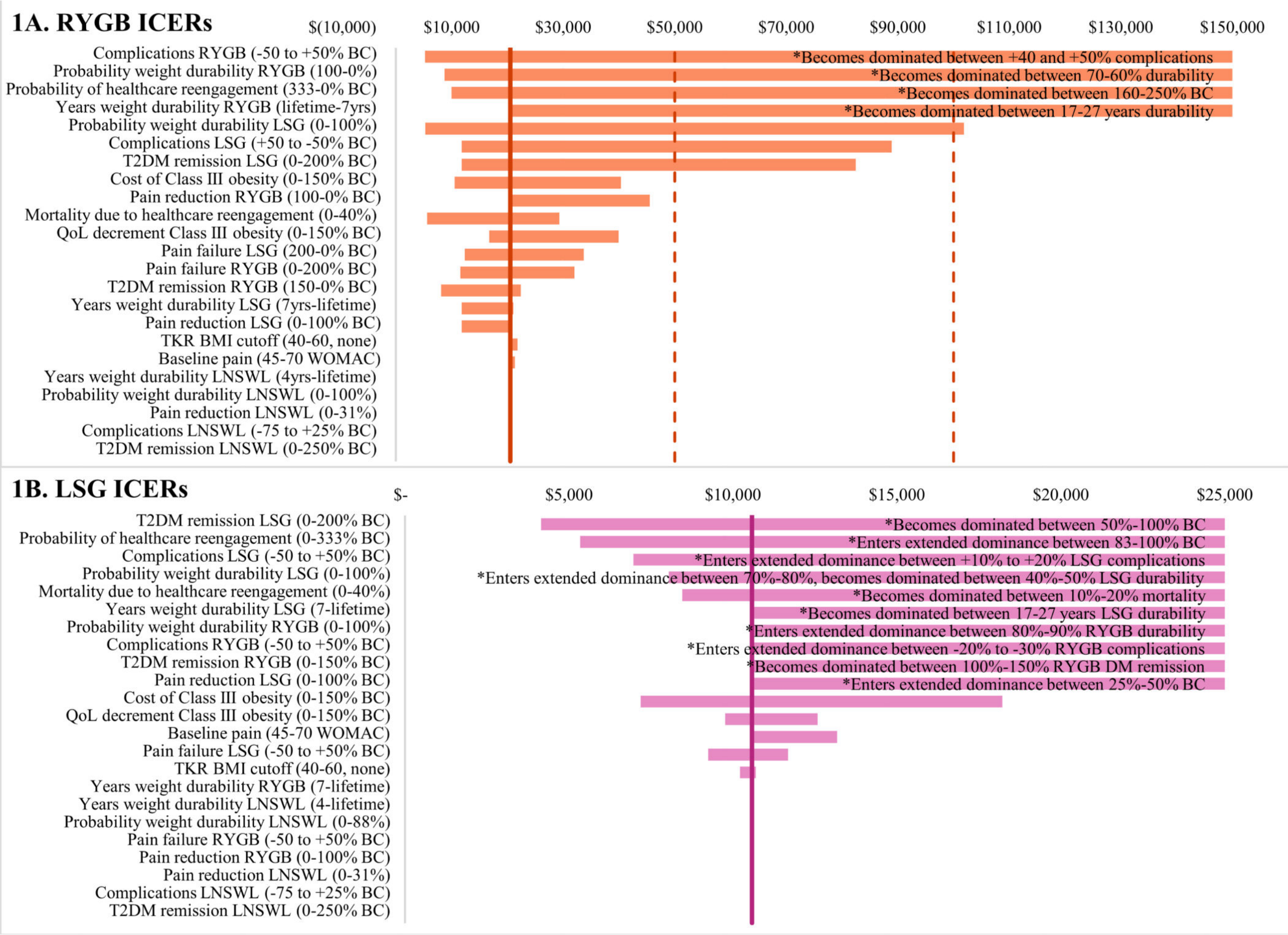

Figure 1. Results of one-way sensitivity analyses

Figure 1a. **Cost-effectiveness of RYGB followed by TKR reevaluation in one-way sensitivity analyses.** This figure shows the ICER of the RYGB strategy as we varied input parameters through the ranges described in Supplementary Table 10. In each analysis, all parameters remained constant at base case values except the parameter shown on the y-axis, which varied through the range of values listed. The leftmost end of each bar displays the ICER at the parameter's most favorable value, and the rightmost end shows the ICER when the parameter is at its least favorable value. The solid vertical line denotes the base case ICER, as reported in Table 2. The dashed vertical lines denote typical willingness to pay thresholds of $50,000/QALY and $100,000/QALY.

*As RYGB becomes less favorable, it is dominated by LSG between the thresholds stated in the bar.

Figure 1b. **Cost-effectiveness of LSG followed by TKR reevaluation in one-way sensitivity analyses.** This figure shows the ICER of the LSG strategy as we varied input parameters through the ranges described in Supplementary Table 10. In each analysis, all parameters remained constant at base case values except the parameter shown on the y-axis, which