Health Technology Assessment of Total Knee Replacement (TKR) in Patients with Osteoarthritis (OA) Knee in India

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Executive Summary

Osteoarthritis knee (OA) is a common degenerative joint condition in India as well as worldwide. Total knee replacement (TKR) is considered to be a reliable treatment for OA knee and is considered to be clinically and cost-effective in developed countries. However, it is necessary to determine whether TKR is cost-effective in India to inform Indian patients, healthcare providers, and policymakers about the significance of TKR. Therefore, this report aimed to determine the cost-effectiveness of TKR compared to non-surgical management using the new cost data available in India, which will help the Indian states to allocate resources efficiently for surgical procedures such as TKR within the ambit of Universal Health Coverage (UHC).

A decision-analytic model-based cost-effective analysis (CEA) was used in patients over 50 years of age with OA knee of KL grade 2 and grade 3 severities. The estimates of transition probabilities, health utility values obtained from existing literature, and cost data in the Indian scenario were imputed into the MARKOV model to calculate the Incremental cost-effective ratio (ICER). Three different scenarios were envisioned based on the age at which TKR is offered and the lifespan of the implant being 20 years. A sensitivity analysis was done involving the cost of different implants and other input parameters.

The net Quality Adjusted Life Years (QALY) gained per OA knee patient who underwent TKR was higher at the age of 50 years for both grades 2 and 3 in all three scenarios. For grade-2 severity, the lowest ICER value of ₹ 36,107 per QALY gain was observed in scenario 1 at 50 years of age and the highest ICER value of ₹ 61,363 per QALY gain was seen at 70 years of age. For grade-3, the lowest ICER value of ₹32,284 per QALY gained was observed in scenario 1 at 50 years of age and the highest ICER value of ₹55,209 per QALY gain was seen at 70 years of age. The results of the sensitivity analysis showed that the ICER value was most sensitive to the cost of non-surgical management followed by the QoL value of the improved state and then by the cost of TKR across different scenarios. In all the scenarios, the ICER was located in the “northeast” quadrant of the decision diagram and below the willingness-to-pay threshold.

Our study concluded that overall TKR is cost-effective when compared to non-surgical management in patients with OA knee in India irrespective of age and types of implants used and whatever be the severity of the disease.

List of Abbreviations

ABPMJAY	Ayushman Bharat Pradhan Mantri Jan Arogya Yojana
CEA	Cost-effectiveness Analysis
GDP	Gross Domestic Product
HTA	Health Technology Assessment
ICER	Incremental Cost-effective Ratio
KL grade	Kellgren Lawrence grade
OA Knee	Osteoarthritis Knee
OPD	Out-Patient Department
QALY	Quality Adjusted Life Years
QoL	Quality of Life
TKR	Total Knee Replacement
UHC	Universal Health Coverage
YLDs	Years Lived with Disabilities

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1 Introduction

1.1 Background

Osteoarthritis (OA) is a degenerative joint disease involving the cartilage and its surrounding tissues and is the single most common cause of disability in the older population (1,2). OA can affect all joints; however, the knee is the most common site of OA, followed by the hand and hip (2,3). Overall, OA of any joint accounted for 3.9% of years lived with disabilities (YLDs) worldwide in 2015 and is the fourth leading cause of YLDs across the globe (1). The global prevalence of OA knee has been estimated to be around 22.9% in individuals aged 40 and above (4). The prevalence of OA knee increases with age and is more common in women (5).

Prevalence of OA in India, among those aged 40 years and above, ranges between 22% and 39% (6). OA knee is among the commonest disabling joint diseases in India as seen globally, and was estimated by a multi-centric Indian study to be ranging between 19% among <50 years old up to 54.1% among 70 years plus population (7). Another study reported the prevalence of OA knee from multiple small studies and reported that the condition of OA knee varied widely across regions of India (8). In India, OA knee was also higher among older women (51%) than their age-matched male counterparts (33.09%) and the rates were higher in the urban population and among people with low physical activity (9). Prevalence estimates of OA knee of India computed by the Global Burden of Disease (GBD) initiative (a global resource for disease-specific and country-specific estimates of different health conditions) are described in detail in subsequent sections.

Symptoms of OA knee include pain that worsens with use and improves with rest; and stiffness that improves after activity. On physical examination, crepitus, swelling, and deformity may be present (10). OA knee is diagnosed based on a clinical and radiological examination that may include X-ray, CT scan, and MRI. Based on radiological findings, OA knee is graded using Kellgren Lawrence (KL) grading system – the most commonly used grading system for OA knee – into four grades. Broadly, grade 1 includes doubtful joint space narrowing, grade 2 indicates possible joint space narrowing and definite osteophytes, grade 3 involves definite joint space narrowing and sclerosis and grade 4 indicates severe sclerosis, definite deformity, and large osteophytes (11).

OA knee is treated conservatively or surgically (12). Conservative management includes medications and physiotherapy (13). On the surgical side, total knee replacement (TKR) is a proven effective treatment of OA knee known to provide substantial symptomatic relief, therefore, leading to considerable patient satisfaction and improved quality of life (QoL) (14). TKR is being applied to treat OA knee for a considerable period. It has undergone many improvements over time, mainly in the quality of prostheses and surgical technique-wise. Many reports have been published over the years, consistently underscoring the clinical effectiveness of TKR along with its evolution over time (15, 16). A systematic review of the literature was also undertaken by the investigators of this study to refresh the evidence of the clinical effectiveness of TKR and to explore the determinants influencing its success. Our review showed that TKR remains effective regardless of the different settings and outcomes used. This review focused on both the short (< 6 months) and long-term (>6 months to 10 years) outcomes of TKR and showed that the greatest improvement was seen between 6 months and 1 year. During the long-term follow-up, although less improvement was observed between one and five years, however, no decline in outcomes post-TKR was observed during any period of the time studied. It was also observed during the review that there was a substantial improvement in the pain and function component as compared to the stiffness component in the operated knee. Similarly, it was found that there was an improvement in all eight domains of QoL measured by a popular scale, except general health. Our review also found that age, gender, comorbidities, and postoperative complications were associated with outcomes of TKR. Summarily, almost all the reports underscore the clinical success of TKR at various follow-up periods. However, the implant used in TKR on an average, needs to be replaced after 20 years, although evidence of its long life is also known. Repeat TKRs may not be offered to all individuals after the "expiry" of their implants based on multiple factors such as age, frailty, comorbidities, etc. and non-surgical conservative management may be the preferred post-expiry choice in such cases.

As a common joint disease, OA knee is associated with a high economic burden, mainly due to disability associated with this chronic degenerative disease leading to income losses as well as the expense for treatment for this condition. Hospitalization, diagnostic procedures, physiotherapy, medications, and non-medical costs such as transport, and auxiliary devices all constitute treatment costs. However, reports on the cost of management of OA knee (except TKR) are not abundant in the body of evidence. For instance, only one study from the USA estimated the management cost to be about US$5294 per person per year in those aged over 65 years and $5704 in patients less than 65 years. Hospitalization costs comprised nearly half of the treatment costs and a third of it was for medications. The non-treatment cost of OA knee was estimated to be around US$4603 per person annually, mainly due to disability-driven work-related economic losses and home-care costs (17).

