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Original Research

Individualized metal implants for focal cartilage lesions in the knee can be cost-effective: A simulation on 47-year-old in a Swedish setting

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ABSTRACT

Objectives: In the aging population, the knee is the joint most commonly causing impaired function and incapacity. While definite treatment by prosthetic replacement is often performed late, symptomatic knee cartilage lesions cause much suffering also in younger ages. Early intervention could, therefore, be instituted at an early stage to the benefit of both patients and society.

Small, metal surface, resurfacing implants have been tested with promising results. A system that features patient-specific implants and surgical instruments shows good clinical results and favorable survival rates. This study aims to assess the cost utility of this metal device compared with microfracture (MFX), being the standard procedure in Sweden.

Methods: We constructed a simulation model in Excel. In the model, a cohort of 47-year-old patients (which is the mean age of patients treated with the metal implant) with symptomatic knee cartilage lesions received either MFX or metal implantation. Outcomes for the cohort were simulated over 40 years, such as in a previously published model based on MFX, and sensitivity analyses (deterministic and probabilistic) of the results were undertaken. Data on transition probabilities, costs, and quality of life were taken from clinical data, published literature, and official price lists. Only direct medical costs were included.

Results: Results from the analysis showed that the metal device is a cost-effective treatment strategy compared with MFX. The incremental cost-effectiveness ratio (ICER) reached acceptable levels at ~5 years postoperatively. Over the full-time horizon of 40 years, the metal device was cost saving with concomitant gains in quality-adjusted life years (QALYs), translating to a dominant treatment strategy. Results were robust according to sensitivity analysis with the initial success rate of up to three years for both metal and MFX having the largest impact.

Conclusions: A metal implant may be a cost-effective treatment alternative for patients in their 40's when compared to MFX in a Swedish setting.

Level of evidence: 5 [1].

What are the new findings?

- An assessment of cost-effectiveness for a patient-specific metal implant is presented to aid decision-making.
- Individualized implants carry a higher initial cost but result in fewer revisions than microfracture, which is still the golden standard in many settings.
- Consequently, although initially more costly, patient-specific implants can be cost-effective for patients in their 40's within a few years when compared with microfracture, as well as a dominant strategy over a lifelong time horizon (better outcome to a lower cost).

Introduction

Knee joint osteoarthritis (OA) is emerging as one of the most prevalent causes of invalidity in the aging population. Definite treatment of

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knee OA is joint replacement after many years of progressively increasing pain and malfunction. This means suffering for the individual and costs for society, with a projected >5-fold increase in the number of knee replacements within 20 years [2]. Attempts for interventions at an earlier stage are well founded.

Evidence is accumulating that focal lesions of the femoral cartilage are the forebears of OA [3,4]. Initial small, circumscriptive lesions in the articular cartilage, often at the apex of the medial femoral condyle [3], progress in a centrifugal process with deterioration first of the affected compartment and later destroying the entire joint [4]. These focal lesions have attracted a huge amount of research and development in recent years. Flaps of periosteum or perichondrium, mosaicplasty Osteochondral Autograft Transfer System (OATS), as well as various cellular treatments by autogenous chondrocyte implantation (ACI), with or without augmentation with membranes or scaffolds, have met with some success, but none has become universally accepted in Sweden. Luring subchondral cells to migrate up into a cartilage lesion by microfracturing (MFX) is a time-honored principal method introduced already in the 1960's. The subchondral bone plate is penetrated by multiple small holes so that metaphyseal multipotent cells can migrate up and fill the chondral defect. The method was further refined by Steadman who devised a complete protocol including also a comprehensive postoperative rehabilitation program [5]. Despite recent findings that the filling, mostly fibrous tissue has rather poor wear characteristics [6], which has triggered a recent challenge [7], and microfracture is still a method of choice in Sweden. Microfracturing is quick, inexpensive, and can be performed "by the way" during an arthroscopy.