varied through the range of values listed. The leftmost end of each bar displays the ICER at the parameter's most favorable value, and the rightmost end shows the ICER when the parameter is at its least favorable value. The solid vertical line denotes the base case ICER, as reported in Table 2.

*As LSG becomes less favorable, it enters extended dominance or becomes dominated by RYGB between the thresholds stated in the bar.

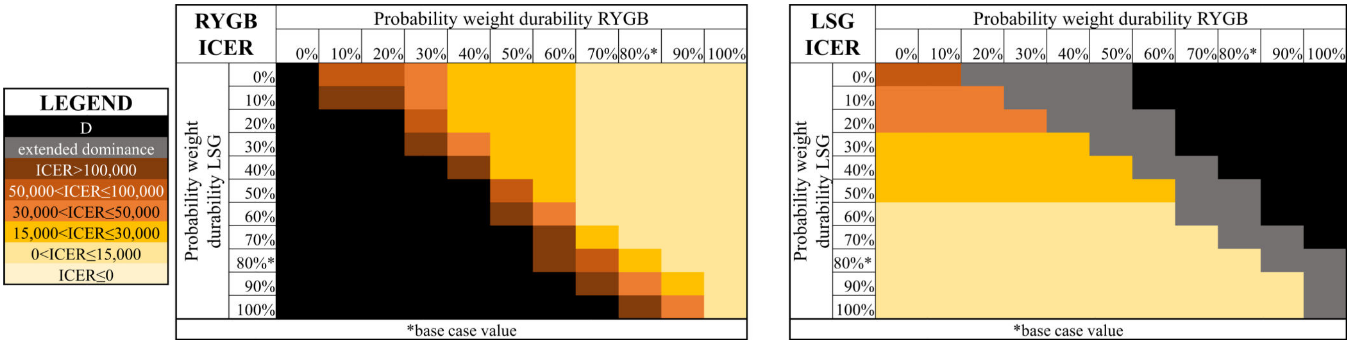

Figure 2. Results of two-way sensitivity analysis: Varying probability of weight durability RYGB vs LSG

Bivariate heatmaps of the probability of weight maintenance after Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG). In the base case, 80% of subjects' weight after year 7 is maintained, while 20% of subjects revert to pre-surgical weight instead of maintaining 7-year weight. All other parameters are held at base case values. The left heatmap shows how RYGB's incremental cost-effectiveness ratio (ICER) is affected by varying the probability of weight durability, and the right shows how the LSG ICER is affected. ICERs were categorized and assigned a color as defined in the key. Results of other two-way sensitivity analyses are reported in Supplementary Material Section 10.3. *Denotes the base case value.