Against this backdrop, total knee replacement (TKR) emerged as the key procedure to overcome the clinical as well as the economic burden of OA knee. The cost of TKR in developed countries such as the USA is estimated to be around $17500 (in 2017) and in European countries like Denmark and the UK around €13149 (in 2020) and £7313 (in 2013) respectively (18–21). Despite the surgeries being expensive, the cost-effectiveness of TKR has been reported by multiple economic evaluation studies, but these studies were mostly conducted in high-income Western nations. Currently, there is very little evidence of the cost-effectiveness of TKR from LMICs, where the costs related to the procedure are also very different, and so are its consequences, as compared to high-income nations.

1.2 Economic Evaluation of health interventions

Cost-effectiveness/cost-utility analyses are some of the main types of economic evaluations used for healthcare. They are comparative analyses of the relative costs and consequences of two or more alternative courses of action. Cost-effectiveness analyses measure the health consequences of an **intervention** in a single natural unit (such as cases averted, or life-years saved). However, a limitation of this is that it is difficult to compare studies investigating interventions targeting different diseases or different stages of care, since their health consequences will be expressed in different units, limiting its potential use for informing policymakers. To address, this specific form of cost-effectiveness known as cost-utility analysis was developed. Cost-utility analyses measure the health consequences with a generic measure of health status, which can account for benefits on both reduced morbidity and mortality, such as DALYs and QALYs. As these metrics can be used for a wide range of diseases, the cost-effectiveness estimates for different healthcare interventions can be directly compared to each other (such as comparing the cost-effectiveness of a malaria intervention to a tuberculosis intervention). In practice, there has been a blurring of the distinctions between cost-effectiveness and cost-utility analyses; as a result, literature on cost-effectiveness often encompasses both these approaches and cost-utility analyses are often referred to as cost-effectiveness analysis (CEA) also. In this report, we have used the more easily-understood phrases like "cost-effective" and "cost-effectiveness" to mean "cost-utility".

1.3 Rationale

Meanwhile, an increasingly aging population and demand for higher functional activity levels among the elderly will further keep escalating the need for TKR, worldwide. There will be also greater demand for TKR in the middle-aged group as well because with increasing obesity across the globe, the age of onset of OA requiring surgery has shifted to the younger side. Hence, in the face of this increasing demand for TKR, there is a need for increasing global availability and accessibility to knee arthroplasty (22). In the year 2010, approximately 700,000 TKR surgeries were performed in the USA, and the demand is predicted to grow to 3.8 million per annum by the year 2030 (23). With regards to India around 1,50,000 TKRs are performed every year (24) currently. But the demand for surgical procedures like TKR will grow exponentially in the fast-growing economy that India is, as the aging Indian population will keep on further aspiring to live a life of better quality, leveraging their ever-burgeoning affordability and growing political clout to demand social and health security from the state. According to a study conducted by Bhandarkar et al. in Mumbai, the prevalence of OA knee increased from 3.31 in 2011 to 3.91 per hundred populations in 2014, a sign of the surge to come in near future. And, most importantly, an egalitarian welfare state like India, committed to providing Universal Health Care (UHC) to all its citizens, will have to gear up to offer an effective therapy like TKR to all its OA knee patients, whoever clinically requires it. An indigenous economic evaluation study estimating the cost-effectiveness of TKR in India and its implications on the health expenditure of the nation can be a good starting point for this purpose.

1.4 Aim and Objectives:

As mentioned above, the clinical and cost-effectiveness of TKR in developed countries have been already proven. However, it is necessary to determine whether TKR is cost-effective in India to inform Indian patients, health care providers, and policymakers. As India strives to cover its entire population with Universal Health Care (UHC), the focus of the report will be to determine the cost-effectiveness of TKR, using the new cost data available in India, which will help the Indian state to allocate resources efficiently for surgical procedures such as TKR within the ambit of UHC.

Therefore, the overarching goal of this study was to conduct a comprehensive economic evaluation of TKR in the Indian context. We assume the earliest average age of OA knee turning severe enough to warrant TKR would be 50 years and the lifespan of the implant to be around 20 years (26), The clinical severity of OA knee is commonly and universally measured with the Kellgren-Lawrence scale, the severity ranging between grades 1 (least severe) to 4 (most severe). TKR is commonly offered to patients suffering from KL grade-3 and also sometimes KL grade-2 severity. Therefore, we aimed to conduct the CEA for these two grades also.

We also aimed to estimate the impact on health-related expenditure to the country if the Indian health system braces to provide TKR to all the Indians who need it.

2 Methodology

The present study considered a decision-analytic model-based CEA of TKR in patients of various age groups suffering from OA knee with different severities and accounting for multiple scenarios.

2.1 Decision-analytic model

A decision-analytic model used for CEA is a biologically plausible sequence of occurrence of health consequences as a result of the decision of undertaking an **intervention**, in our case TKR; and these sequences are compared with that of other interventions, referred to as **comparators**, in our case non-surgical treatment. The Markov model is one of the best decision analytic models and was found to be appropriate for our study. In the Markov model, patients are assumed to reside in one of a finite number of **health states** at any point in time and make transitions between those health states over a series of discrete time intervals or cycles. The probability of transition from one state to another (including the probability of staying in the same state) over a cycle is known as **transition probability**. Thereafter **health utility values** are assigned to each health state. The health utility values are QoL weights assigned to health states, which when multiplied by annualized cycles provide us with the **Quality Adjusted Life Years (QALY)** spent in a health state. The Markov model terminates when it reaches the **absorbing state(s)**, such as death or in our case "expiry" of an implant. The **cost of treatment** is also assigned to each health state. The discounted value of total cost incurred and the QALY gained because of the intervention, generated by the Markov model, as opposed to the comparator, are used to calculate the **incremental cost-effectiveness ratio (ICER)** (27–29), the most common metrics generated by a CEA. Further, the ICER value is illustrated graphically on a four-quadrant diagram known as the **cost-effectiveness graph** for decision-making (30).

2.1.1 Conceptualization of the Markov model for CEA of TKR

For our study, we developed two basic Markov models (Figures 1 and 2), the first model focusing on the intervention (TKR) and the second model focusing on the comparator (non-surgical management). The former model accounted for the progression of a patient with OA knee after TKR and the latter accounted for disease progression in absence of definitive surgical treatment. In both models, the states were represented by **rectangular boxes**, and the transition between the states was shown by the **arrows**. The **loops** indicated the possibility of remaining in a particular state in successive cycles.

The model for non-surgical management consisted of 4 states (OA knee grade-2, OA knee grade-3, and OA knee grade-4, all-cause death) representing the onward progression of OA knee despite non-surgical management (Figure 1). The model for the TKR arm, presented in Figure 2, consisted of 7 states, "OA knee under-going TKR", "improved OA knee", "early failure post-TKR", "late-failure post-TKR", "systemic complication post-TKR", "all-cause death", and "death due to TKR related systemic complications". The transition probability, QoL, and cost matrices (also called **Markov trace**) of both models are presented in the supplementary tables (Supplementary Table 1-2)

The stopping rule in the model was either the expiry period of the implant which was assumed to be 20 years (26) or the death of all the patients which was assumed to be at 100 years. Therefore, each Markov model had 20 yearly cycles.