Small, hard material, surface replacing implants have appeared in the last decade [8]. Good clinical results and low revision numbers have been shown in some reports [13,14].

The long-term disease process of OA is reflected by considerable costs for society, and attempts at calculating the cost-effectiveness of different treatment strategies have been made [9,10].

The objective of the current study was to assess the cost utility from a Swedish health care perspective, of a patient-specific metal implant system (Episurf Medical AB, Sweden). It was hypothesized that such a metal implant may compare favorably with microfracturing.

Methods

Model structure

Based on a previously published model by Gerlier et al., comparing MFX to ACI [10], a decision tree model was constructed in Microsoft Excel, simulating the course over 40 years for a cohort of 47-year-old patients with symptomatic knee cartilage lesions. The model was modified to reflect the comparison of a metal device to MFX and adapted to the Swedish setting. This metal device is indicated for focal lesions up to a size of approximately 7.5 cm^2 in patients aged ≥30 years.

The model was divided into two parts, one describing the initial and mid-term effects on knee-related pain and mobility, and the other describing long-term effects including the eventual development of OA after 15 years. After OA, the model considers the need for total knee replacement (TKR) after 20 years and eventual need for TKR revision either directly (in case of TKR failure) or 15 years after first TKR [10]. The inclusion of these events is in line with Swedish clinical practice. In the model, patients were initially undergoing either MFX or metal implantation. The result of the initial intervention will determine what further events are possible and the probabilities for each. For patients where the metal device is unsuccessful, the most clinically relevant choice of reoperation is unicompartmental knee arthroplasty (UKA). For MFX failures, repeated MFX could be an option, despite poor results [11,12], but to reduce model complexity, we conservatively assume UKA will be used as reoperation also for MFX failures. The model includes a risk of death each year, which is based on age-standardized mortality for Sweden.

Results were expressed in terms of costs and quality-adjusted life years (QALYs) and discounted by 3% per year, according to Swedish health technology assessment guidelines. The model structure is presented in Fig. 1, including baseline assumptions on transition probabilities.

Data on clinical efficacy

Success rates and data on disease development after intervention were collected from the literature.

After the initial intervention, patients in both arms can be either successful or non-successful, the latter including both revised patients and non-responders. Non-responders are defined as patients not showing any improvement in aggregated Knee Injury and Osteoarthritis Outcome Score (KOOS) from baseline.

Patients in both arms are first evaluated at three years after the initial intervention. Patients defined as non-successful at this time include both crude revision rates as well as patients defined as non-responders.

For the metal arm, a crude revision rate of 2.3% has been reported [13] over seven years of clinical use. In addition, the proportion of non-responders (defined as change in aggregated KOOS<0 in a cohort of 75 cases) at two-year follow up was found to be 17% [14]. To include both these aspects in the model, 20% of metal patients were conservatively assumed to be non-successful at three years.

For data on the initial success rate for MFX, a literature review focused on MFX of the knee and long-term outcomes was performed. The search yielded 373 hits that were reviewed for relevance for the current analysis. Key factors for inclusion were relevant patient population (suitable age and from Europe/US), and relevant outcomes reported at three years after surgery. Full details on the search terms, paper exclusion, and other details are provided in Appendix A supplemental material.

Four relevant papers [15–18] were identified, and a weighted average based on the patient population sizes gave a mean probability of 27% for unsuccessful intervention at three years. As for the metal arm, a proportion of patients treated with MFX will be designated as non-responders, i.e., no increase in aggregated KOOS (delta-KOOS≤0). For the MFX arm, we assume the proportion of non-responders to be equal to that of metal (17%). Combining these numbers results in 44% of the MFX patients being unsuccessful after three years. The proportion of non-responders used is supported by Steadman et al., who reported 20% non-responders, excluding revisions for patients undergoing MFX [19].

