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Optimising the current model of care for knee osteoarthritis with the implementation of guideline recommended non-surgical treatments: a model-based health economic evaluation

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Summary

AIMS OF THE STUDY: Structured exercise, education, weight management and painkiller prescription are guideline recommended non-surgical treatments for patients suffering from knee osteoarthritis. Despite its endorsement, uptake of guideline recommended non-surgical treatments remains low. It is unknown whether the implementation of these treatments into the current model of care for knee osteoarthritis would be cost-effective from a Swiss statutory healthcare perspective. We therefore aimed to (1) assess the incremental cost-effectiveness ratio of an optimised model of care incorporating guideline recommended non-surgical treatments in adults with knee osteoarthritis and (2) the effect of total knee replacement (TKR) delay with guideline recommended non-surgical treatments on the cost-effectiveness of the overall model of care.

METHODS: A Markov model from the Swiss statutory healthcare perspective was used to compare an optimised model of care incorporating guideline recommended non-surgical treatments versus the current model of care without standardised guideline recommended non-surgical treatments. Costs were derived from two Swiss health insurers, a national database, and a reimbursement catalogue. Utility values and transition probabilities were extracted from clinical trials and national population data. The main outcome was the incremental cost-effectiveness ratio for three scenarios: “base case” (current model of care vs optimised model of care with no delay of total knee replacement), “two-year delay” (current model of care vs optimised model of care + two-year delay of total knee replacement) and “five-year delay” (current model of care vs optimised model of care + five-year delay of total knee replacement). Costs and utilities were discounted at 3% per year and a time horizon of 70 years was chosen. Probabilistic sensitivity analyses were conducted.

RESULTS: The “base case” scenario led to 0.155 additional quality-adjusted life years (QALYs) per person at an additional cost per person of CHF 341 (ICER = CHF 2,203 / QALY gained). The “two-year delay” scenario led to 0.134 additional QALYs and CHF –14 cost per person. The “five-year delay” scenario led to 0.118 additional QALYs and CHF –501 cost per person. Delay of total knee replacement by two and five years led to an 18% and 36% reduction of revision surgeries, respectively, and had a cost-saving effect.

CONCLUSION: According to this Markov model, the optimisation of the current model of care by implementing guideline recommended non-surgical treatments would likely be cost-effective from a statutory healthcare perspective. If implementing guideline recommended non-surgical treatments delays total knee replacement by two or five years, the amount of revision surgeries may be reduced.

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Introduction

Knee osteoarthritis is a painful condition that leads to loss of function and is one of the most common reasons for disability worldwide [1]. With an estimated overall prevalence of 8.5% and an attribution to 5,150 disability-adjusted life years in 2019 in Switzerland, knee osteoarthritis places a substantial burden on health and the healthcare system [2]. The economic burden of knee osteoarthritis on the Swiss statutory healthcare system was estimated at 1.12 billion CHF in 2011 [3]. The association of osteoarthritis with reduced physical activity levels may promote frailty and/or cardiovascular disease in the aging population, which negatively affects overall health [4].

Current treatment guidelines recommend non-surgical and surgical treatments for patients suffering from knee osteoarthritis [5, 6]. When non-surgical treatment fails to achieve sufficient symptom relief, total knee replacement (TKR) is endorsed [7]. Even though total knee replacement was shown to be highly effective in patients with moderate to severe knee osteoarthritis [8], up to 30% of the operated patients experienced chronic pain after the procedure [9]. Additionally, total knee replacement is associated with adverse events and implants have a limited lifespan leading to implant failure and subsequent revision surgery, which is associated with high costs and less favourable outcomes [10]. The younger the patient who receives a total knee re-

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placement, the higher the risk of revision surgery is in his/her lifetime [11].

Guideline recommended non-surgical treatments are exercise, education about self-management strategies, weight reduction if indicated, painkiller prescription and insoles [5]. Albeit recommended, uptake of guideline recommended non-surgical treatments remains low in clinical practice. Less than 40% of knee osteoarthritis patients receive appropriate non-surgical care in the U.S. [12]. It is currently unknown what proportion of knee osteoarthritis patients receive guideline recommended non-surgical treatments in Switzerland. As of 2019, physiotherapists can be certified as GLA:D© therapists, a certification course that trains therapists in the delivery of guideline recommended non-surgical treatments [13]. By the end of 2022, around 700 therapists had completed this course. With more than 11,000 licensed physiotherapists in Switzerland [14], this is a small proportion and the need for such a certification course may be seen as evidence that the uptake of guideline recommended non-surgical treatments is still low in Switzerland.