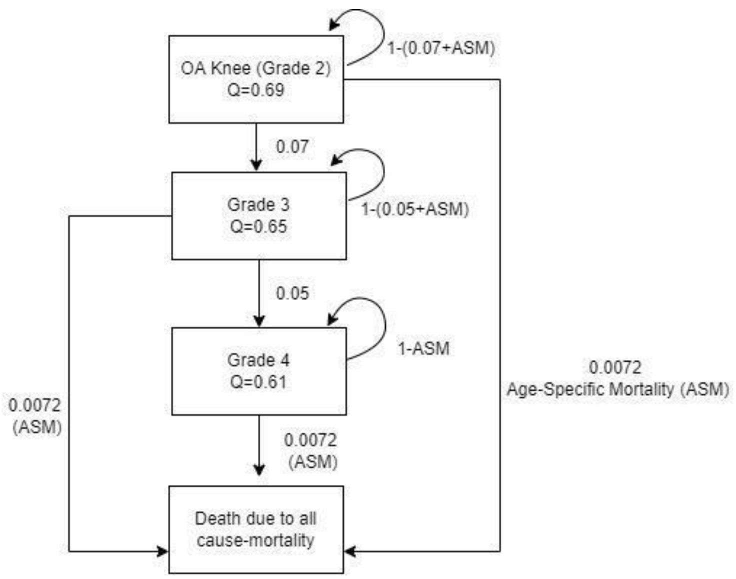


Figure 1. Markov Model for Non-Surgical

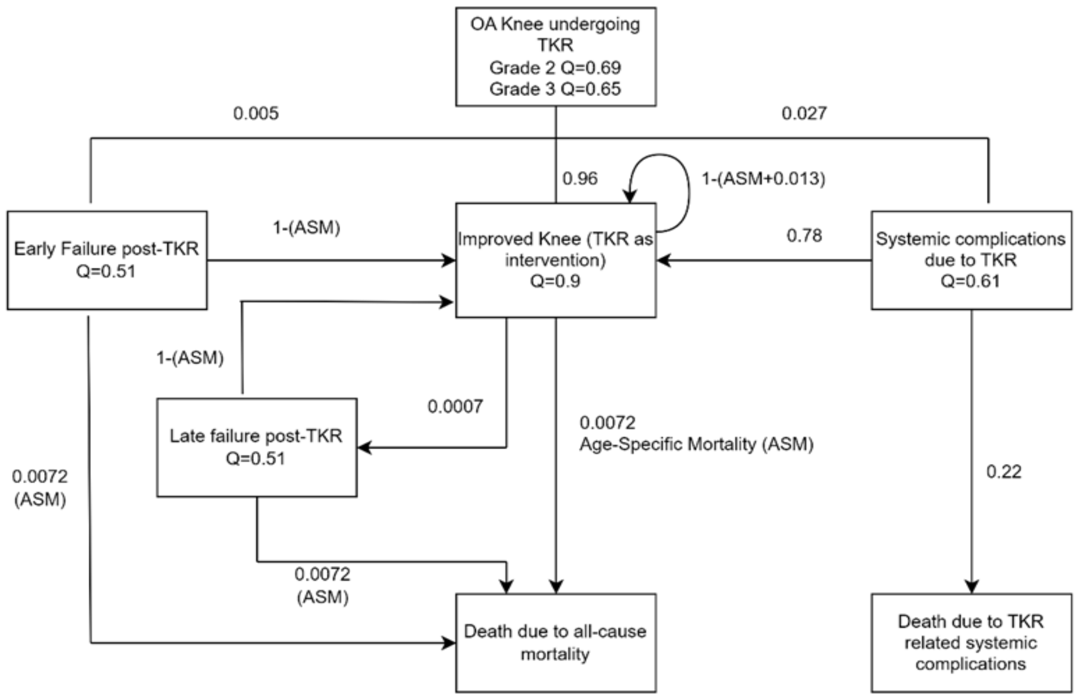


Figure 2: Markov Model for Intervention (Total Knee Replacement)

2.2 Data inputs

Using general principles of evidence-based medicine, estimates of transition probabilities and health utility values of each Markov state were identified and synthesized from existing literature and the models were populated with those values (Fig. 1 & 2). The sources of the individual parameters are detailed below.

Transition probabilities for grade-2 and grade-3

The non-surgical arm consisted of 4 states and 16 possible transitions between these states. However, it is assumed that patients do not recover from the progressive disease of OA knee with conservative management, hence, transitions (in this case improvement) from grade-4 to grade-3 or grade-2 of OA knee were not considered. Therefore, we extracted 8 transition probabilities (see Figure 1 and Supplementary Table 1). Similarly, the TKR intervention arm consisted of 7 states and 49 possible transitions in these health states. As explained earlier, out of the 49 possible transitions, 12 transition probabilities were estimated: (see Figure 2 and Supplementary Table 2). The value of the rest 37 transition probabilities was considered to be zero because of the theoretical impossibility of their transitions.

Health utility values

The QoL for the improved state was allocated to be 0.90. The QoL of OA knee grade 2 and grade 3 were assigned to be 0.69 and 0.65 respectively, based on existing evidence. Patients who died had a QoL of 0. Patients who experienced systemic complications had a QoL of 0.61. QoL for those with early and late failure TKR was 0.51 (Supplementary Table 3).

The all-important health utility value used in the Markov model marking improvement after TKR is from western literature and stood at 0.9 (43–45) as there was no literature containing quality of life and health utility values scores in Indian context during the time of the study.

Since the completion of our study, a recent paper (52) was published in February 2023, which used EQ-5D-5L to determine the quality of life of patients after TKR in a North Indian population. We utilized the EQ-5D scores reported in this paper to derive health utility values of improvement after TKR for the Indian population, which was found to be 0.89. Although this value is slightly lower than the value used in our original Markov model, which was based on Western literature and accommodated at 0.9, the difference between the two values is minimal.

Costing data

The costs of TKR, revision TKR and treatment of systemic complications post-TKR were extracted from the National Health System Cost Database 2014-15 (Supplementary Table 4). The cost per OPD visit for non-surgical management of OA knee was obtained from the National Health System Cost Database 2014-15 (31). All cost values were inflated to 2020-21 based on CPI (consumer price index) health inflation rate (32). The TKR intervention arm involved substantial costs – ₹117041 Indian National Rupee (₹ also expressed as ₹) for TKR, 1.5 times the cost of TKR for revision TKR, and ₹692 for treatment of systemic complications post-TKR. The cost per OPD visit for symptoms of OA knee was ₹324 and it was assumed that the patient required two visits per year. So, the non-surgical treatment has a fixed cost in each annual cycle (2 x ₹324 = ₹648). Hence, the cost obtained from secondary data was used to calculate the total cost and total QALY of treatment for both the arms through Markov model. Further, the total cost and total QALY were discounted at 3% to adjust it to the present value.

2.3 Different Scenarios and age-groups

Given the lifespan of the implant used in TKR being 20 years, we could envision three different scenarios, each representing different combinations of TKR, repeat TKR (up to two repeats), and non-surgical management. Also, as the average age of onset of OA knee of sufficient severity (KL grade 2 onwards) where TKR may be applied is 50 years, we decided to model the outcomes starting with three different cohorts, the starting age of which were 50, 60, and 70 years respectively, as others have done (33). Table *1* describes the possibility of the 6 different scenarios for the TKR arm and three for the non-surgical comparator arm.