Even after a successful intervention, patients may experience long-term problems. After MFX, there is an ongoing deterioration and in a long-term study as much as 75% were revised after 15 years [16]. Based on the previous model providing the framework for this analysis [10], no additional revisions are considered during years 3–15 for patients who are considered successful at three years. Instead, we use reported long-term revision data for MFX as a proxy for the proportion of patients experiencing long-term problems, eventually leading to the development of OA. Two of the papers identified in the literature search [15,16] presented data on long-term revision rates and a weighted average of these results showed that 30% of initially successful patients had long-term problems up to 15 years after MFX.

For the metal implant, the situation can be expected to be different. Studies on a mini-metal device with standardized curvatures have shown high revision rates in some studies [20,21], but non-revised cases show little evidence of knee deterioration, and excellent results after 12 years were reported in two cases [22]. In a series of 64 such first-generation cases, followed for up to ten years, revisions were frequent (42%), but there were no revisions after seven years [23].

For the current metal device, 14 known revisions in 612 performed cases for a crude revision rate of 2.3% after seven years were reported [13]. Also for this series, the revision curve flattened, with little clinical deterioration at 75 months [13]. Hence, for metal resurfacing implants, available data support the notion that failing cases fail rather fast, and once the

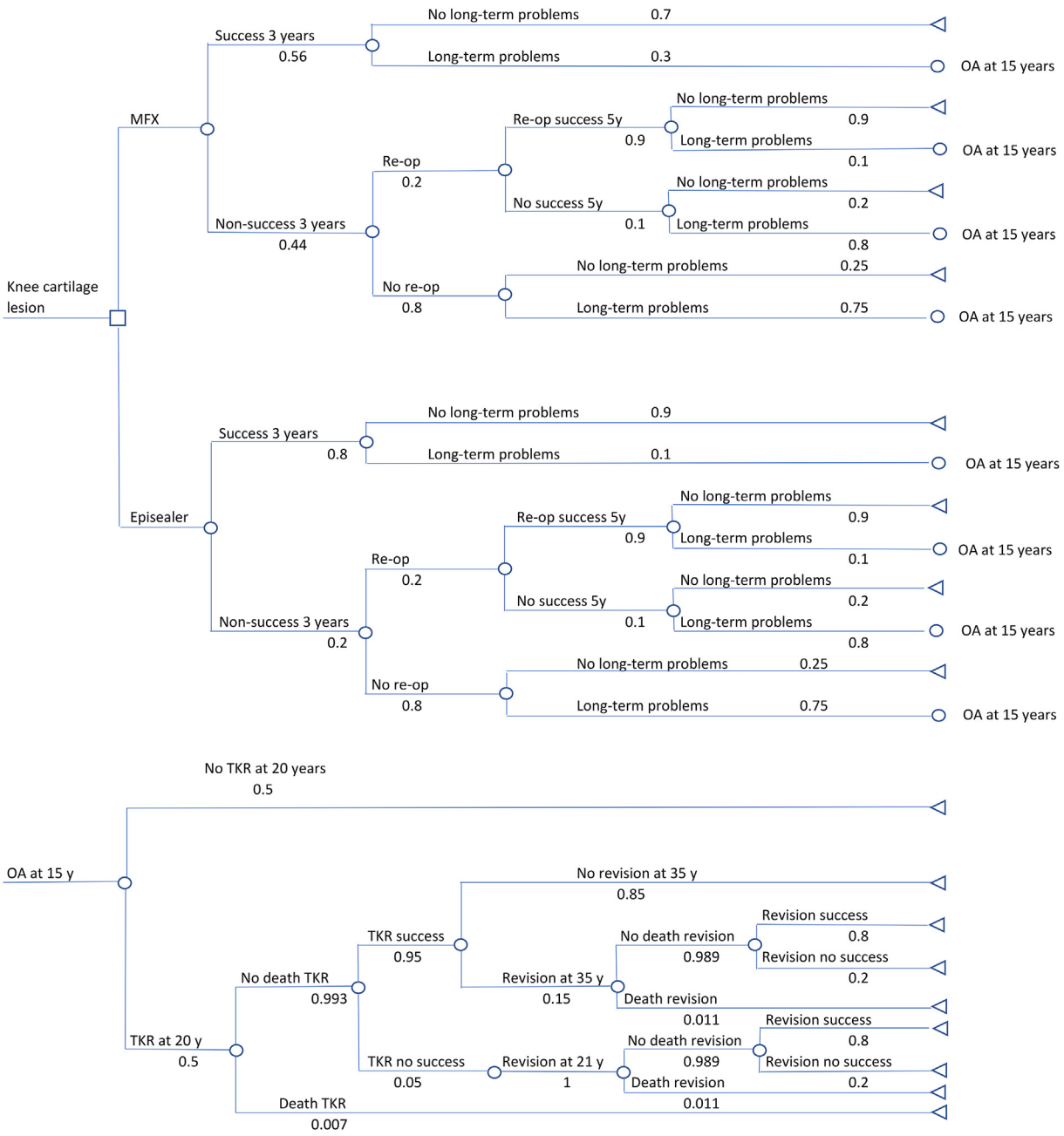

Fig. 1. Model structure and transition probabilities for treatment with MFX and metal, respectively.

failures are gone, the remainders may stay well and last a very long time. Data for the current metal implant after five years show that no further deterioration has occurred [24]. For the model analysis, we have assumed that 10% of the successful metal implants will experience long-term problems at 15 years. This assumption was tested in a scenario analysis.

Most non-successful cases are not revised, at least not in the short term. The preoperative level of life quality, KOOS QoL [14], is such that patients in both study arms usually choose to cope rather than venture another large operation like a TKR. Also, non-success generally refers to patients neither experiencing improvement nor worsening of symptoms. In the short term (<5 years) we have, in line with previous reports [14–18,25], assumed 20% incidence of reoperation following non-success for both arms. For both arms, it is assumed that revision is UKA or TKR, and that the results are similar to primary procedures. Both UKA and TKR outcomes are well documented. From the Swedish Knee Registry, it is known that about 10% of a mixed UKA/TKR cohort will be revised after ten years [26].