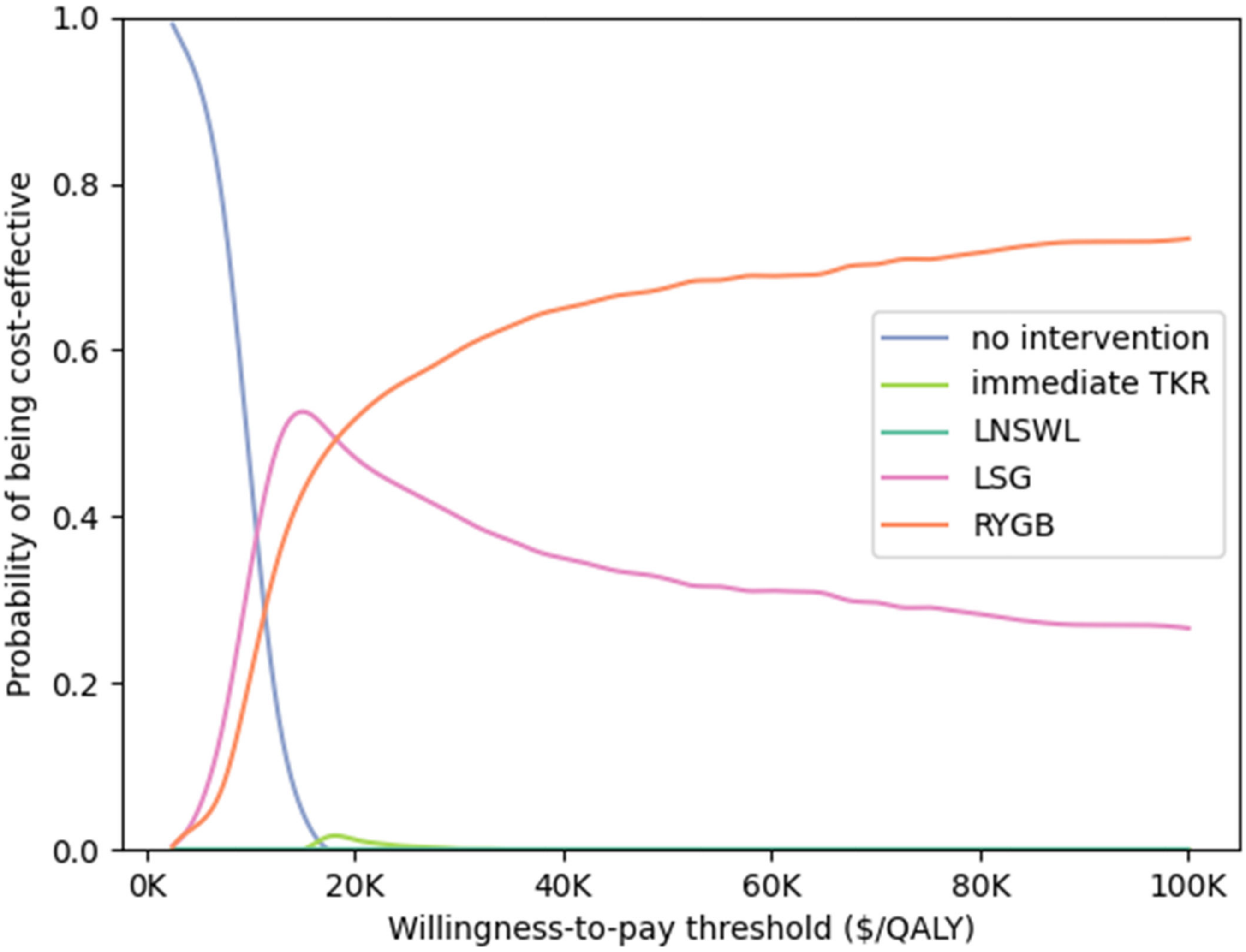

Figure 3. Cost-effectiveness acceptability curve

We performed a probabilistic sensitivity analysis of weight loss strategies in a cohort with average starting BMI of 46.6 kg/m^2 considering TKR. We did 1,000 simulations, taking independent draws of model input parameters from the distributions specified in Supplementary Table 11. We calculated incremental cost-effectiveness ratios (ICERs) for each simulation comparing the no intervention (blue line), immediate TKR (green line), LNSWL (teal line), LSG (pink line), and RYGB (orange line). At each willingness-to-pay (WTP) threshold, a strategy was considered cost-effective if it produced the greatest quality-adjusted life expectancy while retaining an ICER below the WTP threshold. The proportion of simulations in which a given strategy was cost-effective at each WTP threshold is plotted against WTP thresholds on the x-axis ($/QALY).