A recent systematic review by Mazzei et al. [15] including 23 health economic evaluations concluded that guideline recommended non-surgical treatments are cost-effective and implementation should be encouraged. The authors commented that cost-effectiveness, from a healthcare perspective, may be underestimated if guideline recommended non-surgical treatments delay total knee replacement. Even though there is some evidence that guideline recommended non-surgical treatments can delay total knee replacement in eligible patients [16, 17], more research is needed to draw any firm conclusions. Yet, it seems plausible that the delay of total knee replacement through guideline recommended non-surgical treatments is possible and the cost-effectiveness may be even greater when analysed in the context of total knee replacement delay as this likely reduces the amount of revision surgeries needed [11].

Considering the potential effect of guideline recommended non-surgical treatments in delaying total knee replacement and the insufficient implementation of guideline recommended non-surgical treatments in the current model of care for knee osteoarthritis in Switzerland, the aim of this health economic evaluation was to answer the following research questions:

- Is a model of care optimised by the implementation of guideline recommended non-surgical treatments cost-effective from a Swiss statutory healthcare perspective?
- What is the effect of total knee replacement delay by guideline recommended non-surgical treatments on the cost-effectiveness?

Methods

Overview and model

We report this health economic evaluation according to the Consolidated Health Economic Evaluation Reporting Standards [18] and have constructed a Markov model following the recommendations of the International Society for Pharmacoeconomic and Outcome Research [19]. Effectiveness (expressed as quality-adjusted life years [QALYs]), treatment costs, and transition probabilities have been determined for two model of care consisting of surgical and non-surgical treatments for knee osteoarthritis: A) the current model of care in which non-surgical treatment primarily consists of painkillers and written advice and B) an optimised model of care in which guideline recommended non-surgical treatments are implemented.

We coded a state-transition Markov model in RStudio (Version 1.3.1093) [20]. Data manipulation and plots were realised using the “tidyverse” package (Version 1.3.0) [21]. The model represents the various states for patients with knee osteoarthritis in the healthcare system. A major advantage of using Markov modelling is that it encompasses the whole lifetime of each patient allowing us to implement delays with so called “tunnel states” [22]. The structure of the developed model is based on previously published studies [23–25].

Figure 1 depicts a detailed description of the model. We conducted the analysis from the statutory Swiss healthcare perspective. Outcomes were reported as incremental cost-effectiveness ratio which describes the additional costs per quality-adjusted life year gained. The cycle time was defined as one year with a time horizon of 70 years which is considered lifelong.

Based on a health economic evaluation conducted in the context of Switzerland [26], we decided to apply a discount rate of 3% to costs and health-utilities gained starting from the second year and a willingness to pay threshold of CHF 100,000.

No study protocol was registered or published.

Patient population

The population of interest were individuals at risk of developing symptomatic radiographic-confirmed knee osteoarthritis living in Switzerland aged 40 years in 2019. We chose this starting age because the prevalence of knee osteoarthritis in patients younger than 40 is very low [27]. Absolute population numbers were derived from the Swiss Federal Statistics database from 2019 [28].

Cost data

Because the statutory healthcare perspective was chosen for this health economic evaluation, only direct costs were considered while indirect costs and intangible costs were omitted. Cost data were calculated using the following formula: Cost = unit consumed x unit price (i.e., non-aggregated form). Costs were expressed in 2019 Swiss francs.

Non-surgical treatments for knee osteoarthritis are delivered in an outpatient setting. Outpatient costs are listed by the physician outpatient services catalogue, which is used for the reimbursement of individual statutory healthcare services in Switzerland [29]. Because of Swiss privacy legislation, it is not possible to link individual healthcare services to a diagnosis. Nevertheless, to estimate the costs attributed to outpatient treatments we contacted various clinical experts (orthopaedic surgeons, physicians, physiotherapists). The costs accumulated during the time individuals were successfully treated with non-surgical measures, reflected by the “Successful non-surgical treatment” state, were based on expert opinion.

Surgical treatments (total knee replacement and revision surgery) are delivered in an inpatient setting. Unlike outpatient treatments, inpatient reimbursement is regulated by "diagnosis related groups" (DRG). DRGs are classifications of specific case groups based on diagnoses and treatments. Reimbursements are paid as a flat rate depending on diagnosis, of which publicly accessible databases are available [30]. To separate costs related to total knee replacement versus revision surgery we used insurance claims provided by two health insurance providers, which together hold a market share of 14.4% (i.e., 1,226,535 individuals in Switzerland in 2019 [31]). DRG code I43C was used to calculate costs related to total knee replacement while revision surgery costs were retrieved through DRG codes I04A, I04B, I43A and I43B. We made assumptions regarding the cost incurring after total knee replacement and revision surgery, reflected by "Successful TKR" and "Successful revision" states. Table 1 provides an overview of the costs used in the model. A detailed description of the cost estimation can be found in Appendix 1.

