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ORIGINAL ARTICLE

COST-UTILITY ANALYSIS OF ARTHROSCOPIC MATRIX-BASED MENISCUS REPAIR (AMMR) IN THE PERSPECTIVE OF POLISH NATIONAL HEALTH SERVICE AND PRIVATE PATIENTS – 10-YEAR HORIZON

ANALIZA UŻYTECZNOŚCI KOSZTÓW ARTROSKOPOWEJ TECHNIKI BIOLOGICZNEGO LECZENIA ŁĄKOTKI (AMMR) W PERSPEKTYWIE PŁATNIKA PRYWATNEGO I NARODOWEGO FUNDUSZU ZDROWIA – HORYZONT 10-CIO LETNI

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ABSTRACT

Introduction

Clinical data has indicated that Arthroscopic Matrix-based Meniscus Repair (AMMR) offers a means to preserve the meniscus in patients who would otherwise be scheduled for meniscectomy, although AMMR has significant upfront costs.

Aim

The objective of this study was to estimate the cost-effectiveness of AMMR in Poland in both the National Health Service (PNHS) and from the perspective of private patients (PP).

Material and methods

A Markov health-state model was developed to evaluate the cost-utility analysis of AMMR compared to meniscectomy (ME) for patients with a complex meniscus tear, using a 10-years horizon, modelling a cohort of 1000 patients. Initial probabilities and clinical course were simulated based on previously published data. A literature review identified different clinical outcome probabilities and health-related utility scores associated with each health state. Cost-effectiveness was presented as an indicator of Incremental Cost-Utility Ratio (ICUR). Costs were taken from published sources for the perspective of PNHS and from a private clinic offers for the perspective of PP.

Results

In the 10-year horizon, AMMR was associated with an increase in discounted quality-adjusted life-years (QALYs) to 7 778.25 compared to 7 454.33 for ME. In both perspectives, (PNHS and PP) the ICUR cost is smaller than willingness to pay (WTP) parameter (PNHS-ICUR = 34.212.92 versus PP-ICUR = 29.897.36).

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Conclusions:
Despite the increase in costs, the procedure is cost-effective at standard thresholds used in Poland for analyzed perspectives.

Keywords: knee; meniscus; collagen matrix; cost-effectiveness; economic analysis; Markov model

STRESZCZENIE

Wstęp
Dane kliniczne wskazują, że artroskopowa technika biologicznego leczenia uszkodzeń łąkotki z użyciem błony kolagenowej (AMMR) pozwala na zachowanie łąkotki u pacjentów, którzy w przeciwnym razie zostaliby zakwalifikowani do jej częściowego lub całkowitego usunięcia (ME). Jest to istotne dla opóźnienia rozwoju zmiana zwyrodnieniowych stawu kolanowego. Procedura AMMR wiąże się jednak ze znacznymi kosztami początkowymi.

Cel
Celem pracy była ocena opłacalności procedury AMMR w Polsce zarówno z perspektywy płatnika prywatnego (PP) jak i Narodowego Funduszu Zdrowia (NFZ).

Materiał i metody
Analizę ekonomiczną przeprowadzono w formie analizy kosztów-użyteczności. Koszty oraz efekty zdrowotne dla porównywanych procedur zostały wyznaczone w oparciu o opracowany model Markowa, z wykorzystaniem 10-letniego horyzontu czasowego dla kohorty 1000 pacjentów. Wstępne prawdopodobieństwa i przebieg kliniczny zostały zasymulowane na podstawie wcześniej opublikowanych danych. Dane dla kosztów leczenia zostały pobrane z opublikowanych przez NFZ źródeł oraz z ofert prywatnych klinik dla perspektywy PP. Efektywność kosztowa została przedstawiona jako wartość przyrostowego wskaźnika użyteczności kosztów (ICUR).

Wyniki
W horyzoncie 10-letnim, leczenie procedurą AMMR wiązało się z większą wartością wskaźnika stanu zdrowia, wyrażającego długość życia skorygowaną o jego jakość (QALYs) wynoszącą 7 778,25 w porównaniu z 7 454,33 w przypadku procedury ME. W obu perspektywach płatniczych (NFZ i PP) koszt ICUR okazał się mniejszy niż parametr gotowości do zapłaty (WTP) (NFZ-ICUR = 34 212,92 w porównaniu z PP-ICUR = 29 897,36).

Wniosek
Pomimo początkowych wyższych kosztów leczenia, procedura AMMR jest opłacalna przy standardowych progach stosowanych w Polsce dla obu analizowanych perspektyw płatniczych.

Słowa kluczowe: kolano; łąkotka; błona kolagenowa; opłacalność; analiza ekonomiczna; model Markowa

Introduction

It's not an exaggeration to say that the menisci are vital to the proper functioning of the knee, as the menisci augment contact area, joint congruity and stability, transmit load, absorb shock and aid in joint lubrication (Renstrom *et al.*, 1990; Markes *et al.*, 2020).