For patients where the initial intervention (metal or MFX) was unsuccessful and where no reoperation was conducted, no further intervention is considered during the first 15 years of the model. The probabilities for long-term problems after unsuccessful intervention and no reoperation for the two interventions in the model were set to 75% for both arms. Data on probabilities after OA at 15 years were based on the original model [10] and data from the Swedish Knee Registry [16,26]. A summary of input parameters and relevant sources is provided in Table 1.

Data on utility scores

Utility scores, i.e., the quality of life associated with different states and outcomes, are summarized in Table 2. These were derived from a relevant patient population using the SF-36 questionnaire [10]. After a successful procedure, irrespectively of whether after MFX, metal, or UKA, patients are assumed to have the same utility, corresponding to good knee status. Utility for patients with no long-term problems was assumed to be the same as for

Table 1
Probabilities used in the model (given as percent).

Model parameter	MFX	Metal	Source
Success rate of initial intervention at three years	56	80	[13–18,25]
Long-term problems (−15 years) after successful intervention	30	10	Based on assumption [15,16]
Reoperation (UKA) after unsuccessful initial intervention	20	20	[14–18,25]
Success rate of UKA	90	90	[26]
Long-term problems after successful UKA	10	10	Based on assumption [26]
Long-term problems after unsuccessful UKA	80	80	Based on assumption [26]
Long-term problems after unsuccessful initial intervention and no UKA	75	75	Based on assumption [10]
TKR (at 20 years) if developed OA	50	50	[10,26]
TKR revision one year after a failed TKR	100	100	[10,26]
TKR revision 15 years after successful TKR	15	15	[10,26]
Success rate of TKR	95	95	[10,26]
Success rate of TKR revision	80	80	[10,26]
Death during TKR	0.7	0.7	[10,26]
Death during TKR revision	1.1	1.1	[10,26]

good knee status. Patients with unsuccessful interventions (irrespectively of MFX, metal, or UKA) or long-term problems were assigned the utility of poor knee status. The utility was age adjusted using data on the Swedish population health-related quality of life [27]. The adjustment was performed using a multiplicative approach, where the mean reported utility for the model starting age (47 years) was set to 1.