Utility data

To represent utilities for successful non-surgical treatment, we used data from a randomised controlled trial (RCT) that reported data calculated for Denmark [32]. We decided to use data from this trial because it resembled the treatment regimens used in our models and Denmark, like Switzerland, is a western high-income country. In this trial, patients (n = 100) with symptomatic knee osteoarthritis and radiographic confirmed knee OA (Kellgren&Lawrence

Figure 1: Conceptualisation of the proposed Markov model visualising the current model of care and the proposed optimised model of care. The difference between current model of care and the optimised model of care is the addition of more extensive guideline recommended non-surgical treatments. By evaluating the cost-effectiveness of the whole model of care the dynamics between the surgical and non-surgical treatments can be investigated. In our scenario analysis, we analysed the effect a delay of total knee replacement (TKR) by guideline recommended non-surgical treatments by two and five years on the cost-effectiveness of the whole model of care. The delay of TKR is modelled by adding tunnel states after "Successful non-surgical care". For Switzerland a "willingness to pay" threshold of 100,000 CHF was considered. CHF: Swiss francs; KOA: knee osteoarthritis

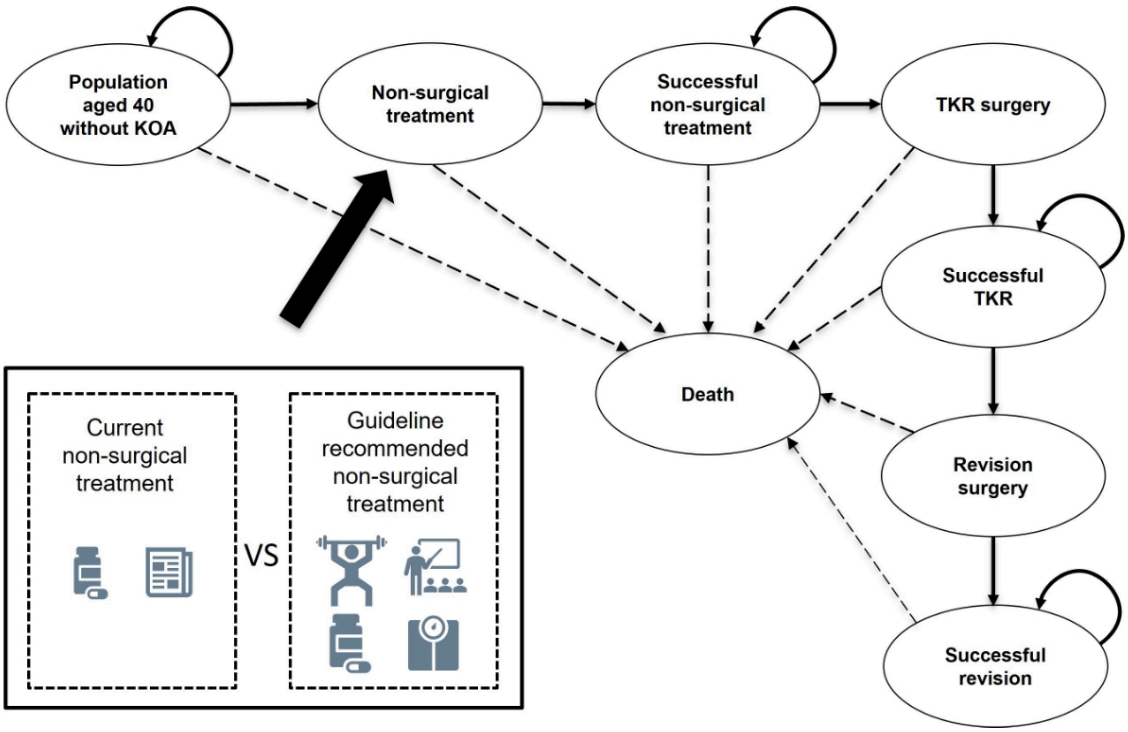


Table 1:
Overview of cost data used in the model. For both, optimised model of care and current model of care, clinical experts were contacted to make valuation assumptions. When available, data was drawn from health-insurance claims. Costs described under "Successful non-surgical treatment" reflect statutory healthcare spending that occurs in the state when patients are successfully managed with non-surgical care and are therefore lower than the intervention costs which only are applied for one year. All costs are occurring in one year and are expressed in 2019 Swiss francs (CHF).