Unfortunately, meniscal lesions are one of the more common knee injuries (Kim *et al.*, 2011). While meniscectomy, either partial or complete, has been a treatment option for a long time, there is substantial evidence to indicate that meniscectomy leads to increased degeneration of articular cartilage and osteoarthritis (Han *et al.*, 2010) along with a greater frequency of total knee replacement (Katz *et al.*, 2020).

The MOON Cohort study concluded that 30% of medial meniscal tears and 10% of lateral meniscal tears are eligible for all-biological repair; 35% of medial meniscal tears and 35% of lateral meniscal tears are eligible for an advanced repair technique, and 35% of medial meniscal tears and 55% of lateral meniscal tears are eligible for a scaffold replacement (Fetzer *et al.*, 2009). Despite a growing emphasis on meniscal preservation, the majority of meniscus tears observed at the time of arthroscopy are treated with partial meniscectomy. Current treatment algorithms are dictated by the tear morphology, proximity to the meniscal blood supply, length and stability of tear, and the presence of degeneration with complex meniscal lesions frequently resulting in partial or total meniscectomy (Burgess *et al.*, 2020). This would seem to be in contrast to a consensus that recommended that patients with a symptomatic knee and a degenerative meniscus lesion should not have a meniscectomy proposed as a first-line treatment (Beaufils *et al.*, 2017).

In 2010, a fully arthroscopic technique of an arthroscopic matrix-based meniscus repair (AMMR) and the injection of bone marrow aspirate into the area of the meniscal lesion developed (Piontek *et al.*, 2012). The 2 and 5-year follow-up data demonstrate that the AMMR technique is safe and can offer an additional tool to save the meniscus in the patients otherwise scheduled for meniscectomy (Piontek *et al.*, 2016; Ciemniewska-Gorzela *et al.*, 2020). Although the introduction of the AMMR technique offers another treatment option, it has large upfront costs. While the benefits of meniscal preservation through meniscal repair are apparent and widely accepted, the substantially elevated cost of AMMR meniscal repair leaves uncertainty about its relative health-economic benefit and overall long-term advantage compared to partial meniscectomy, especially among middle-aged and older patient populations.

Considering the role of health economics with regard to treatment options, this has been applied to outcomes following surgical treatment of meniscal lesions. Using age-specific per-patient cost and quality-adjusted life-years (QALYs) projected for the 30-year horizon, computations suggest that payers would save approximately $43 million annually if 10% of current meniscectomies could be performed as meniscal repairs (Feeley *et al.*, 2016).

Therefore, the objective of this study was to estimate the cost-effectiveness of AMMR in Poland in the Polish National Health Service (PNHS) and from the perspective of private patients (PP).

Aim

The Markov model was used to investigate the lifetime cost-effectiveness of AMMR compared with ME by the possible prevention of symptomatic osteoarthritis in patients with an irreparable meniscal lesion. Clinical data used in the model were derived from several population-based studies and 1 case series of AMMR treatment. If the event probabilities were provided over a time period longer than 1 year, we calculated the 1-year probability of the event, assuming a fixed rate with respect to time. The probabilities of death were taken from the tables of life expectancy (2017) published by the Polish Office for National Statistics. For AMMR, ME, 1y post-TKR and post revision TKR procedures, the probability of death associated with the medical procedure was taken into account, with a probability of 0.003. The cost-effectiveness of AMMR was calculated for both PNHS and PP. The study was conducted in accordance with the 2013 Consolidated Health Economic Evaluation Reporting Standards statements.

AMMR probabilities and QALYs

The data source for AMMR was a study that assessed 54 consecutive patients. The mean follow-up was 5.92 years (range: 3.56–8.34). Six patients were lost to follow-up, and 4 patients underwent arthroscopic debridement for persistent knee pain and swelling, thus they were considered treatment failures. Kaplan-Meier survival analysis assessed the survivorship after AMMR with an overall survival rate of 88% at final follow-up. The EuroQoL 5-dimension 5-level (EQ-5D-5L) scores were assessed in 44 patients, and the scores were converted to utility values ranging from 0.594 (the worst health state) to 1.000 (full health). The mean EQ-5D-5L utility values were 0.9 ± 0.1 (Ciemniewska-Gorzela *et al.*, 2020).

Systematic Review of the Literature

A systematic review of the literature was conducted and focused on the cost-effectiveness of meniscus treatment strategies. The utilities (Table 1) and event rates (Table 2) were based on the published literature. Tables 1 and 2 summarizes the key input parameters and references.

Costs

We used the average procedure cost from a private clinic to obtain the direct costs of AMMR. We recorded the number of physical therapy sessions for each patient. We used the rate per session provided by a local physical therapy clinic and PNHS. We also recorded any hyaluronic acid injections and any aids purchased for the treated knee such as orthotics, crutches, braces or other medical treatment for knee osteoarthritis (OA).