Data on costs

Data on costs used in the model were calculated based on official Swedish price lists [28,29] and are displayed in Table 3. Rehabilitation for MFX is based on the description by Steadman [5]. The number of physiotherapy (PT) visits differs between the groups and is poorly reported. This is due to the fact that various rehab activities over a three-month period are inherent to MFX [5]. Rehab after metal surgery is limited to normal postoperative routines after an arthrotomy. Costs collected in Swedish Crowns (SEK) were converted to Euros (EUR, €) using the average conversion rate in 2021 (1 EUR = 10.49 SEK).

Sensitivity analysis

To evaluate the effects of parameter uncertainties on outcomes, it is necessary to perform deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA). For DSA, each of the parameters is varied separately to identify the main drivers in the model, while PSA evaluates the underlying uncertainty in the model. The parameters included in the DSA were varied by ± 20%, except for utility values where high and low boundaries were implemented such that a worse health state could never have a higher utility than a better health state. The probabilistic analysis uses information on model parameter uncertainties (beta distributions were used for probabilities, and gamma distributions were used for costs). Input values and results for the PSA are summarized in Appendix A supplemental material (Table A4, Fig. A3).

Results

Results of the analyses are presented in terms of costs, gained QALYs, and incremental cost-effectiveness ratio (ICER). In the base case analysis, the total cost for the metal device was €11,424, while the total cost for MFX was €12,182, resulting in cost savings of €758 over a forty-year time horizon. The total QALYs were 16.063 for metal and 15.277 for MFX, an incremental gain of 0.786 QALY resulting in metal-dominating MFX.

Table 2
Utility scores used in the model.

State/outcome	Utility score
Post-operatively (first year)	0.76
Good knee status	0.817
Poor knee status	0.691
OA	0.52
After successful TKR	0.68

As can be expected, initially, the ICER is high but decline over time due to cost savings and accumulated QALYs (Fig. 2A). There is no formal willingness to pay (WTP) for a QALY in Sweden, and the threshold is flexible and mainly guided by disease severity. For knee lesions, a reasonable threshold is assumed to be around SEK 200,000 (~€19,000). With that benchmark, Metal is cost-effective from five years post-surgery and a dominant treatment strategy over a life-long time horizon (i.e., cost-saving and better clinical outcome). For clarity, only a time horizon of ten years is shown in the figure.

DSA showed that the results were robust. To account for the dominance in the analysis, a net monetary benefit (NMB) approach was taken to include effects on both costs and QALYs (Fig. 2B). For this analysis, the same benchmark regarding acceptable WTP for a QALY of SEK 200,000 (~€19,000) was used. The main drivers of the model results are the success rates for metal and MFX, followed by the utility values for good and poor knee status. Specific DSA results for costs and QALYs, respectively, are shown in Appendix A supplemental material (Fig. A2).

Several scenario analyses were undertaken to further assess the robustness of the results

Firstly, the impact of a higher proportion of patients experiencing long-term problems after successful metal implantation was investigated. Here, the proportion of patients with long-term problems was conservatively set to 30% instead of the 10% used in the base case. In this scenario analysis, metal implantation resulted in an incremental cost of €1,345, a QALY gain of 0.307, and an ICER of €4385. Like the base case analysis, the ICER fell below the threshold for cost-effectiveness after less than five years.