Table 1. Scenarios based on the expiry of the implant

	Age at which TKR was conducted for the first time		
Scenarios	50 years	60 years	70 years
1. TKR implant expires in 20 years (cycles) and all live patients continue with non-surgical treatment up to death.	Possible	Possible	Possible
2. First TKR implant expires in 20 years and then a second repeat TKR is conducted on those patients who are likely to live for another 20 years or more. The second TKR implant expires in another 20 years following which all live patients continue with non-surgical treatment up to death.	Possible	Possible	Not possible
3. First TKR implant expires in 20 years and a second repeat TKR is conducted on those patients who are likely to live for another 20 years or more. The second TKR implant expires in another 20 years and a third repeat TKR is conducted on those patients who are likely to live for another 20 years or more. The third TKR implant expires in another 20 years following which all live patients continue with non-surgical treatment up to death.	Possible	Not possible	Not possible

2.4 Sensitivity analysis

A univariate Deterministic Sensitivity Analysis (DSA) was carried out. All three input variables, transition probability, health utility values, and cost were either selected from published literature or national repository, however, these values had variations; especially the price varied between the different types of implants. With regards to the transition probability and utility values, these were derived from other countries in absence of India-specific values, hence, we presumed that the input parameters may differ in the Indian setting. Also, these values were bounded by upper and lower limits of their uncertainty intervals (95% confidence intervals in most cases). To capture this variation of input values, we conducted the DSA. It was carried out for Grade 2 only because it was found that TKR for grade 3 was anyway more cost-effective than grade 2, so if the estimates from sensitivity analysis for grade 2 was cost-effective then it is definitely cost-effective for the estimates for grade 3. DSA changed the different input variables of TKR intervention and non-surgical arm by 50%. The results were presented using tornado plot.

The cost of different types of implants ranged between ₹55000 and ₹77000 with specific cost ceilings of ₹54720, ₹56490 and ₹76600 for Cobalt-chromium, High flexibility implants and Zirconium-Titanium respectively (34). A 50% increase in the cost of TKR (₹175561) would include the cost escalation due to different types of TKR implants. Therefore, the sensitivity analysis of different input variables of both TKR and non-surgical arms was estimated based on 50% variation (see Supplementary Tables 1-4).

2.5 Decision Diagram

The decision diagram presents the ICER values of different scenarios and grades vis-à-vis different thresholds. The per capita GDP of India was INR 1,28829/- at current price in 2020-21. Normally, three times of per capita GDP is assumed to be the willingness to pay (WTP) threshold value. Anything less than one per capita GDP is considered highly cost-effective. (WHO-CHOICE). The ICERs derived from sensitivity analyses were also presented through the decision diagram (we present only the ICER with highest increase from DSA estimates).

2.6 Budget Impact Analysis

The budget expenditure for TKR surgery was calculated based on the cumulative prevalence of OA knee (plus annual incidence), care seeking by OA knee patients and administration of TKR for those conditions in the Indian context; and the cost of TKR surgery. As per the Global Burden of Disease data for OA knee the cumulative prevalence was 37636296 and annual incidence was 2471445 among 50+ Indians. These estimates are in line with the Indian studies mentioned in the background section. Out of the total cumulative prevalence of OA knee, only 2% of the patients are likely to opt for TKR if it is provided through UHC. The budget expenditure is calculated by multiplying the number of people going for surgery annually and the average TKR cost minus the expenditure on non-surgical treatment. All the estimates related to the budget expenditure of TKR surgery were predicted up to 2029. This was calculated from the data available at Sample Registration System, extrapolated for 2023-2029 by accounting for the average growth rate to the total population. The details of Indians expected to undergo TKR annually and its cost-wise implications nationally are explained in detail in a supplementary table 9.

3 Results

3.1 Grade-wise and age-wise ICER values

The net QALY gained per OA knee patient who underwent TKR was higher at the age of 50 years in all three scenarios in both grade-2 and grade-3 severity as compared to the patients starting at 60 and 70 years of age. At the age of 50, for grade-2, the highest net QALY gain of 3.8 was noted in scenarios 2 and 3, however, scenario 3 had a higher incremental cost (₹177,894) when compared to scenario 2 (₹174,182) while for grade-3 the highest net QALY gain of 4.3 was in scenario 3. For grade-2, a notable 18% less QALY was gained in scenario 1 when compared to scenario 2, however, with a 35% less cost also. Further, differences in the increments in QALY and costs in both grades between scenario 1 and scenario 2 narrowed with age.

Based on the six scenarios (3 scenarios for age 50 and 2 scenarios for age 60 and one for age 70), for grade-2, the lowest ICER value of ₹36,107 per QALY gained was observed in scenario 1 at 50 years of age, followed by an ICER value of ₹43,518 per QALY gained in scenario 1 at 60 years of age. The highest ICER value of ₹61,363 per QALY gain was seen at 70 years of age. Similarly, for grade-3, the lowest ICER value of ₹32,284 per QALY gained was observed in scenario 1 at 50 years of age, followed by an ICER value of ₹38,386 per QALY gained in scenario 1 at 60 years of age. The highest ICER value of ₹55,209 per QALY gain was seen at 70 years of age (see Table – 2).

For grade-2, the ICER per QALY gained had increased by 20% from 50 to 60 years of age and by 70% between 50 and 70 years of age in scenario 1. On the other hand, in scenario 2 a 15% increase in ICER was noted between 50 and 60 years of age.

All the ICER values across the scenarios for both grades were below the threshold value which was assumed to be three times the per capita GDP of India (3X 1,28,829 = ₹3,86,487).

Table 2: Incremental Cost Effectiveness Ratio (ICER)

Patient's Age	Grade-2			Grade-3		
	Scenario-1 (Single TKR)	**Scenario-2 (Double TKR)**	**Scenario-3(Triple TKR)**	**Scenario-1 (Single TKR)**	**Scenario-2 (Double TKR)**	**Scenario-3(Triple TKR)**
	Net QALY gain			Net QALY gain		
50	3.1	3.8	3.8	3.4	4.2	4.3
60	2.6	2.8		2.9	3.2	
70	1.9			2.1		
	Extra cost (in INR)			Extra cost (in INR)		
50	111158	174182	177894	111158	174182	177894
60	112175	149635		112175	149635	
70	113766			113766		
	ICER (INR per QALY gained)			ICER (INR per QALY gained)		
50	36108	46136	46912	32284	41051	41735
60	43518	52943		38386	46609	
70	61363			53458		

3.2 Deterministic Sensitivity Analysis (DSA)

The results of the sensitivity analysis showed that the ICER value was most sensitive to a reduction in the cost of non-surgical management followed by the QoL value of the improved state and then by the cost of TKR across different scenarios. On the other hand, the other input values had an impact of less than 5% on the ICER values. (See Figure 3a for Scenario 1, figure 3b for Scenario 2, and Figure 3c for Scenario 3). A 50% decline in the cost of non-surgical (₹324 per year) management of OA knee led to 89%, 74%, and 69% increases in the value of ICER among 50-, 60-, and 70-year-olds. Similarly, a 50% decline in the QoL value of the improved state (from 0.9 to 0.795) led to a more than 80% increase in the ICER value across all scenarios. Meanwhile, a 50% increase in the cost of TKR intervention resulted in only a 10% increase in ICER. The ICER values generated by the different sensitivity analyses were consistently lower than the per capita GDP of India.