We recorded healthcare resource use at each of the follow-up visits (3, 6, 12, 24 and 60 months), including inpatient hospitalizations and physical therapy. Costs, except for AMMR, were taken from the published sources for perspective of PNHS and the private clinic offers for the perspective of private patients' payment. Currently, AMMR is not a standard treatment for meniscal lesions, consequently, there is no standard PNHS reimbursement. Therefore, we used the costs of AMMR based on PP in both treatment perspectives. We estimated the total cost for each patient over the entire study period. All costs are presented in the fiscal year 2017 using the currency of Polish złoty (PLN).

Table 1. Model Parameters – costs and utility.

State	cost PNHS [PLN]	cost PP [PLN]	utility	Source
IndexProcedure	0	0	0	
AMMR	18 955	21 055	0.579	
ME	7 012	10 380	0.579	
Between_AMMR_and_ME	0	0	0.9	Ciemniewska-Gorzela *et al.* 2020
no_OA	0	0	0.9 – (0.01* (state_time-1))	Rongen *et al.* 2016; Bendich *et al.* 2018
OA_1y	3 313.07	3 805.4	0.636	
OA_rehabilitation	3 313.07	3 805.4	0.7	Hermans *et al.* 2012
postTKR_1	22 352	36 795	0.68	Feeley *et al.* 2016
postTKR_2	220	495	0.84	
postTKR_3	220	495	0.83	
postTKR_4	220	495	0.82	
postTKR_5	220	495	0.81	
postTKR_6	220	495	0.8	
postTKR_7	220	495	0.79	
postTKR_8	220	495	0.78	
postTKR_9	220	495	0.77	
postTKR_10	220	495	0.76	
postTKR_11	220	495	0.75	
R_TKR	31 703	36 075	0.61	Feeley *et al.* 2016
R_TKR_rehabilitation	220	495	0.74	Feeley *et al.* 2016
Heath	0	0	0	

Table 2. Model Parameters – event rates.

Strategy	From	To	Probability	Source
model_AMMR	IndexProcedure	AMMR	1	Ciemniewska-Gorzela *et al.* 2020
model_AMMR	IndexProcedure	ME	0	Ciemniewska-Gorzela *et al.* 2020
Both	AMMR	ME	0.02	Ciemniewska-Gorzela *et al.* 2020
Both	Between_AMMR_and_ME	ME	0.0213	Ciemniewska-Gorzela *et al.* 2020
Both	AMMR	Between_AMMR_ and_ME	C	Ciemniewska-Gorzela *et al.* 2020
Both	Between_AMMR_and_ME	Between_AMMR_ and_ME	C	Ciemniewska-Gorzela *et al.* 2020
Both	Between_AMMR_and_ME	OA_rehabilitation	0.0053	Ciemniewska-Gorzela *et al.* 2020
Both	ME	no_OA	C	Bendich *et al.* 2018
Both	no_OA	no_OA	C	
Both	ME	OA_1y	0.018	Bendich *et al.* 2018
Both	AMMR	OA_rehabilitation	0	Ciemniewska-Gorzela *et al.* 2020
Both	no_OA	OA_rehabilitation	0.018	
Both	OA_1y	OA_rehabilitation	C	
Both	OA_rehabilitation	OA_rehabilitation	C	
Both	OA_1y	postTKR_1	0.14	
Both	OA_rehabilitation	postTKR_1	0.0937	Bendich *et al.* 2018
Both	postTKR_1	postTKR_2	C	
Both	postTKR_2	postTKR_3	C	
Both	postTKR_3	postTKR_4	C	
Both	postTKR_4	postTKR_5	C	
Both	postTKR_5	postTKR_6	C	
Both	postTKR_6	postTKR_7	C	
Both	postTKR_7	postTKR_8	C	
Both	postTKR_8	postTKR_9	C	
Both	postTKR_9	postTKR_10	C	
Both	postTKR_10	postTKR_11	C	
Both	postTKR_11	postTKR_11	C	
Both	postTKR_1	R_TKR	0.019	
Both	postTKR_2	R_TKR	0.019	
Both	postTKR_3	R_TKR	0.019	
Both	postTKR_4	R_TKR	0.019	
Both	postTKR_5	R_TKR	0.010	
Both	postTKR_6	R_TKR	0.010	
Both	postTKR_7	R_TKR	0.010	
Both	postTKR_8	R_TKR	0.010	
Both	postTKR_9	R_TKR	0.010	
Both	postTKR_10	R_TKR	0.009	
Both	postTKR_11	R_TKR	0.006	
Both	R_TKR	R_TKR_rehabilitation	C	
Both	R_TKR_rehabilitation	R_TKR_rehabilitation	C	
Both	AMMR	Heath	combine_probs (mr, mr_med)	Ciemniewska-Gorzela *et al.* 2020
Both	ME	Heath	combine_probs (mr, mr_med)	
Both	Between_AMMR_and_ME	Heath	mr	
Both	no_OA	Heath	mr	
Both	OA_1y	Heath	mr	
Both	OA_rehabilitation	Heath	mr	
Both	postTKR_1	Heath	combine_probs (mr, mr_med)	
Both	postTKR_2	Heath	mr	
Both	postTKR_3	Heath	mr	
Both	postTKR_4	Heath	mr	
Both	postTKR_5	Heath	mr	
Both	postTKR_6	Heath	mr	
Both	postTKR_7	Heath	mr	
Both	postTKR_8	Heath	mr	
Both	postTKR_9	Heath	mr	
Both	postTKR_10	Heath	mr	
Both	postTKR_11	Heath	mr	
Both	R_TKR	Heath	combine_probs (mr, mr_med)	
Both	R_TKR_rehabilitation	Heath	mr	
Both	death	Heath	1	
model_ME	IndexProcedure	AMMR	0	
model_ME	IndexProcedure	ME	1	