State	Source	Current model of care	Source	Optimised model of care
Non-surgical treatment	Health insurance claims	CHF 222	Health insurance claims	CHF 1,209
Successful non-surgical treatment	Expert opinion	CHF 200	Expert opinion	CHF 200
TKR surgery	Health insurance claims	CHF 18,326 (SD = CHF 1,606, SE = CHF 46)	Health insurance claims	CHF 18,326 (SD = CHF 1,606, SE = CHF 46)
Successful TKR	Expert opinion	CHF 500	Expert opinion	CHF 500
Revision surgery	Health insurance claims	CHF 28,776 (SD = CHF 6,436, SE = CHF 536)	Health insurance claims	CHF 28,776 (SD = CHF 6,436, SE = CHF 536)
Successful revision	Expert opinion	CHF 500	Expert opinion	CHF 500

SD: standard deviation; SE: standard error; TKR: total knee replacement score ≥1) not eligible for total knee replacement were either randomised to current non-surgical care (painkiller prescription, written/oral advice) or guideline recommended non-surgical treatments (exercise, dietary intervention, insoles, painkillers, education classes). The proportion of women was 51% and mean age of the total sample was 66 years (SD 8.9 years). During the follow-up of 12 months, health utilities were assessed using the EuroQol 5-Dimensions 5-Levels (EQ5D-5L) questionnaire for both groups. At the end of the follow-up, health utility gains of the guideline recommended non-surgical treatments-group were higher (+0.125) compared to the usual care group (+0.091). We used these values for the "Successful non-surgical treatment" state for the current model of care and the optimised model of care, respectively, in our model.

For total knee replacement and revision surgery, another RCT from the same research group was used to extract health utility data for successful total knee replacement [16]. In this trial, patients (n = 100) eligible for total knee replacement (pain and Kellgren & Lawrence score ≥2) were either randomised to immediate total knee replacement or a period of guideline recommended non-surgical treatments with the option of total knee replacement at any time. The proportion of women was 62% and mean age of the total sample was 66.4 years (SD = 8.7). Health utilities were reported for both groups after a follow-up period of 24 months using the EQ5D-5L. Quality-adjusted life year values of the total knee replacement group after 12 months were extracted and imputed in the model as health utility value of the "Successful TKR" state.

The health utilities (using EQ5D-5L) for "Revision surgery" were derived from a study that gathered follow-up data of patients (n = 5,398) receiving revision surgery in a hospital in New York, USA [33]. During the year of surgery, we assumed patients to have baseline utilities as mobility is usually severely restricted during the first months after surgery. Table 2 depicts utility values used in the model.

Transition probabilities

The first state in our model accounts for all males and females living in Switzerland aged 40 years in 2019 without symptomatic knee osteoarthritis. Pooled global incidence for symptomatic radiographically confirmed knee osteoarthritis was reported as 0.02% per year in individuals aged over 20 years [27]. This incidence was used for all ages and for males and females. Using the incidence, the annual number of individuals making the transition from the general population to non-surgical treatment because of the development of knee osteoarthritis was calculated. It was assumed that persons with symptomatic knee osteoarthritis seek help from their physician and receive non-surgical care. The same transition probability for non-surgical treatment was used for current model of care and optimised model of care.

We calculated age-specific probabilities for the transition from the "Successful non-surgical treatment" state towards the "TKR surgery" state as follows:

(1) Define the number of persons living in Switzerland in 2019 by age group and gender.

(2) Establish the prevalence of symptomatic radiographically confirmed knee osteoarthritis by age group and gender for western Europe using data from the Global Burden of Disease Study [1].

(3) Estimate the number of persons living with symptomatic radiographically confirmed knee osteoarthritis by age group and gender by multiplication of population at risk with prevalence.

(4) Assess the number of total knee replacement in Switzerland in 2019 by age group and gender [34].

(5) Assess the probability for undergoing total knee replacement by dividing the number of TKR by estimated persons having symptomatic radiographically confirmed knee osteoarthritis:

number of total knee replacements 2019 / population 2019 × prevalence knee osteoarthritis

Steps 1 to 5 described above allowed us to calculate the age and gender specific proportion of individuals with symptomatic knee osteoarthritis who received total knee replacement in Switzerland in 2019. These proportions were then used as model input. The obtained transition probabilities are in line with incidence rates for total knee replacements published elsewhere [35]. See Appendix 2 for more detail.

We used preliminary data from the "Swiss National Hip and Knee Surgery" database (SIRIS) [34] to calculate age-specific annual probabilities for the transition from "Successful TKR" to "Revision surgery". Currently, cumulative revision risks for a follow-up period of 8 years are available, which we used for our calculations. The same annual revision probability was used for optimised model of care and current model of care model calculations. See Appendix 3 for more detail.

For the transition probability from any state to death, crude age-specific mortality rates in Switzerland for 2019 were calculated using population data from the Federal Statistical Office [28] according to the following formula:

Table 2:
Overview of utility values used in the model. The utility for successful non-surgical treatment differs between current model of care and optimised model of care. In the optimised model of care, guideline recommended non-surgical treatments results in a higher treatment effect [32]. All other utility values remain the same for the current model of care and the optimised model of care.