Secondly, a scenario analysis using a higher value for the utility after successful TKR (0.79) was performed. Here, the QALY gain was reduced to 0.716, while the cost-saving was unchanged, maintaining the dominant result.

Thirdly, the impact of different sources used for MFX success rate was assessed. Using the study by van Lauwe et al. [17] resulted in an ICER €332, while the corresponding number using the Knutsen paper [15] was €569. For the two more recent and larger studies [16,18], the results remained dominant.

Discussion

We found a favorable cost utility situation for the metal device over a 40-year time span, as compared to MFX. Considering the fact that the underlying lesions often are of traumatic etiology, occurring early in life (25–30 years of age), a long time span is relevant for the analysis and has previously been applied for the same context [10]. However, few modern

Table 3
Costs used in the model.

Item or intervention	Cost (EUR)	Comment	Source or rationale
PT visit	76	Visits to other health care personnel	[3,29]
Health care visit	172	Physician visit	[3,29]
Drugs (per year)	238	Assumption based on average dosing.	
Microfracture intervention	2229	DRG H12O, other knee surgery	[4,28]
Metal intervention	3380	DRG H10O, larger knee surgery	[4,28]
Metal device	2861		Episurf
UKA intervention	7806	DRG H04N, primary knee prothesis	[4,28]
TKR intervention	7806	DRG H04N, primary knee prothesis	[4,28]
TKR revision	15,599	DRG H03N, secondary knee prothesis	[4,28]
States			
Microfracture	3755	Incl. 20 PT visits	
Metal	6623	Incl. device and 5 PT visits	
Annual cost after successful intervention	410	1 health care visit + drugs	Identical for MFX, Metal, and UKA
Annual cost after unsuccessful intervention	753	3 health care visits + drugs	Identical for MFX, Metal, and UKA
Annual cost for no LT problems	0	No visits or drugs	
Annual cost for LT problems	753	3 health care visits + drugs	
Annual cost for OA	410	1 health care visit + drugs	
TKR cost	11,620	Incl. 50 PT visits	
Annual cost after successful TKR	410	1 health care visit + drugs	
TKR revision	19,413	Incl. 50 PT visits	

Abbreviations: LT, long-term; PT, physiotherapist.

medical technologies have been in use for 40 years, and therefore some assumptions must be made.

Although long-term modeling will introduce uncertainty into the results, the metal device is a cost-effective treatment option in a Swedish setting with a time horizon as short as five years, well within the time frame of available long-term data, both for intervention and comparator.

Due to the dominant outcome, NMB analysis as well as separate DSAs were performed for cost and QALY results.