Decision-Analytic Model and Economic Evaluation

Markov models are decision-analytic models where various outcomes can occur over an extended period, which, in this case, would be a patient moving between mutually exclusive health states. Cost-utility analysis is the preferred type of health economic evaluation in medicine. It compares not just costs and health outcomes but also types of interventions in a ratio: the incremental cost-utility ratio (ICUR) (PLN/QALY). As a measure of health outcome, effectiveness is measured in QALYs ranging from 0 (death) to 1 (perfect health). In a Markov model, a cohort of simulated participants is initially allocated to each treatment strategy and subsequently assigned to mutually exclusive health states based on the estimated transition probabilities.

During each cycle, participants accrue utilities according to their respective health states. At the end of each yearly cycle, patients are reassigned between the states. For this study, we created a Markov model to project strategy-specific progression to symptomatic osteoarthritis, total knee replacement (TKR), and revision TKR in a cohort (n = 1000) of 40-year-old patients presenting with complex meniscus tears but no OA at the time of treatment (Figure 1). In the base case, patients start in the non-osteoarthritis state after the index procedure (if any) and have a strategy-specific probability of progressing to osteoarthritis. According to the case series results and literature search, failure rates of AMMR and progression to knee osteoarthritis for ME and AMMR were accounted for. We assumed that any failure would require revision surgery and that meniscectomy would be performed in case AMMR failed. Patients with OA have a certain sex-stratified probability of undergoing TKR. In the status, post-TKR implied that there is a probability of the revision arthroplasty. Utilities, costs, and event rates were based on the literature and analysis of public research and case series results. Tables 1 and 2 summarize the key input parameters (Table 1, 2). The analysis used a 10-year time frame as a base case and explored the effects of parameter uncertainty. Costs were discounted at 5% and effects at 3.50% per annum, in line with health economic guidelines in Poland. Peoples' willingness to pay (WTP) for health care quality improvements was 125.955 PLN. (Polish Agency for Health Technology Assessment and Tariff System 2020) Calculations were done in R (version 3.6.0) with packages heemod (version 0.9.4) and ggplot2.

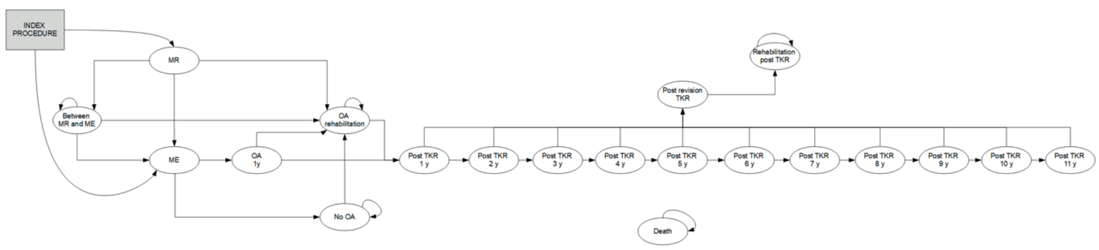

Figure 1. The model structure: a combination of a decision tree and a Markov model. In the base case, all patients start in the status post (s/p) index procedure state and can experience osteoarthritis (OA), a revision, or both. All patients with OA can progress to TKR, and there are up to 2 TKR revisions possible. ME = meniscectomy; AMMR = meniscus repair.

Results

The results (total costs PNHS, total costs private, total utility) are presented as a sum of the values for 1000 patients. ICUR was counted for PNHS costs and private costs separately, using the formula:

It presents the cost of gaining one utility point (QALY) by one person.

The costs of AMMR are higher than ME in both PNHS and PP (Table 3). Patients' utility after AMMR is higher as a result of better functioning.

Table 3. Base model: costs and utilities.

	cost PNHS	cost PP	utility	strategy
1	20.737.931.34	23.571.294.22	7.778.24	model_AMMR
2	9.655.688.28	13.886.946.62	7.454.33	model_ME

In both perspectives, (PNHS and PP) the ICUR cost is smaller than WTP parameter (PNHS-ICUR = 34.212.92 versus PP-ICUR = 29.897.36). The cost per QALY gained when a new treatment is administered and calculated at 34.212.92 PLN in the PNHS finance system and 29.897.36 PLN in the private healthcare system. This calculation suggests that choosing AMMR should be preferred.