Figure 3a: Tornado plot with 50% deviation from the base with single TKR

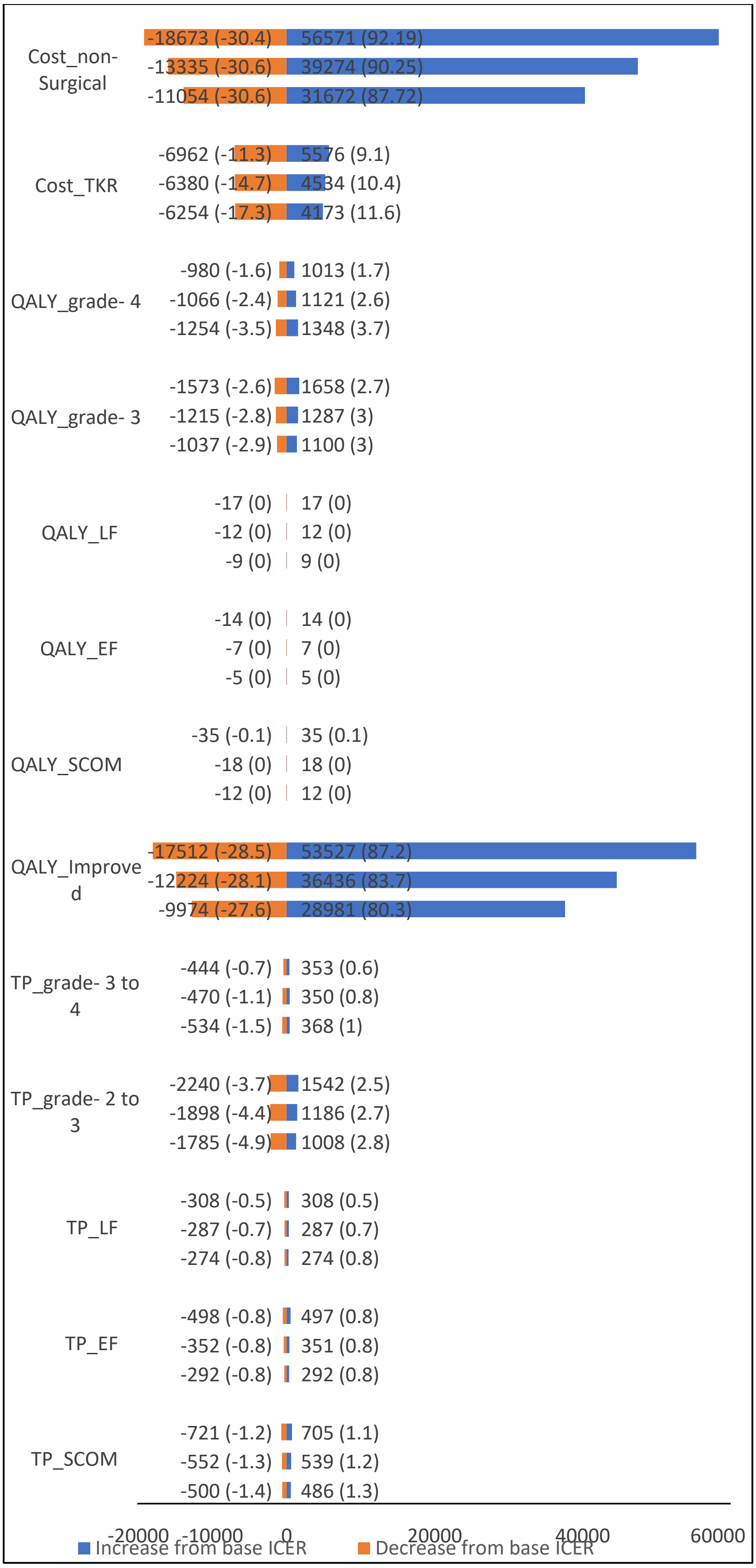


Figure 3b: Tornado plot with 50% deviation from the base in double TKR

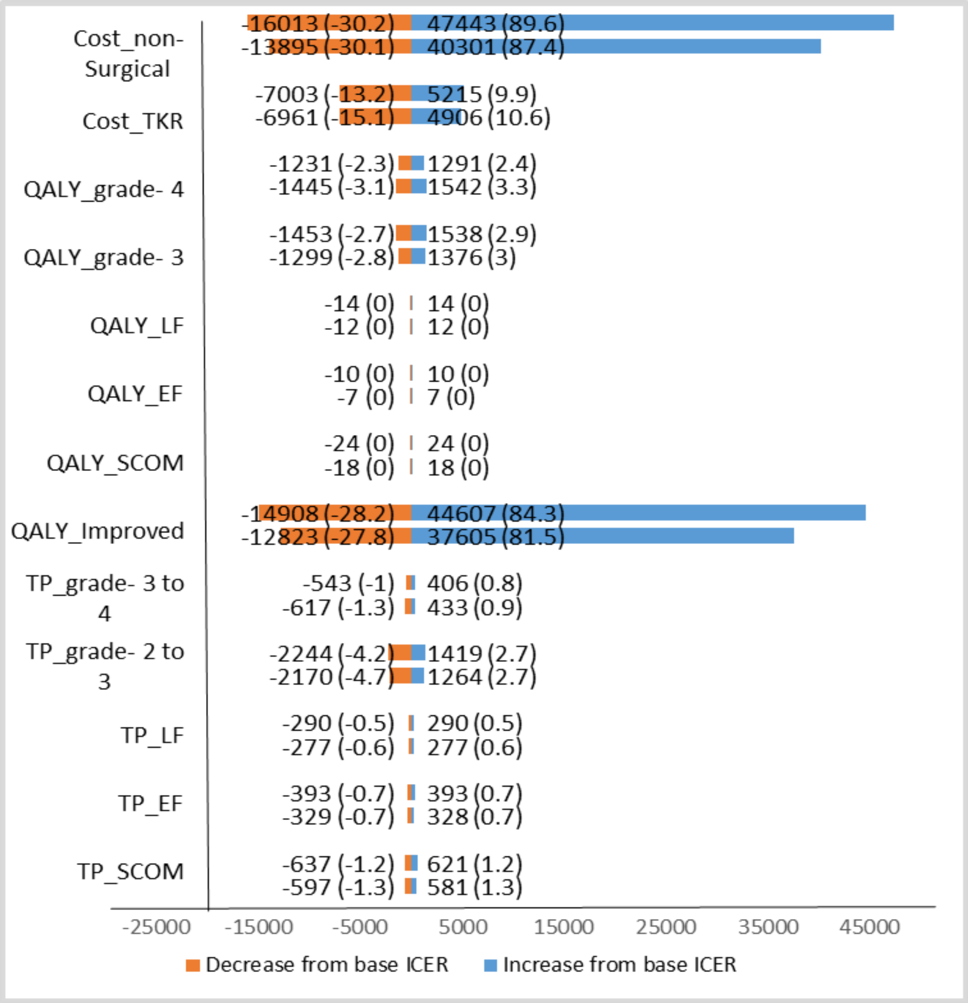
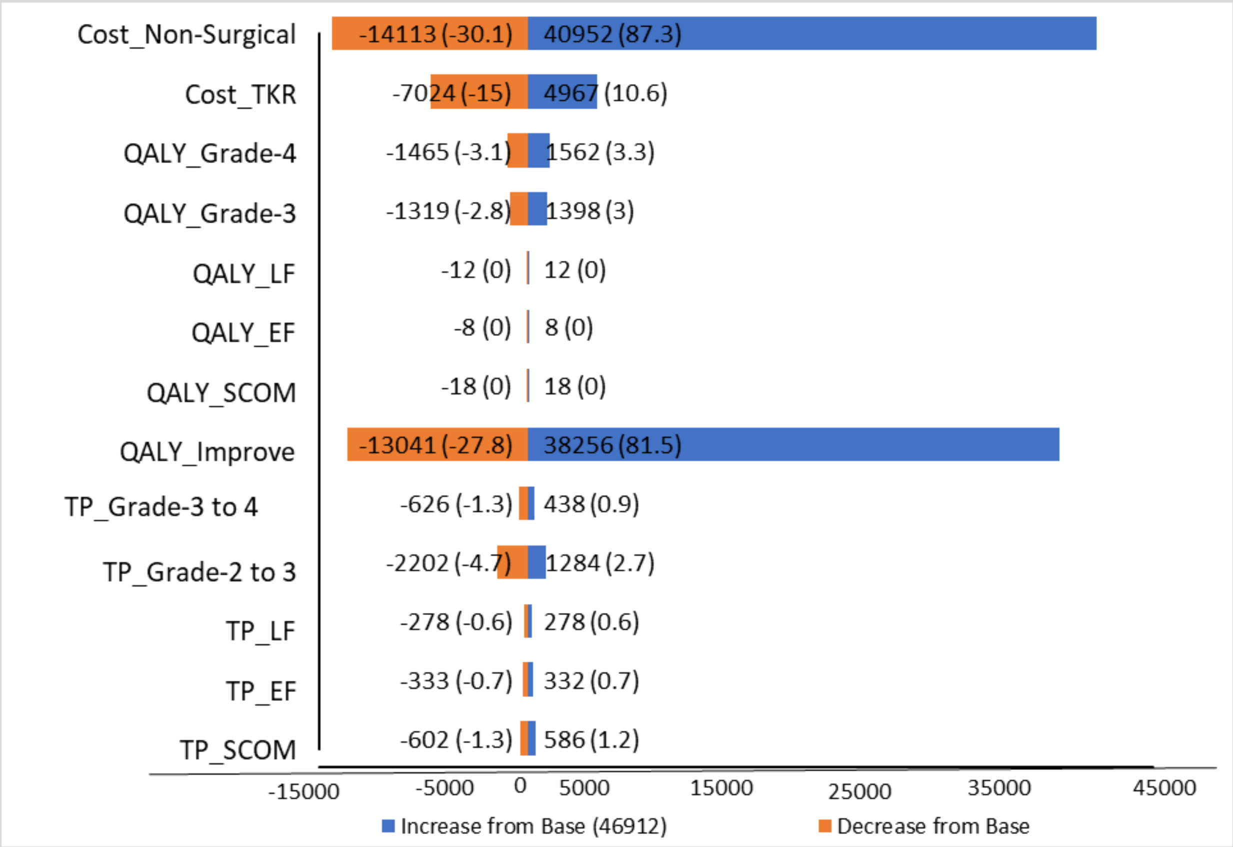