Table 1:

Key model inputs

Population Characteristics	**Mean (SD[*])**	**Derived from sources**
Age (years)	58.8 (4.5)	
Female	79.9%	
Race/Ethnicity		
White non-Hispanic	88%	
White Hispanic	3%	
Black non-Hispanic	4.5%	
Black Hispanic	4.5%	
BMI (kg/m^2)		(1)
White, male	45.0 (5.2)	
White, female	43.0 (4.9)	
Black, male	45.1 (4.9)	
Black, female	44.3 (5.2)	
Hispanic, male	42.9 (2.6)	
Hispanic, female	46.5 (5.2)	
Starting WOMAC knee pain [†]	54 (15)	
Annual QoL decrement for BMI≥40kg/m^2	−0.0375	(57)
Additional non-OA[¶] related annual costs by BMI[**]		
35≤BMI<40kg/m^2	$2,114	(58)
BMI≥40kg/m^2	$3,695	(58)
RYGB[‡] Intervention Parameters		
Weight loss trajectory efficacies		
Upper limit of BMI lost	23–47%	(6)
Mean % weight loss regained	0–30%	(6)
Initial pain reduction [Ω]	31% (39%)	(31)
Type II Diabetes		
Remission	70%	(6)
Complications		
Probability of any complication year 1 (years 2+)	20.5% (6.8%)	(32, 33)
Costs [**]		
Cost of surgery	$22,774	(34)
Surgeon’s fees	$1,963	(35)
Anesthesiologist fees	$1,351	(36)
Physician visits	$158	(37)
Dietary supplements	$98	(37)
LSG[§] Intervention Parameters		
Weight loss trajectory efficacies		
Upper limit of BMI lost	19–38%	(6, 38)

Population Characteristics	**Mean (SD[*])**	**Derived from sources**
Mean % weight loss regained	0–60%	(6, 38)
Initial pain reduction [Ω]	31% (39%)	(31)
Type II Diabetes		
Remission	51%	(39)
Complications		
Probability of any complication year 1 (years 2+)	8.1% (3.3%)	(32, 33)
Costs [**]		
Cost of surgery	$20,291	(34)
Surgeon’s fees	$1,222	(35)
Anesthesiologist fees	$1,081	(36)
Physician visits	$158	(37)
Dietary supplements	$98	(37)
Lifestyle non-surgical weight loss Intervention Parameters		
Weight loss trajectory efficacies		
Upper limit of BMI lost	5–15%	(40)
Mean % weight loss regained	62%	(40)
Initial pain reduction [Ω]	0% (0%)	Assumption
Type II Diabetes		
Remission	8.8%	(44)
Complications due to orlistat		
Probability of any complication year 1 (years 2+)	89.4% (56.3%)	(46)
Costs [**]		
Year 1	$3,154	(47)
Years 2–4	$1,861	(47)
Annual cost of orlistat	$5,562	(48, 49)