Demographic analysis
The only changing variable was gender; all other parameters remained the same.

The group "only males" was exactly the base group. Here the results were repeated in order to compare the results with that of females easily. Costs and utilities were similar but not identical. This is due to the fact that mortality rates were higher for men. The conclusions were the same as in the base case. ICUR for men was higher (ICUR for males for PNHS= 34 212.9 and for PP = 29.897.4; ICUR for females for PNHS = 33.495.4 and for PP = 29.253.83); therefore, sensitivity have been analyzed only in the male group (as a worse case).

A population consisting of 22.92% females and 77.08 males was analyzed. All other parameters remained the same. ICUR for this population was smaller then for men only (ICUR for mixed population for PNHS = 34.045.9 and for PP = 29.747.6). Again, the conclusions were the same as in the base case.

Changed discounting rates
In the sensitivity analysis, the following values of cost discounting rate and utility discounting rate are analyzed:

- 5% both
- 0% both
- 5% for costs and 0% for utility

Costs: 5%, utilities: 5%
Discounting of the costs remained the same. Discounting rate of utility increased, so the total utility for 10 years for 1000 patients decreased (Table 4).

Table 4. Discounting rate 5%: costs and utilities.

	cost PNHS	cost private	QALY	.n_indiv	strategy
1	20.737.931.34	23.571.294.22	7.268.72	1000	model_AMMR
2	**96.55.688.28**	13.886.946.62	6.976.04	1000	model_ME

ICUR increased (PNHS ICUR = 37.865.53, PP ICUR = 33.089.24), but is still significantly smaller than WTP.

Costs: 0%, utilities: 0%
Discounting rates decreased, so the total costs and total utility for 10 years for 1000 patients increased [Table 5].

Table 5. Discounting rate 0%: costs and utilities.

	cost PNHS	cost private	QALY	.n_indiv	strategy
1	2.347.052.40	24.423.561.50	9.218.47	1000	model_AMMR
2	10.666.840.88	15.236.302.65	8.803.95	1000	model_ME

ICUR decreased (PNHS ICUR = 25.765.22, PP ICUR = 22.163.58), and is significantly smaller than WTP.

Costs: 5%, utilities: 0%
Discounting rates of costs remained the same; therefore, no change in costs is observed. The discounting rate of utility decreased; therefore, the total utility for 10 years for 1000 patients increased [Table 6].

Table 6. Discounting rate 5% and 0%: costs and utilities.

	cost PNHS	cost private	QALY	.n_indiv	strategy
1	20.737.931.34	23.571.294.22	9.218.47	1000	model_AMMR
2	9.655.688.28	13.886.946.62	8.803.95	1000	model_ME

ICUR decreased (PNHS ICUR = 26.735.09, PP ICUR = 23.362.77), and is significantly smaller than WTP.

Deterministic sensitivity analysis (DSA)
Deterministic sensitivity analysis was used to check the impact of changing one parameter in the model at a time. For example, the model was run for age = 20 years while retaining all other parameters from the base case. The results, however, are presented together for easier comparison.

Values of parameters
The probability of transition from state "AMMR" to state "ME" was changed: lower value = 0.5, higher value = twice the initial first value [Table 7].

Some outcome parameters were influenced only by a part of the parameters. For example, the value of QALY does not influence the cost. The most significant impact on ICER in the case of PNHS costs has an upper value of QALY in the state "no_OA" and a lower value of QALY in the state "Between_AMMR_and_ME". In the first case, we can see that the QALY increased in the ME scenario greatly, thus, increasing the ICER to a value above "willingness to pay". In the second case, we see that changing QALY of the state "Between_AMMR_and_ME" to a lower value may cause a situation in which patients in the ME scenario had higher QALYs than in the AMMR scenario (ICUR drops below 0). As shown, the model is very sensitive to the exact values of these 2 parameters, as they define the patient's QOL after each of the surgeries if no other medical condition has to be later taken into account (for example, OA or TKR). In the case of PNHS costs, the change of other parameters did not take values greater than WTP or smaller than zero.

Similar results were seen for PP costs, as the QALY for patients undergoing AMMR is affected greatly by the exact value of QALY in the condition "Between_AMMR_and_ME". A higher initial age of the patients results in a lower total QALY because the higher mortality rate of older people shortens the length of time they are observed in the model, gaining any positive QALY value. Likewise, sex also impacts the model through a difference in mortality rates. Increasing the value of transition between AMMR and OA rehabilitation causes fewer patients to go to the state "Between_AMMR_and_ME" (which has a larger QALY), thus causing the total cost of QALY of the population to decrease. In ME, the cost of QALY is affected especially by the initial age, cost of QALY in the state "no_OA" and "sex".