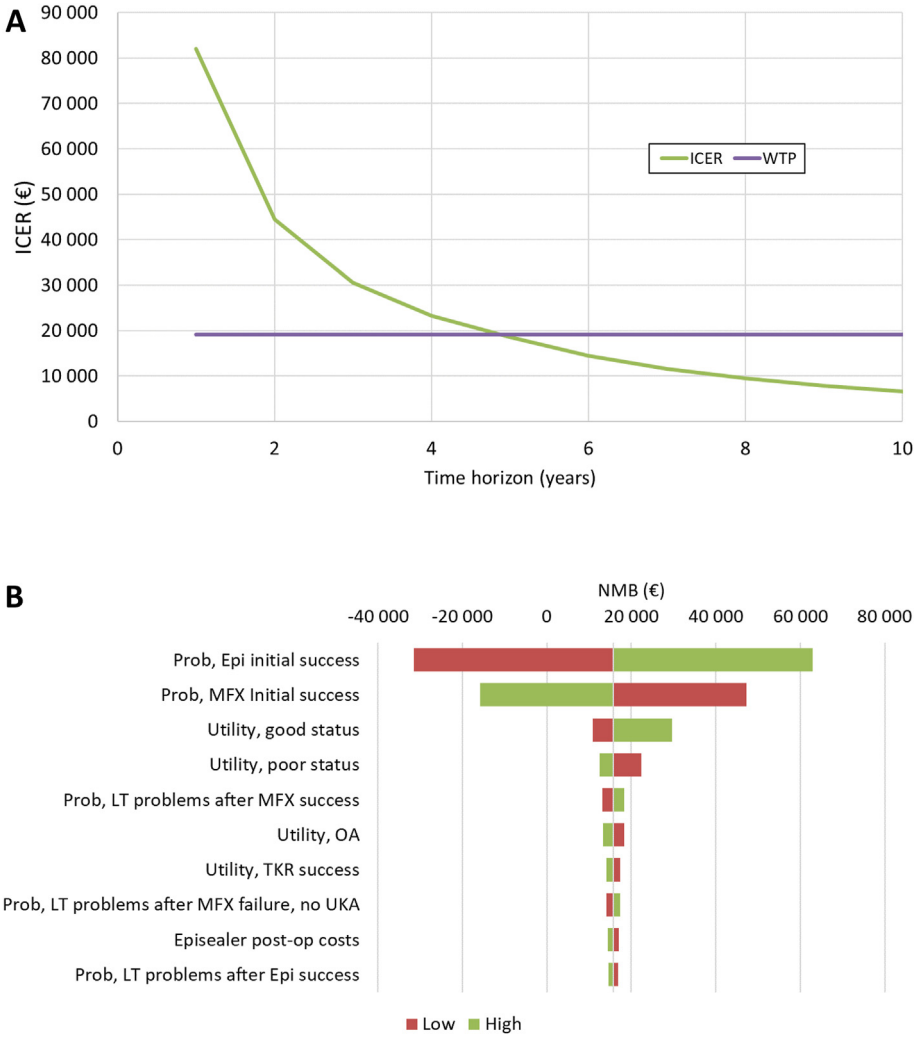

Fig. 2. A) Development of ICER over time and **(B)** results of deterministic sensitivity analysis.

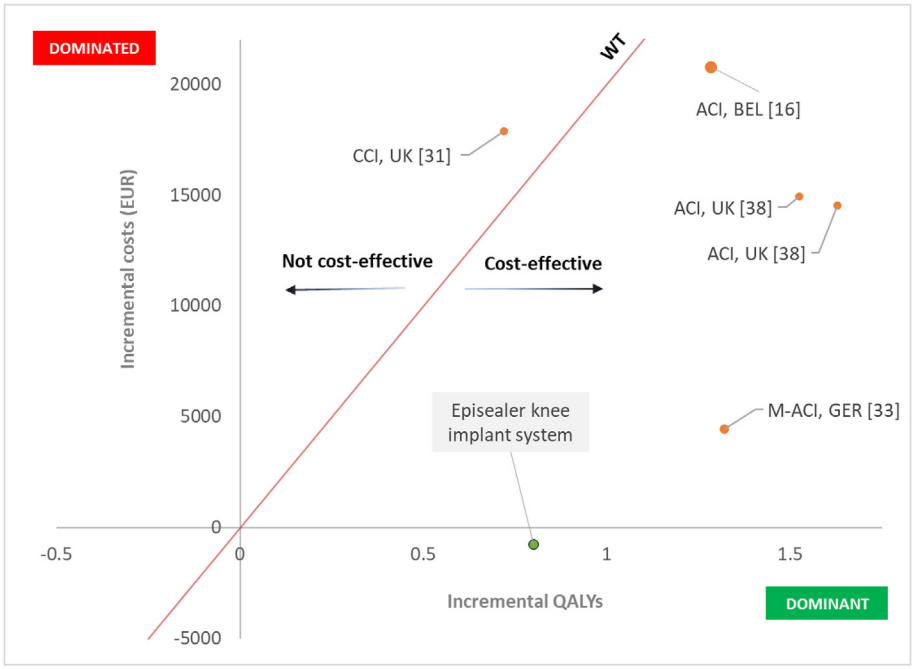

Fig. 3. Cost-effectiveness of experimental interventions compared to microfracture
Abbreviations: ACI = Autologous chondrocyte implantation, CCI = characterized chondrocyte implantation, M-ACI = matrix-induced autologous chondrocyte implantation, QALY = quality-adjusted life year, WTP = willingness to pay
Countries: BEL (Belgium), GER (Germany), UK (United Kingdom). The WTP for a QALY (threshold) in the figure is set at 20,000 EUR.