Total Knee Replacement Parameters					
Structural efficacy					**post RYGB/LSG**
		BMI<30	**BMI 30–40**	**BMI>40**	
Structural	50–65 years	98.3% (97.3%)	98.2% (97.2%)	97.9% (96.7%)	96.7% (94.8%)
success year 1[⁂]	>65 years	99.1% (98.6%)	99.1% (98.5%)	98.9% (98.3%)	98.3% (97.3%)
Structural failure	50–65 years	1.3% (1.3%)	1.4% (1.4%)	1.6% (1.6%)	2.4% (2.4%)
years 2+[⁂]	>65 years	0.3% (0.3%)	0.3% (0.3%)	0.4% (0.4%)	0.5% (0.5%)
Derived from sources		(1, 18, 59)	(1, 18, 59)	(1, 18, 59)	(28, 59)
Complications					
Pulmonary embolism		0.54%	0.75%	0.75%	0.79%/0.82%
Pneumonia		0.40%	0.32%	0.38%	0.64%/0.29%
Readmission		3.38%	3.23%	4.23%	3.93%/4.27%
Opioid overdose[⁂]		0.02% (0.15%)	0.02% (0.15%)	0.02% (0.15%)	0.02% (0.15%)
Deep venous thrombosis		0.94%	0.92%	0.71%	0.75%/0.70%
Wound dehiscence		0.15%	0.19%	0.35%	0.23%/0.29%

Population Characteristics		**Mean (SD[*])**		**Derived from sources**
Periprosthetic joint infection	0.23%	0.28%	0.53%	0.22%/0.44%
Death	0.10%	0.11%	0.13%	0.18%/0.12%
Derived from sources	(18, 27)	(18, 27)	(18, 27)	(28, 30)
Costs [**]				
Cost in year 1	$19,038	$19,327	$19,711	$19,327
Cost in years 2+	$176	$176	$176	$176
Derived from sources	(1, 60)	(1, 60)	(1, 60)	(1, 60)

[*] SD: Standard Deviation

[†] Starting pain according to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale (0 = best, 100 = worst).

[¶] OA: osteoarthritis of the knee

[‡] Roux-En-Y Gastric Bypass

[§] Laparoscopic Sleeve Gastrectomy

[Ω] Initial relative pain reduction was not stratified by weight loss in LABS. See Appendix Sections 4.2.3 and 5.2.3 for greater detail.

[**] All costs reported in 2020 USD

[***] Probability for patients WITH chronic opioid use history is reported in parentheses

Table 2.

Results of the cost-effectiveness of weight loss interventions prior to total knee replacement for patients with class III obesity

Base case (Mean BMI = 47 $\mathrm{kg/m^2}$)						
Strategy	**QALE**	**Cost**	**ICER (\$/QALY)**	**% TKR**	**Age at TKR**	**BMI at TKR**
No weight loss, no TKR	9.38	\$241,262				
Immediate TKR	10.13	\$253,977	ed*	79.4%	59.8	44.9
LNSWL followed by TKR evaluation	10.28	\$258,107	ed*	81.4%	60.4	41.9
LSG followed by TKR evaluation	11.02	\$258,609	\$10,600	50.5%	62.1	36.3
RYGB followed by TKR evaluation	11.25	\$263,216	\$20,500	51.9%	62.1	34.5
Mean BMI = 42 $\mathrm{kg/m^2}$						
Strategy	**QALE**	**Cost**	**ICER (\$/QALY)**	**% TKR**	**Age at TKR**	**BMI at TKR**
No weight loss, no TKR	9.82	\$227,578				
Immediate TKR	10.72	\$242,022	ed*	91.1%	59.6	41.6
LNSWL followed by TKR evaluation	10.90	\$244,350	ed*	92.1%	60.2	38.9
LSG followed by TKR evaluation	11.53	\$244,540	\$9,900	57.3%	61.9	33.7
RYGB followed by TKR evaluation	11.71	\$250,805	\$35,100	57.4%	61.8	32.0

* Strategies that are eliminated due to extended dominance (denoted with “ed”) are ruled out because they result in a higher ICER than a strategy with a greater QALE benefit.

We calculated ICERs as the ratio of the difference in lifetime costs to the difference in QALE between two strategies. Strategies are ordered by increasing cost and ICERs are calculated, after which some strategies may be excluded due to “strong dominance” or “extended dominance”. The remaining strategies’ ICERs are recalculated (for example, after immediate TKR and LNSWL strategies are excluded, the LSG ICER is then calculated with respect to the *no weight loss, no TKR* strategy, and this ICER is reported). ICERs are rounded to the nearest hundred.