The greatest costs were observed for increasing probability of transition from the state "AMMR to OA_rehabilitation". A large increase in costs was also caused by increasing the cost of an AMMR surgery. Increasing initial age decreased the costs due to the higher probability of mortality, as deaths occurred before further medical treatment was needed. The costs of ME were mostly affected by the exact value of the AMMR/ME treatment.

Probabilistic sensitivity analysis (PSA)
Beta-distribution, as a distribution defined on the interval [0,1], was used for all transition

Table 7. DSA: parameter values.

PARAMETER	BASE CASE	LOW	HIGH
age_init	40	20	60
Sex	male	male	female
AMMR_ME	0.02	0.010	0.04
AMMR_OA_rehabilitation	0	0	0.1
OA_rehabilitation_postTKR_1	0.0937	0.058	0.1294
Between_AMMR_and_ME_OA_rehabilitation	0.0053	0.00265	0.0106
Between_AMMR_and_ME_ME	0.0213	0.0053	0.0426
cost PNHS _AMMR	18.955	1.000	21.000
cost PNHS _ME	7.012	6.000	8.000
cost PNHS _postTKR_1	22.352	21.000	24.000
cost PNHS_postTKR_1	31.703	30.000	33.000
cost private_AMMR	21.055	20.000	23.000
cost private_ME	10.380	9.000	12.000
cost private_postTKR_1	36.795	35.000	39.000
cost private_R_TKR	36.075	35.000	39.000
QALY_Between_AMMR_and_ME	0.9	0.716	1
QALY_no_OA	0.9 – (0.01*(state_time-1))	0.8	0.9

probabilities and QALYs, with the mean equal to the point estimates used in the base case.

Normal distribution was used for all costs in the private healthcare system, with reasoning based on Central Limiting Theorem. Since QALY in the state "no_OA" affects mainly ME, a worst-case will be presented: QALY in "no_AO" not dropping in subsequent years.

Costs results

AMMR is more cost-effective than ME for the base-case value of willingness to pay. Only for small values of willingness to pay is the ME strategy favoured.

The following figure (Figure 3) shows that the simulated AMMR strategy is more costly than the base case ME strategy. QALY (named "Effect" in figure 3) was usually higher in AMMR, but not always.

The results in the private healthcare system are similar (Figures 4 and 5).

AMMR was more expensive in every simulation than the ME (Figure 4). The QALY (annotated as "effect" on the graph in figure 5) (Figure 5) was usually greater in AMMR, but not always. In some cases, it was significantly smaller than in ME. It needs to be mentioned that this result may be significantly impacted

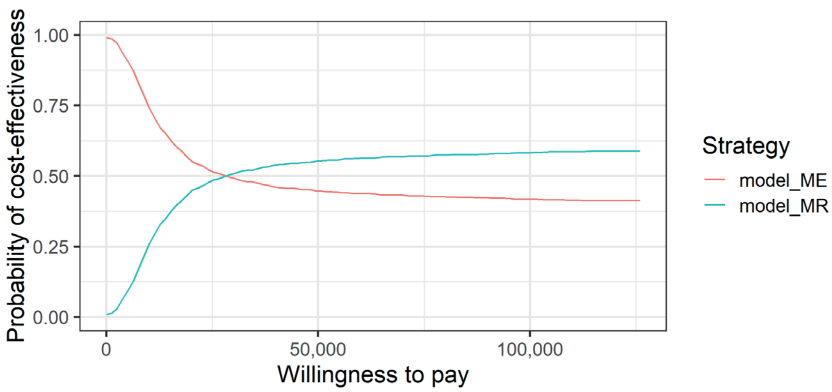

Figure 2. Probability of cost effectiveness vs willingness to pay (PNHS costs), 10 years horizon (model_MR = model_AMMR).