Figure 3c: Tornado plot with 50% deviation in triple TKR



3.3 Decision diagram

In all six scenarios, for grade-2 and grade-3, the net QALY gained and the incremental cost was positive, which suggests that extra cost had to be borne to gain QALY. Therefore, the ICER was located in the "northeast" quadrant of the graph (see Figure 4a and 4b). All the ICERs for our six scenarios were very much below the willingness-to-pay threshold value, which was three-time per capita GDP (PCGDP) of India, (PCGDP was ₹128829 at the current price in 2020-21). They were all below one PCGDP of India, which is considered as "highly cost-effective". The lowest ICER was Rs 32,284 (single TKR, 50 years and grade 3) –which was less than 25% of PCGDP while the highest ICER was Rs 61, 363 (Single TKR, 70 years, grade 2) which was less than 50% of PCGDP **.** Therefore, all ICERs for all scenarios (all grades, all age groups, all combinations of treatment) were much less than WTP threshold value**.** Even when all the input parameters were inflated or reduced to 50%, the net QALY gained despite remaining in the northeast quadrant of the graph was never more than PCGDP (Supplementary Table 10).

Figure 4a: Decision diagram for grade-2 severity

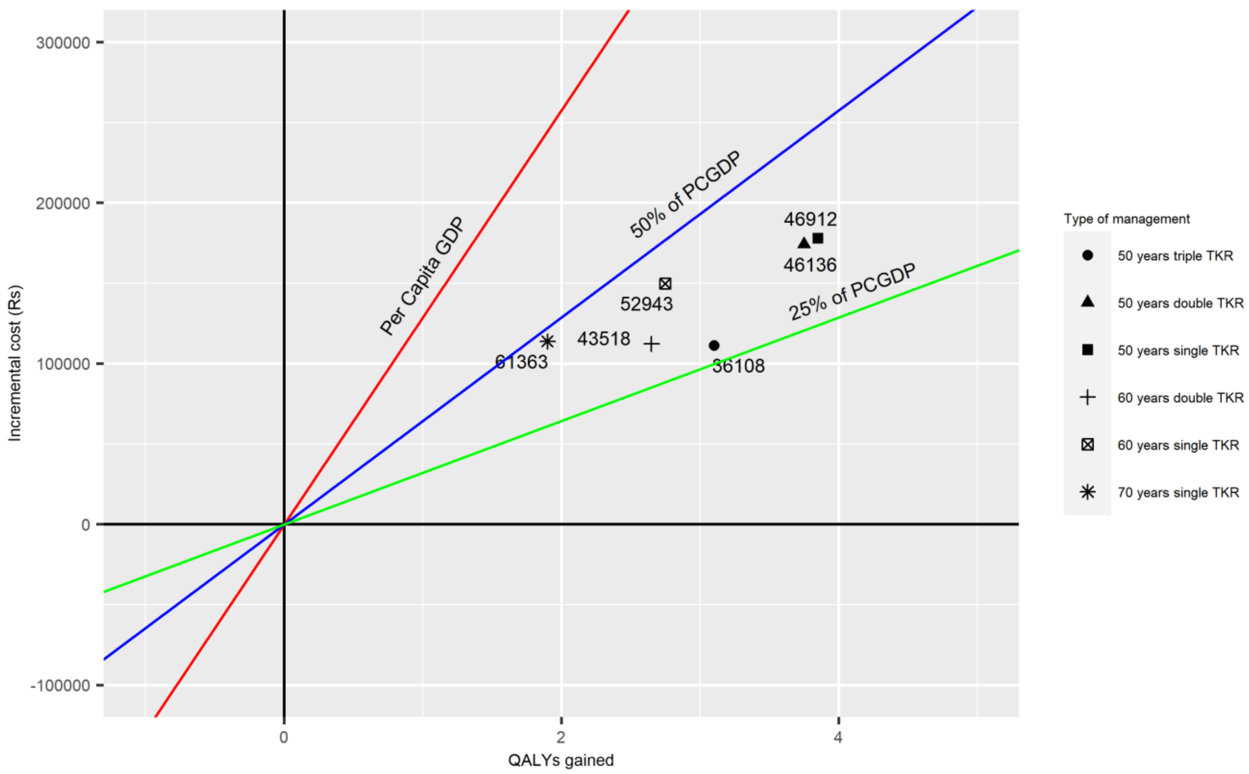
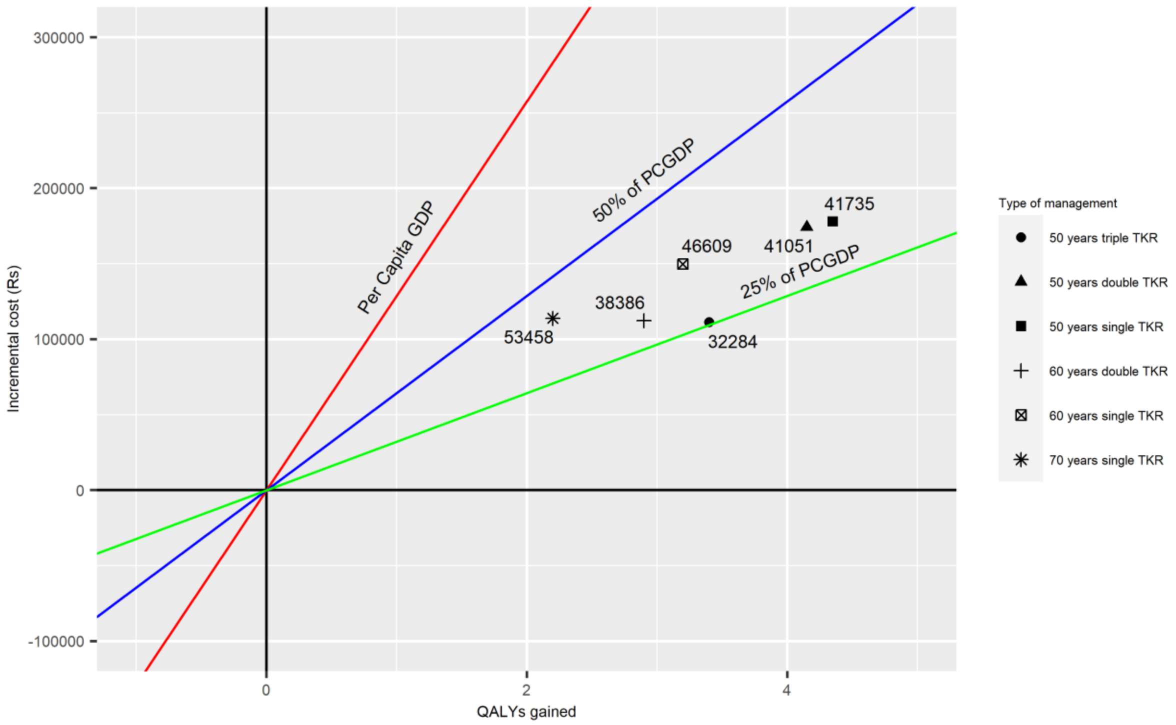