State	Current model of care	Optimised model of care
Non-surgical treatment [32]	0.658	0.658
Successful non-surgical treatment[32]	+0.091 (SD = 0.158, SE = 0.025)	+0.125 (SD = 0.108, SE = 0.017)
TKR surgery	0.658	0.658
Successful TKR [16]	+0.22 (SD = 0.151, SE = 0.024)	+0.22 (SD = 0.151, SE = 0.024)
Revision surgery	0.658	0.658
Successful revision [33]	+0.102	+0.102

SD: standard deviation; SE: standard error; TKR: total knee replacement *deaths in age group (2019) / persons in age group (2019)*

See Appendix 1 for more detail.

Table 3 provides an overview of all transition probabilities used in the model.

Scenario analysis

In this health economic evaluation three different scenarios were defined. Scenario one is described as “base case”. In this scenario the incremental cost-effectiveness ratio for optimised model of care vs current model of care without delay of total knee replacement has been calculated. The second and third scenario were calculated under the assumption that guideline recommended non-surgical treatments can delay total knee replacement by two or by five years, respectively.

Sensitivity analysis

We evaluated model robustness by probabilistic sensitivity analysis (PSA) with 10,000 iterations on cost and health utility parameters. We used beta distribution for health utilities and transition probabilities because the imputed values were not close to zero and calculated by the method of moments [36]. For cost data we used gamma distributions, as recommended by guidelines [36]. PSA was conducted for all three proposed scenarios.

The developed model has been validated technically and clinically. To ensure technical validity, two differently coded models within RStudio were used to compare the outcomes and the coded model was checked for errors by the last author. Clinical validation was performed by a primary care physician, an orthopaedic surgeon and a physiotherapist specialised in knee osteoarthritis treatments.

Results

Calculations from the model for the current model of care resulted in CHF 4,465 cost per person and 16.92 quality-adjusted life years per person over a period of 70 years. Calculations for optimised model of care with no delay of total knee replacement resulted in CHF 4,806 cost per person and 17.07 QALY per person. Therefore, the “base case” scenario yielded higher costs (+CHF 341) and higher QALY gains (+0.155) over 70 years resulting in an incremental cost-effectiveness ratio of CHF 2,203 per additional QALY gained. This incremental cost-effectiveness ratio falls in the north-eastern quadrant of the cost-effectiveness plane (figure 2).

In the “two-year delay” scenario cost per person was CHF 4,451 and QUALY per person was 17.07 calculated over a period of 70 years. In comparison to the current model of care, cost reduction was CHF –14 and quality-adjusted life year gain per person was +0.13. The incremental cost-effectiveness ratio of the “two-year delay” equals to CHF –101 per additional QALY gained and dominates current model of care (figure 2).

In the “five-year delay” scenario cost per person was CHF 3,964 and quality-adjusted life years per person was 17.03

Figure 2: Cost-effectiveness plane showing the incremental cost-effectiveness ratio for all three scenarios and the results of the probabilistic sensitivity analysis (PSA). The incremental cost-effectiveness ratio for the “base case” scenario equals to 2,203 CHF per quality-adjusted life year (QALY). The other scenarios simulating a “two-year delay” and “five-year delay” yield an incremental cost-effectiveness ratio of –101 CHF per QALY and –4,267 CHF per QALY, respectively. The PSA was run with 10,000 iterations. Cost and utility data was altered according to its standard errors. CHF: Swiss francs

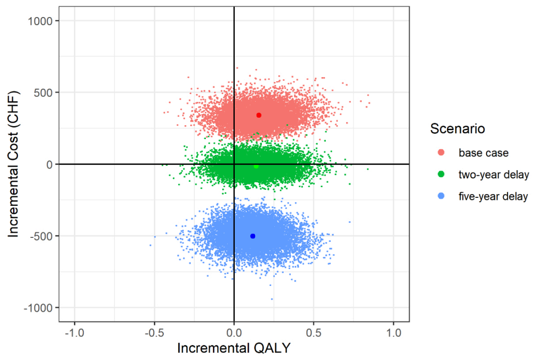


Table 3:
Overview of the transition probabilities used in the model. Age-specific probabilities were used if available.

Probabilities			Annual probability OMOC/CMOC
Population aged 40 without knee osteoarthritis	To non-surgical treatment [27]		0.02
	To death [28]		Age-specific mortality CH 2019
Successful non-surgical treatment	To total knee replacement [28, 34]	40–44	0.004
		45–54	0.008
		55–64	0.025
		65–74	0.049
		75–84	0.057
		85+	0.022
	To death [28]		Age-specific mortality CH 2019
Successful TKR	To revision [34]	40–44	0.021
		45–55	0.015625
		55–64	0.011625
		65–74	0.008125
		75–84	0.005375
		85+	0.0035
	To death [28]		Age-specific mortality CH 2019
Successful revision	To death [28]		Age-specific mortality CH 2019

CH: Switzerland; CMOC: current model of care; OMOC: optimised model of care; TKR: total knee replacement calculated over a period of 70 years. Comparing the "five-year delay" scenario with current model of care, a cost reduction of CHF –501 and a QALY gain per person of +0.12 was found. The corresponding incremental cost-effectiveness ratio of the "five-year delay scenario" equals extra CHF –4,267 per additional QALY gained when compared to the current model of care scenario (i.e., "dominant") and falls in the south-eastern quadrant of the cost-effectiveness plane (Figure 2). The computed main results are reported in table 4.