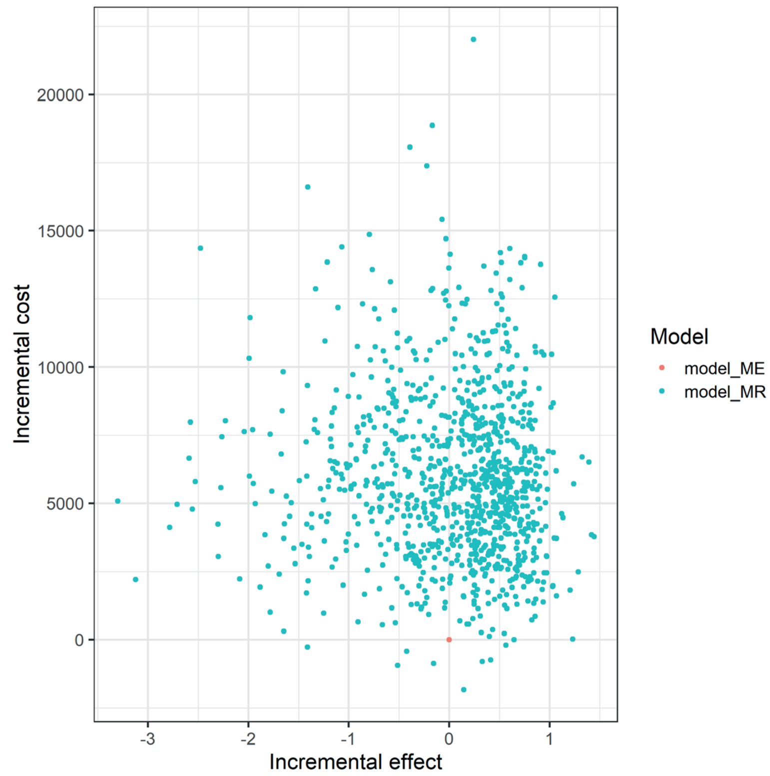

Figure 3. Incremental cost vs incremental effect (PNHS costs), 10 years horizon (model_MR = model_AMMR).

Figure 4. Probability of cost-effectiveness vs willingness to pay (PP costs), 10 years horizon (model_MR = model_AMMR).

by the value of QALY in the state "no_OA" taken into account in the sensitivity analysis.

Discussion

Our analysis has shown that meniscal repair via AMMR has the potential to reduce the overall treatment costs to both PNHS and PP. These findings confirmed that AMMR meniscal repair is the dominant treatment strategy. Another important finding is that QALY after a successful AMMR is a major factor influencing ICER. Therefore, if the goal is cost savings after meniscal repair, then rehabilitation and lifestyle following surgery should be a focus. This is another reason to including rehabilitation protocol as a critical part of meniscal treatment, whether in PNHS or PP. Moreover, our results indicate

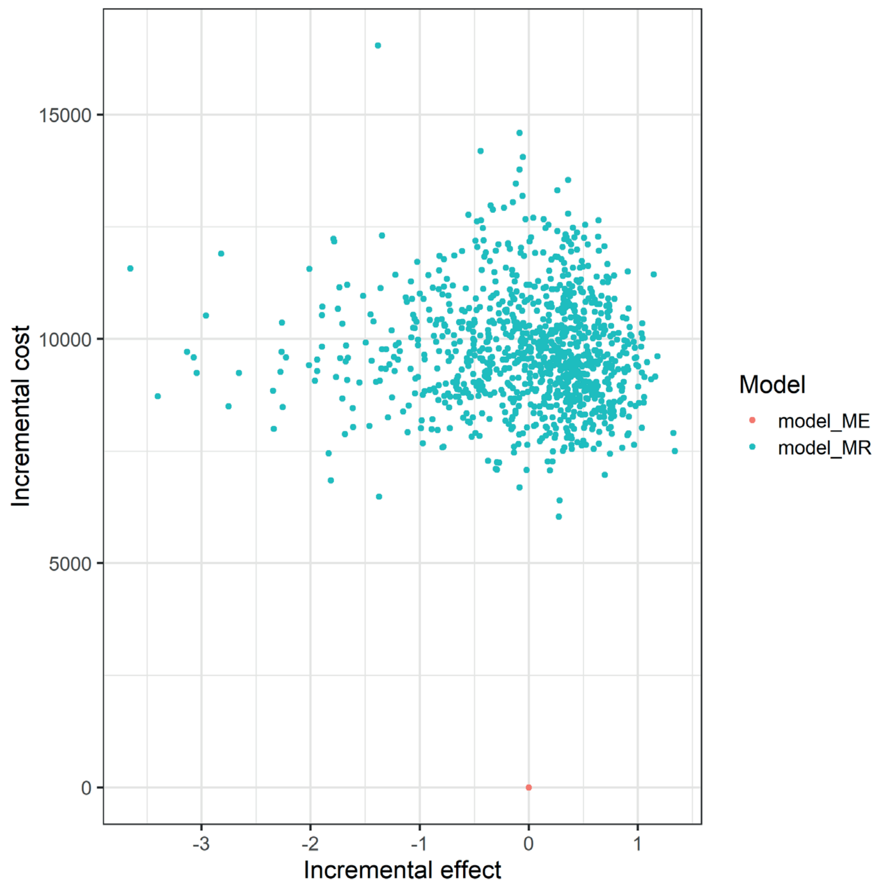

Figure 5. Incremental cost vs incremental effect (PP costs), 10 years horizon (model_MR = model_AMMR).

that the AMMR model is more sensitive to the cost of AMMR surgery than the costs of ME, TKA and OA non-operative therapies.