Figure 4b: Decision diagram for grade-3 severity



3.4 Budget Impact Analysis

We extrapolated the population suffering from OA knee based on the cumulative prevalence of OA knee. It was found that 4.77 crore population above the age of 50 years is likely to have OA knee in 2023. Approximately, 2% of this sub-population (9.54 lakhs) will be prescribed or will access TKR surgery. To provide TKR to this population the expected cost will be around INR 11,174 crore in 2023. So, we have predicted that the TKR-eligible population will increase to 11.9 lakhs by 2029 and so the expenditure requirement also increases to INR 13,930 crores in the same year.

BIA shows total expenditure required by the national government to provide OA knee as part of the national government health programme or purchase care from the private sector. As per our estimate, total expenditure would be INR 11714 Cr in the year 2023-24. In 2023-24, total projected expenditure for OA knee would be 2.63% of total union and state government health expenditure.

Table 3: Budget Impact Analysis

	Total Population	Population aged 50+(19.0678%)	Prevalence of OA knee among 50+ (14.772%) and Incidence Rate (0.97%)	Prevalence of TKR	Budget Expenditure (in Crores)
2023	1430186364	263449359	47737025	954740	11741
2024	1441633609	265558014	50312938	1006259	12112
2025	1453172478	267683546	51903209	1038064	12480
2026	1464803704	269826092	53482458	1069649	12846
2027	1476528027	271985786	55051071	1101021	13210
2028	1488346192	274162766	56609429	1132189	13571
2029	1500258949	276357172	58157905	1163158	13930

4 Conclusion

The main aim of this study was to conduct a health technology assessment of TKR in the Indian context and determine the cost-effectiveness through different scenarios, based on the possibility of multiple replacements, the severity of the disease, and the age groups at which TKR is being done. Our study suggested that TKR is cost-effective in the Indian setting among all the scenarios, ages, and severities considered. TKR is most effective when the individual is 50 years old, suffering from KL Grade 3 OA knee with only one-time replacement followed by conservative management after the expiry of the implant. However, TKR is so clinically effective and also overwhelmingly cost-effective in the Indian setting, because all ICER estimates are below the willingness-to-pay threshold, that it should be offered to every individual whoever is clinically eligible for it.

Our study showed that TKR is cost-effective. across all the scenarios for both grades This result correlates with those in high-income countries such as the USA, UK, and Canada, where TKR has been proven to be cost-effective (35–37). A similar finding was also observed by a study conducted in China, which showed that TKR is highly cost-effective being RMB ¥3237.37/QALY gained, which was less than 10% of per capita GDP needed to gain 1 QALY by TKR (38). Concerning age, our finding was corroborated by another study, which showed differences in ICER, comparable to our study, when TKR at an earlier age was compared to late TKR (33). Therefore, it can be concluded that TKR is cost-effective for younger patients as well (39). It was also interesting to observe that the cost of TKR in the Indian scenario was much lower as compared to the Western settings. This might be due to the higher cost of living including the higher cost of implants and service charges for TKR surgery in those nations.

It is not very common for a person to undergo TKR surgery more than once in the Indian setting. In addition to this, in a clinical scenario, the chance of a person with degenerative OA knee undergoing more than one TKR is unlikely since the implant is likely to last for a longer period unless there is extensive physical activity. However, our study concluded that irrespective of the age groups, grades, and scenarios envisioned (which included multiple TKRs also), the ICER value of TKR was below the threshold value and therefore, TKR can be unambiguously considered cost-effective across all age groups, and severities.

A sensitivity analysis showed that despite the 50% unfavorable changes in all input parameters (QALY, transition probabilities, and cost), the ICER was consistently below the threshold value.

Our study was the first to evaluate the cost-effectiveness of TKR compared to non-surgical management among different age groups and the severity of disease in the Indian context. Our study was also the first to do a sensitivity analysis involving the cost of different TKR implants in India since various types of implants are used in the surgery depending on the condition of the patient. The cost-effectiveness analysis was done using the cost data from different regions of India, thereby making the results generalizable throughout the country. This study was also the first to determine the cost-effectiveness of TKR among different scenarios to establish whether multiple TKR surgeries are cost-effective when compared to non-surgical management.

Our study has a few limitations. Since the data for transition probabilities and QoL were obtained from Western countries, the generalization of these data to developing countries like India might not be precise. But, it is unlikely that transition probabilities will vary humongously to distort our estimates because the demographic profiles and health system of India are gradually catching up with its high income counterparts. Moreover, utility values derived from a very recent article on TKR from India displayed very similar utility values as that reported by the western studies. In addition to this, the sensitivity analyses done by this study further strengthen the conclusions because, in any of the sensitivity analyses, the ICER does not cross the threshold value.