Figure 2 presents the results of the PSA (10,000 iterations for each scenario) in a cost-effectiveness plane for all scenarios. Of the simulated incremental cost-effectiveness ratios of the "base case" scenario 15.8% fell into the south-eastern and 59.2% in the north-eastern quadrant. For the "two-year delay" scenario 27.3% fell into the south-eastern and 45.1% in the north-eastern quadrant, while for the "five-year delay" scenario 79.2% fell in the south-eastern and 0% in the north-eastern quadrant.

The modelled delay of total knee replacement by two and five years resulted in a reduction of revision surgeries by 18% and 36%, respectively. Figure 3 depicts the number of revision surgeries for each scenario.

In the cost-effectiveness acceptability analysis, we assumed a "willingness to pay" threshold of CHF 100,000 for Switzerland [26]. Based on this threshold, the probability for cost-effectiveness with the "base case" scenario equals 0.75, for the "two-year delay" scenario the probability is 0.72, and the probability is 0.79 for the "five-year delay" scenario (figure 4). All input parameters that were included in the probabilistic sensitivity analysis are reported in table 5.

According to our model the lifetime probability to develop radiographically confirmed symptomatic knee osteoarthritis was 57% and the lifetime probability for total knee replacement after diagnosed knee osteoarthritis was 55.7%.

Discussion

This Markov modelling study is, to the best of our knowledge, the first to estimate the cost-effectiveness of a com-

Figure 3: Number of revision surgeries for each scenario and model cycle. The "two-year delay" scenario and "five-year delay" scenario resulted in a reduction of revision surgeries by 18% and 36% respectively when compared to the "base case scenario".

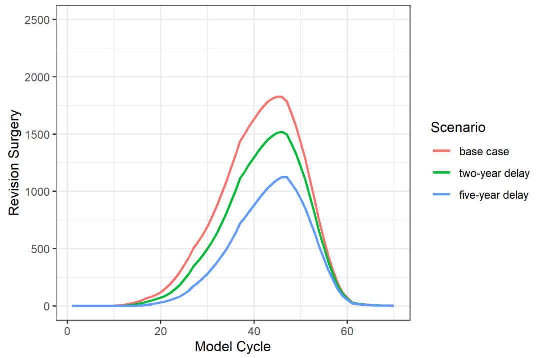


Figure 4: Cost-effectiveness acceptability curve of the three analysed scenarios.QALY: quality-adjusted life year

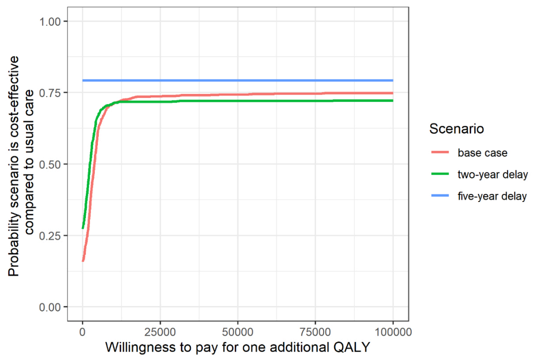


Table 4:
Overview of the calculated results for the three proposed scenarios. Current model of care versus optimised model of care without delay, with two-year delay and with five-year delay of TKR. Incremental cost-effectiveness ratio, cost and QALY are reported per person and over the modelling time horizon of 70 years.

Model	Per person cost	Per person QALY	
Current model of care	4,465	16.92	
OMOC no delay	4,806	17.07	
OMOC two-year delay	4,451	17.06	
OMOC five-year delay	3,964	17.03	
Scenario	**ICER**	**Cost delta**	**QALY delta**
Base case (CMOC vs OMOC no delay)	2,203	341	0.155
Two-year delay (CMOC vs OMOC two-year delay)	–101	–14	0.134
Five-year delay (CMOC vs OMOC five-year delay)	–4,267	–501	0.118

CMOC: current model of care; OMOC: optimised model of care; TKR: total knee replacement; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year

Table 5:
Input parameters included in the probabilistic sensitivity analysis (PSA) with the distribution type applied.