As shown in the DSA, the initial success rate of the metal device and MFX is a critical parameter for the model results. The data on success rate for the metal device can be considered reliable evidence, being based on published data derived from a growing number of implanted devices [13] complemented with conservative assumptions based on post-implant patient-reported outcomes. For MFX, a literature overview was conducted to provide input, and four valid studies were used as model inputs.

While the metal device presents as a dominant strategy, assessments of other experimental treatment options compared to MFX have resulted in better health outcomes albeit more costly over a corresponding time horizon. ICERs between ~£14,000 [30] and €16,229 [10] have been reported for ACI as compared to MFX, while Elvidge et al. found similar results for characterized chondrocyte implantation (CCI) with an ICER of £21,245 vs. MFX [31]. A recent publication on cost-effectiveness of a third-generation ACI and matrix-induced autologous chondrocyte implantation (M-ACI) reported an ICER of € 3376 vs. MFX [32]. To put into context, hip and knee arthroplasty are considered to be some of the most cost-effective procedures of all with a cost per QALY of € 6710 for hips and €13,995 for knees already at one-year post-surgery [33].

An illustration of incremental costs, incremental QALYs, and ICERs for all identified assessments of cost-effectiveness vs. MFX (lifelong time horizon) is shown in Fig. 3.

The metal device was here shown to be more cost-effective than the biological methods mentioned above, and there are several reasons for this. First, a metal device does not depend on the slow development and maturation of new tissue over a period of 12–24 months. In fact, after MFX, three months of monitored rehabilitation form an integral part of the procedure [5].

There are a number of limitations in the current study

Any probe into the far future requires some assumptions regarding long-term results, etc. This paper is to a considerable extent based on published data, and a conservative approach has been applied. A scenario analysis with a highly conservative approach showed that treatment with metal device would still be cost-effective in a time frame very similar to the base case, about 5–6 years.

Our model was designed in similarity to a previous study using microfracture as a comparator [10]. This may not reflect a logical scenario for some, arguing that ACI/MACI, OATS/Allografts may be intermediate alternatives. The inclusion of such intermediates would, however, results in an excessively complicated analysis.

The analysis included no indirect costs, and only direct medical costs were included in the health care analysis. Bone and cartilage lesion in the knee due to OA can severely impair the ability of the patient to work and participate in activities of daily life [34] and can be expected to be relevant for the target population of the metal device who are of working age. Although work impairment can be argued to be addressed by the data on quality of life in some small part, no costs for productivity losses are included in the current analysis, which means that the estimated ICER is likely conservative.

With the extensive preoperative assessment of each patient, including MRI and a 3D visualization of the patient's femoral knee, it is anticipated that better patient selection will be possible with increasing number of procedures and outcomes data. Such optimization would likely improve clinical outcome and cost-effectiveness further.

We conclude that a metal implant may be a cost-effective treatment alternative for patients in their 40's when compared to MFX in a Swedish setting.

Availability of data and materials

Not applicable.

Authors' contributions

All three authors have contributed to study design, analysis, and writing the manuscript. The manuscript has been read and approved by all three authors before submission.

Consent for publication

Not applicable.

Competing interests

LB has no competing interests. At the time of writing, DG was an employee of PharmaLex Sweden, supporting Episurf Medical with

consultancy services. LR is a board member and owns stocks in Episurf Medical.

Ethics approval and consent to participate

Not applicable.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jisako.2023.02.006.

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