Since the burden of OA knee has been increasing in India, it is essential to determine the effective method of treatment for OA knee to improve the patient’s QoL. When compared to non-surgical management, TKR has been proven to be both clinically effective as well as cost-effective. The demand for TKR surgery has also been increasing in India due to the aging population and the demand for a better quality of life. It is also considerably cost-effective at a younger age and it ought to be offered at a lower clinical grade of OA knee if the clinician and the patient decides and it will still be below the willingness to pay (WTP) threshold.

As India aims to achieve Universal Health Coverage, there is a need to cover the entire population through insurance mechanisms like Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (ABPMJAY) — a government scheme to provide medical coverage especially to the underprivileged. This Health Technology Assessment (HTA) report is crucial in providing insight into the judicious allocation of resources and pricing for TKR as it established the cost-effectiveness of TKR in the Indian context using the cost data from India.

To conclude, our study suggests that overall TKR is cost-effective when compared to non-surgical management in patients with OA knee in India irrespective of age, the severity of the disease, and the types of implants used.

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Supplementary Tables

Supplementary Table 1: Transition Probability of OA knee without intervention (non-surgical)

Start State	End State	Transition probability (50% variation)	Reference	Remark
OA knee (grade 2)	OA knee (grade 2)	0.91	(40)	1- (age-specific all-cause mortality + Movement to OA knee grade 3)
OA knee (grade 2)	OA knee (grade 3)	0.07 (0.035 -0.105)	(40)	
OA knee (grade 3)	OA knee (grade 3)	0.93	(40)	1- (age-specific all-cause mortality + Movement to OA knee grade 4)
OA knee (grade 3)	OA knee (grade 4)	0.05 (0.025 -0.075)	(40)	
OA knee (grade 4)	OA knee (grade 4)	0.98		1- (age-specific all-cause mortality)
OA knee (grade 2) OA knee (grade 3) OA knee (grade 4)	Death (Age specific all-cause mortality)	50-54 – 0.0072 55-59 – 0.013 60-64 – 0.018 65-69 – 0.030 70-74 – 0.043 75 – 79 – 0.070 80-84 – 0.099 85+ - 0.18	(41)	

Supplementary Table 2: Transition Probability of OA Knee with Intervention (TKR)

Start State	End State	Transition probability (50% variation)	Reference	Remarks
OA knee	Systemic complications	0.027 (0.0135 - 0.0405)	(42)	
OA knee	Improved knee	0.968		1-(0.027+0.05) [1-(OA knee to systemic complications + OA knee to early failure)]
OA knee	Early failure	0.005 (0.0025 - 0.0075)	(43)	(43) (yearly TP- 0.01/2= 0.05)
Improved knee	Late failure	0.000722 (0.000361 - 0.001083)	(43)	(43) (yearly TP – 0.013/18 = 0.0007)
Systemic complications	Improved	0.78	Assumed 100% recovery from early failure	1- 0.22 (1- systemic complications to death due to TKR)
Early failure	Improved			1- age-specific all-cause mortality
Late failure	Improved			1- age-specific all-cause mortality
Improved	Improved			1- (age-specific all-cause mortality + Late failure)
Early failure Late failure Improved	Death due to all-cause mortality	50-54–0.0072 55-59 – 0.013 60-64 – 0.018 65-69 – 0.030 70-74 – 0.043 75–79 – 0.070 80-84 – 0.099 85+ - 0.18	(41)	
Systemic complications	Death due to TKR-related systemic complications	0.22	(42)	0.006/0.027 [TKR intervention to death / OA knee to systemic complications]

Supplementary Table 3: QoL value for each state of OA knee

State	**QoL estimates (50% variation)**	**Reference**	**Remarks**
OA knee (Grade 2)	0.69	(43–47)	
OA knee (grade 3)	0.65 (0.63 -0.67)	(48)	Calculated based on the proportionate change from grade 2 of QALYs; data from Nikolic et al (48) (based on QALYs of grade 1 or 2 = 0.786 and grade 3 or 4 =0.712)
OA knee (grade 4)	0.61 (0.57 -0.65)	(48)	Calculated based on the proportionate change from grade 2 of QALYs; data from Nikolic et al (48) (based on QALYs of grade 1 or 2 = 0.786 and grade 3 or 4 =0.712)
Improved state (TKR)	0.9 (0.795 -0.99)	(43–45)	
Systemic complications	0.61 (0.57 -0.65)	(49)	Percentage decline in value from QALYs of OA knee = 0.69
Early failure	0.51 (0.42 -0.6)	(50)	
Late failure	0.51 (0.42 -0.6)	(50)	
Death	0	(51)	

Supplementary Table 4: Cost data for surgical and non-surgical management (31)

	Cost 2014-15 (actual)	Cost 2020-21 (inflation-adjusted)	Cost 2020-21 _with a 50% reduction	Cost 2020-21 _with 50% increment
TKR_Surgery	84497	117041	58520	175561
Systemic complication	614	692	346	1038
Revised_TKR_Surgery	126745	175561	87781	263342
Revised_TKR_Surgery	126745	175561	87781	263342
Non-surgical OPD (per visit)	468	648	324	972

Supplementary Table 5: Transition Probability Matrix for TKR arm among the 50-54 age group

Health States	OA	SCOMP	TKRD	EF	LF	Improved	Death	Check
OA	0	0.0270	0	0.005	0	0.961	0.007	1
SCOMP	0	0	0.22	0	0	0.780	0	1
TKRD	0	0	1.00	0	0	0	0	1
EF	0	0	0	0	0	0.993	0.007	1
LF	0	0	0	0	0	0.993	0.007	1
Improved	0	0	0	0	0.0007	0.992	0.007	1
Death	0	0	0	0	0	0	1	1

Supplementary Table 6: Transition Probability matrix for non-surgical arm among the 50-54 age group

Health State	Grade-2	Grade-3	Grade-4	Death	Check
Grade-2	0.923	0.070	0	0.007	1
Grade-3	0	0.943	0.050	0.007	1
Grade-4	0	0	0.993	0.007	1
Death	0	0	0	1	1

Supplementary Table 7: QoL and Cost of TKR arm per cycle (Year)

Health States	QoL value	Cost (in rupees)
SCOMP	0.61	692
TKRD	0	0
EF	0.51	175561
LF	0.51	175561
Improved through TKR surgery	0.9	117041
Death	0	0

Supplementary Table 8: QoL and Cost of Non-surgical arm per cycle (Year)

Health States	QoL value	Cost (in rupees)
Grade-2	0.69	648
Grade-3	0.65	648
Grade-4	0.61	648
Death	0	0

Supplementary Table 9: Prevalence and Incidence of OA Knee from GBD 2019

	Prevalence				Incidence		
	All ages	50-69 years		70+ years	All ages	50-69 years	70+ years
India	46852407 (53716759-40542598)	26345223 (31178669-21854929)		11291073 (13170701-9644621)	4178678 (4792078-3625948)	2005227 (2472157-1589511)	1846844 (2270149-1479925)

Supplementary Table 10: Increased ICERs after sensitivity analysis for grade-2 severity

Type of management	Base ICER	Maximum increase in ICER	Increased ICER	Location of increased ICER with regards to per capita GDP
50 single TKR	36108	31672	67780	below 1
50 double TKR	46136	40301	86437	below 1
50 triple TKR	46912	40952	87864	below 1
60 single TKR	43518	39274	82792	below 1
60 double TKR	52943	47443	100386	below 1
70 single TKR	61363	56571	117934	below 1 (at 50% GSDP)