			SD / SE	Distribution
Cost (CHF)	TKR surgery	18,326	1,606 / 46	γ
	Revision surgery	28,776	6,436 / 536	γ
Utility	Successful non-surgical treatment	CMOC 0.749	CMOC 0.158 / 0.0246	β
		OMOC 0.783	OMOC 0.108 / 0.0168	β
	Successful TKR	0.878	0.151 / 0.023	β
Transition probability	Population aged 40 without knee osteoarthritis			
	To non-surgical treatment	0.02	SE = 0.00510	β

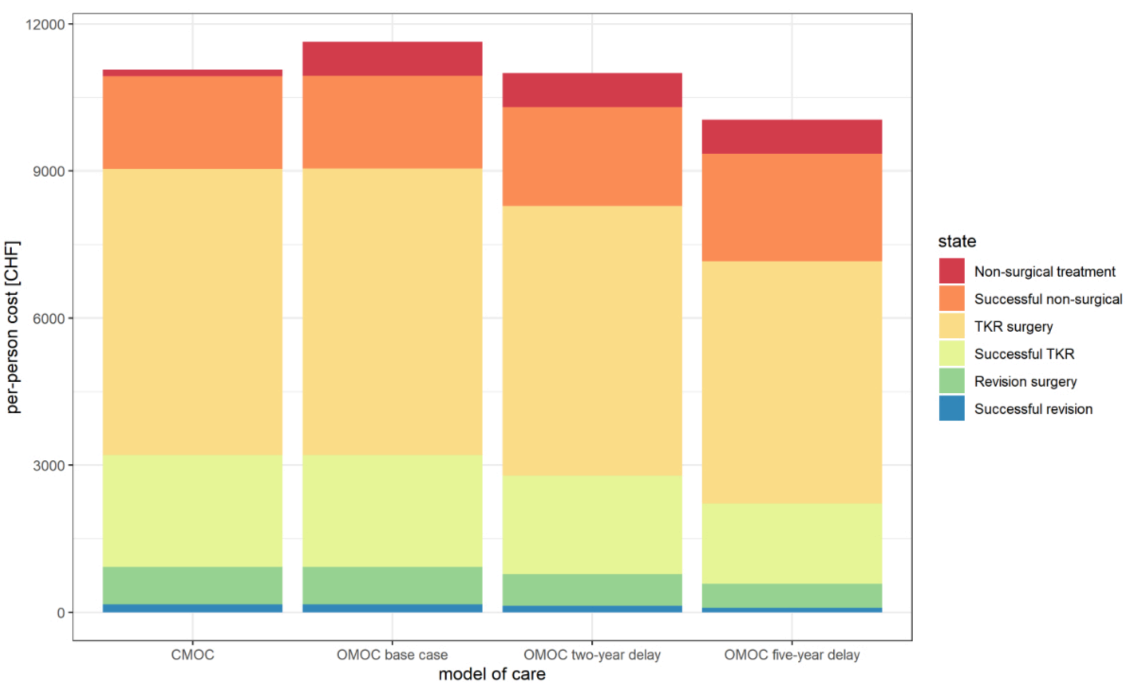
CHF: Swiss francs; CMOC: current model of care; OMOC: optimised model of care; SD: standard deviation; SE: standard error; TKR: total knee replacement plete model of care involving both non-surgical and surgical treatments for knee osteoarthritis. We conducted model calculations for three different scenarios. The first scenario represented the implementation of guideline recommended non-surgical treatments with no delay on total knee replacement. The second and third scenarios represented the implementation of guideline recommended non-surgical treatments with a delay of total knee replacement by two and five years, respectively. The incremental cost-effectiveness ratio for the "base case" (current model of care versus optimised model of care with no delay of total knee replacement) was extra CHF 2,203 per additional quality-adjusted life year gained, which is highly cost-effective considering a "willingness to pay" threshold of CHF 100,000 per QALY in Switzerland [26]. The "two-year delay" and the "five-year delay" scenario both resulted in dominant incremental cost-effectiveness ratios and had a cost-saving effect. In all three scenarios, the incremental cost-effectiveness ratios were calculated over 70 years from the Swiss statutory healthcare perspective and dominated the current model of care. The achieved QALY gains over the modelling period are in line with other studies using a lifetime horizon [25].

Regarding undiscounted costs per person for each scenario, most costs were due to total knee replacement surgery (figure 5). This is explained by the high procedure costs. Another important share of costs was related to the "Successful non-surgical" state. Despite these costs being low, many individuals remain in this state for a long time accumulating costs. The effect of total knee replacement delay is most prominently reflected in the costs caused by "Revision surgery". These costs were reduced by 55% with a delay of total knee replacement of five years when compared to current model of care.