Although many older patients may not be candidates for meniscal repair because of the nature of their tears (e.g., degenerative), our data suggest that it may be beneficial to consider meniscal repair for some older patients, despite previous treatment guidelines considering partial meniscectomy to be sufficient. Recent studies have suggested that meniscal repair can be successful even in older patients, highlighting the importance of understanding the economic implications of meniscal debridement versus repair (Steadman *et al.*, 2015). This has been highlighted by recent studies evaluating outcomes in older patients undergoing meniscal repair (Kurzweil *et al.*, 2014; Steadman *et al.*, 2015). Finally, clinical studies have shown that repair of meniscal root avulsions in patients older than 50 years leads to significantly improved clinical results compared to meniscectomy (Kim *et al.*, 2011; Chung *et al.*, 2015). Thus, indications of repair may be expanding, and the cost-effectiveness of a more aggressive repair strategy highlights the benefits of attempting repair in older patients. Although other tear patterns, such as radial tears and horizontal tears, do not have clear indications, some studies suggest good outcomes with partial meniscectomy (Lee *et al.*, 2019). The results of our study suggest that it is likely beneficial to consider AMMR for tear patterns that may be amenable to repair, even with higher failure rates, in order to decrease the risk of OA progression (Goebel *et al.*, 2017), and reduce overall healthcare costs. If only a small share of the tears currently treated with meniscectomy would instead be treated with repair, substantial long-term savings can be expected alongside improvement in long-term outcomes (Pujol *et al.*, 2015; Feeley *et al.*, 2016; Hagmeijer *et al.*, 2019; Momaya *et al.*, 2019).

There is a clear consensus in orthopaedics that the menisci are important stabilizers of the knee; therefore, preservation of the menisci is essential to the preservation of the knee joint. While meniscal repair is preferred to partial or complete meniscectomy, this is not always possible given that only the periphery of the meniscus (the red-red and red-white zones) has vascular supply (Feeley *et al.*, 2016). The extent of meniscal resection has been directly linked to OA progression; therefore, subtotal and total meniscectomy is a primary risk factor for knee degeneration and progression to early TKR (Papalia *et al.*, 2011). For patients with irreparable meniscal tears who require subtotal or complete meniscectomy, meniscus allograft transplant (MAT) or meniscal scaffolds offer the potential for joint preservation (Southworth *et al.*, 2020). Although limited, the clinical data demonstrates that AMMR can offer an additional tool to save the meniscus in patients otherwise scheduled for meniscectomy. Currently, AMMR is not a standard treatment for meniscal lesions, and there is no clear view on total resource utilization. Meniscal scaffolds, MAT and AMMR procedures are more expensive than ME or non-operative treatment. The cost-effectiveness of meniscus scaffolds or MAT procedures were evaluated for the prevention of osteoarthritis as well as the treatment of chronic symptoms in patients with irreparable meniscus injurie but the results of the current health technology assessment suggest that these treatments should currently not be implemented on a large scale (Rongen *et al.*, 2016; Waugh *et al.*, 2019). However, these studies identified the most influential variables that could be included in order to assess the economic value of those procedures more accurately. While our results demonstrate that AMMR can offer a cost-effective tool for meniscal preservation, it would be beneficial to compare the cost-effectiveness of meniscal scaffolds, MAT and AMMR.

This study has several limitations. First, this is a mathematical simulation and simplifies health states and transitions in a way that may not always reflect all pathways of disease progression. Since few of our assumptions are based on high-level evidence, we performed sensitivity analyses around key assumptions such as annualized rate of OA in AMMR-treated knees. To evaluate the efficacy of AMMR, we were limited to the use of experimental data from 1 study (Ciemniewska-Gorzela *et al.*, 2020). However, the models can be improved as additional clinical data regarding AMMR becomes available. Next, our costs come from a single private clinic and the PNHS database. As a result, the payment may not reflect generalizable costs. To account for this, we performed a sensitivity analysis around these costs. Third, we used private payers cost data to estimate the costs of AMMR surgery for both payment perspectives. Additionally, because of the long-term perspective of this model, part of the care for late-stage events, including expensive treatments such as TKRs and revision TKRs, will be covered by PNHS.

Further, private payer costs for these treatments will likely be higher, so that our projections take a conservative approach and rather underestimate potential savings. Our study follows the same general methodological approach as previous health-economic modelling studies that evaluated the clinical and cost-effectiveness of TKR-related treatments in end-stage OA (Dong *et al.*, 2006; Peersman *et al.*, 2014; Persson *et al.*, 2018). In the established practice for chronic conditions, such analyses begin with short-term clinical data and employ model-based extrapolations to project outcomes over a long-term horizon (Dong *et al.*, 2006; Hermans *et al.*, 2012; Feeley *et al.*, 2016; Rongen *et al.*, 2016; Bendich *et al.*, 2018; Persson *et al.*, 2018). Given the constraints of the model, it does not take into account certain patient-reported factors, including a patient preference for meniscal debridement or repair, nor does it apply a cost value to overall satisfaction.

In summary, our model-based projection suggests that AMMR meniscal repair provides better outcomes and lower overall costs, making it a cost-effective strategy and the dominating treatment strategy for most patients. Even among older patients and those whose treatment may have a high risk of failure, AMMR should be considered in order to decrease the overall risk of OA progression and capture financial benefits for the healthcare system.

Conclusions

Despite the increase in costs, the procedure is cost-effective at standard thresholds used in Poland for analyzed perspectives.

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