The observed reduction of revision surgeries by 18% in the "two-year delay" and 36% in the "five-year delay" scenario is due the fact that revision risk is cumulative and consequently becomes higher the longer the implant is in use, which rises in parallel with a younger age of implantation [11]. Our calculated reduction is supported by the results of Gademan et al. [39], who reported a reduction of revision surgeries by 17% when modelling the delay of total knee replacement by five years in individuals under 75 using joint registry data from the Netherlands. The difference to our results may be explained by higher total knee replacement rates (+58% in Switzerland versus the Netherlands [40]) and the assumption in this present health economic evaluation was that total knee replacement was delayed for all ages. There is great consent that the need for revision surgery should be kept at the lowest possible rate as it is considered an expensive and challenging procedure with often unreproducible results [41]. Revision rates are therefore frequently used to determine the outcome of total knee replacement [42].

The modelled lifetime probability to develop radiographically confirmed symptomatic knee osteoarthritis (57%) is somewhat higher than reported in the study of Murphy et al. using data from a cohort of 3,068 U.S. participants reporting a lifetime probability of 44.7% (95% CI 40%–49%) [37]. The probability for total knee replacement after diagnosed knee osteoarthritis in our model was 55.7%. This result is in line with the study of Weinstein et al. who reported 52.2% for males and 50.6% for females using the Osteoarthritis Policy Model, a validated comput-

Figure 5: Costs per person (undiscounted) for each scenario and the current model of care (CMOC). The optimised model of care calculated under "base case" conditions, meaning with no delay of total knee replacement (TKR), results in the highest overall costs (CHF 11,634). This is due the more intensive non-surgical treatment costs. The optimised model of care calculated with a delay of TKR by two years results in lower costs per person (CHF 10,997) and the optimised model of care calculated with a delay of TKR by five years reduces the total costs even further (CHF 10,044). The reduction of costs by these two scenarios can be explained because of less TKR and revision surgeries performed. CHF: Swiss francs; TKR: total knee replacement



er simulation model of knee osteoarthritis based on U.S. data [38].

Our findings suggest that an investment in more intensive, guideline recommended non-surgical treatments is likely to be cost- effective in the context of the Swiss statutory healthcare system. If guideline recommended non-surgical treatments lead to a delay of total knee replacement, for which robust empirical evidence is still lacking, it may prevent a significant amount of revision surgeries and therefore has the potential to enhance total knee replacement outcomes and save costs. The developed model shows that non-surgical and surgical care should be delivered in an integrated manner with the aim to select patients for total knee replacement only after appropriate non-surgical care has failed. As clear indications for total knee replacement are still missing and the decision to undergo surgery is mostly influenced by the patient's willingness [43, 44], it is vital to provide guideline recommended non-surgical treatments before total knee replacement is considered.

The reported results must be interpreted with caution because modelling studies always have limitations. First, we did not account for costs that are associated with inpatient rehabilitation after total knee replacement. Not accounting for these costs may have underestimated the cost-effectiveness of guideline recommended non-surgical treatments, as some studies suggest that up to 50% are referred to inpatient rehabilitation after total knee replacement [45].

Second, we did not adjust our model for patients who had already received total knee replacement and were therefore cured from knee osteoarthritis. This may have led to an overestimation of the performed total knee replacement surgeries in our model and therefore overestimated the cost-effectiveness of guideline recommended non-surgical treatments.

Third, we assumed that total knee replacement is the only available surgical treatment option. Nevertheless, in 2019, 2,908 partial knee replacements were implanted in Switzerland for the treatment of knee osteoarthritis (total knee replacement 15,378, partial knee replacements 2,908) and its usage is currently rising [34]. In addition to partial knee replacements, high tibial osteotomy is also a commonly performed surgical option for which we did not account for.

Fourth, other Markov models included re-revision surgery, for which we did not account for [46]. The assumption that all revisions are successful (meaning no re-revision is needed) is very conservative. In fact, re-revision surgery after revision surgery are six times more likely to be needed than revision surgery after total knee replacement [41]. Again, the lack of accounting for re-revision surgery is likely to have underestimated cost-effectiveness of guideline recommended non-surgical treatments.

Fifth, conclusions drawn from modelling studies need to be interpreted with caution. A narrow perspective was taken in this analysis and utility data from Denmark and the U.S. were used which were not degraded with rising age. This limits the model's generalisability. To confirm our results, long-term data in the context of the Swiss statutory healthcare system is needed. Like the Swiss Implant Registry, which provides reliable data regarding total knee replacement and revision surgery, a national health record or an extension of this registry would be needed to provide data on how patients move through the healthcare system after they have been diagnosed with knee osteoarthritis.

Conclusion

According to this Markov model, the implementation of guideline recommended non-surgical treatments in Switzerland would likely be cost-effective from a statutory healthcare perspective. If implementing guideline recommended non-surgical treatments leads to delaying total knee replacement by two or five years, we would achieve a cost-saving effect and a reduction of needed revision surgeries by 18% and 36%, respectively.

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Potential competing interests

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Appendices: Supplementary data

The Appendices 1-4 are available for download as separate files at https://doi.org/10.57187/smw.2023.40059.