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Review

Arthroscopic partial meniscectomy vs non-surgical or sham treatment in patients with MRI-confirmed degenerative meniscus tears: a systematic review and meta-analysis with individual participant data from 605 randomised patients

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SUMMARY

Objective: To identify subgroups of patients with magnetic resonance imaging (MRI)-confirmed degenerative meniscus tears who may benefit from arthroscopic partial meniscectomy (APM) in comparison with non-surgical or sham treatment.
Methods: Individual participant data (IPD) from four RCTs were pooled (605 patients, mean age: 55 (SD: 7.5), 52.4% female) as to investigate the effectiveness of APM in patients with MRI-confirmed degenerative meniscus tears compared to non-surgical or sham treatment. Primary outcomes were knee pain, overall knee function, and health-related quality of life, at 24 months follow-up (0–100). The IPD were analysed in a one- and two-stage meta-analyses. Identification of potential subgroups was performed by testing interaction effects of predefined patient characteristics (e.g., age, gender, mechanical symptoms) and APM for each outcome. Additionally, generalized linear mixed-model trees were used for subgroup detection.
Results: The APM group showed a small improvement over the non-surgical or sham group on knee pain at 24 months follow-up (2.5 points (95% CI: 0.8–4.2) and 2.2 points (95% CI: 0.9–3.6), one- and two-stage analysis, respectively). Overall knee function and health-related quality of life did not differ between the two groups. Across all outcomes, no relevant subgroup of patients who benefitted from APM was detected. The generalized linear mixed-model trees did also not identify a subgroup.
Conclusions: No relevant subgroup of patients was identified that benefitted from APM compared to non-surgical or sham treatment. Since we were not able to identify any subgroup that benefitted from

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APM, we recommend a restrained policy regarding meniscectomy in patients with degenerative meniscus tears.

Background

Arthroscopic partial meniscectomy (APM) is one of the most commonly performed orthopaedic procedures in which a part of the meniscus is surgically removed[1–3]. In middle-aged and elderly patients without a history of acute knee trauma, these tears are typically the result of a degenerative process in the knee and often observed by magnetic resonance imaging (MRI)[4,5]. Degenerative meniscus tears detected on MRI are not necessarily the cause of symptoms in these patients[6]. Indeed, degenerative meniscus tears are frequent incidental findings in asymptomatic knees[7,8].

Evidence from randomised controlled trials (RCTs) and systematic reviews does not demonstrate a clear benefit from APM compared to exercise therapy, corticosteroid injections or sham surgery for patients with MRI-confirmed degenerative meniscus tears[9,10,19,11–18]. In 2017, an expert panel strongly recommended against the use of APM in nearly all patients with degenerative knee disease[20], but several guidelines still support this procedure or do not make a clear statement against its use[21,22]. Although average treatment effects of trials demonstrate no relevant effect, there may be subgroups of patients who benefit from the procedure. Unfortunately, the individual trials performed so far were too small for valid and reliable subgroup identification[23].

A meta-analysis of the participant patient data (IPDMA) from original trials enables the opportunity to identify potential subgroups that are most likely to benefit from APM[24]. The identification of any such subgroup(s) can assist physicians to select individual patients that may benefit from APM and thereby improve the outcomes for that particular subgroup, while avoiding unneeded surgery for others. We therefore aimed to identify subgroups of patients with degenerative meniscus tears who might benefit from APM.

Methods

Study inclusion and characteristics

This international collaborative IPDMA was registered in PROSPERO (registration number: CRD42017067240) and the study protocol was published elsewhere[25]. This IPDMA is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data (PRISMA-IPD) guidelines[26]. We performed a systematic search for eligible trials in Medline, Embase, CINAHL, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) for which we used the search strategy described by Thorlund *et al.*[27] The last search was performed in December 2020. The detailed search strategy is described in the published protocol and is depicted in Additional file 1[25].

Studies were eligible for inclusion if the study was 1) an RCT evaluating the effectiveness of APM in persons with MRI-confirmed degenerative meniscus tears, 2) the comparative treatment was either non-surgical (pain and/or anti-inflammatory medication, exercise programs, and/or watchful waiting) or sham surgery, and 3) MRI verification of the meniscus tear was performed before patient inclusion. Studies that involved participants with traumatic meniscal tears, defined as being the result of a specific traumatic incident, were excluded. Moreover, there were no restrictions on publication date, type of setting, length of follow up, or language.

The original investigators of the ten eligible trials were requested to collaborate and share their trial data[9–18]. If no reply was received after the first invitation, three additional inquiries were sent with a 14-day interval, including inquiries sent to alternative email addresses identified for the corresponding author, co-authors, and affiliated institution in the original publication. Of the ten trials, eight responded and five were willing and able to share the anonymous individual participant data[12,13,16–18]. Before sharing the de-identified patient data, a data transfer agreement was signed by all parties, that included the goal of the study and the intended use of the data.

From each of the five studies of which the individual participant data (IPD) was available, the patient characteristics (age, gender, history of knee symptoms, physical activity level, body mass index (BMI)), radiographic information on knee osteoarthritis (Kellgren–Lawrence (KL) grade), clinical variables (type and location of meniscal tear, duration and severity of symptoms, mechanical symptoms), health-related quality of life scores (derived from the EuroQol-5 dimensions (EQ-5D) or 36-Item Short Form Survey (SF-36)), overall knee specific scores (Knee injury and Osteoarthritis Outcome Scale (KOOS), Subjective Knee Form of the International Knee Documentation Committee (IKDC) or the Lysholm knee score scale) and trial information (assigned treatment, sample size, setting, crossover etc.) were collected and harmonized. Eventually, we had to exclude one study with 3 months follow-up ($n = 17$) because we were unable to combine this study with the four studies that had 24 months of follow-up[13].

Data from the five trials of which IPD was not available and the one excluded study with 3 months follow-up were collected from the published trial reports, both at baseline and follow-up visits[9–11,13–15].

IPD integrity & risk of bias assessment

All IPD were validated to match the results of the original publication. Inconsistencies were discussed and resolved with the original investigators. To assess the risk of bias for the individual studies, we used the latest version of the Cochrane risk-of-bias tool for randomised trials (RoB 2)[28]. The potential for publication bias and small study effects was examined by visual inspection of a contour-enhanced funnel plot[29,30]. To enable the assessment of homogeneity/heterogeneity between the included trials the study characteristics of the included RCTs were compared and described.

Outcomes and effect measures

The primary outcomes were knee pain, overall knee function and quality of life at 24 months of follow-up. The secondary outcomes were mental health scores and adverse events. The included studies assessed these outcomes but used different instruments/questionnaires. Therefore, it was necessary to transform the outcomes of the studies to a uniform scale (0–100, with 0 being the worst score and 100 the best score) before they could be

combined[31]. For the knee pain score, the visual analogue scale (VAS) pain score and KOOS pain subdomain were used[32]. For the overall knee function score, the KOOS4 composite score, Lysholm knee score scale or IKDC were used. The health-related quality of life score was measured using the SF-36-physical component score. The mental health outcome was derived from the SF-36-mental component scores.

Statistical analysis

The four included trials had both systematically and sporadically missing data. Systematically missing variables were not imputed. Studies with systematically missing outcomes were excluded from the analyses. Sporadically missing data were imputed using multilevel multiple imputations by chained equations assuming that data were missing at random (MAR)[33–36]. Age, gender, and BMI had no missing values, while Tegner Activity Scale and walking ability were missing for 92 and 121 patients, respectively. The pain and overall knee function outcome were sporadically missing at 24 months follow-up. The health-related quality of life score and mental health score were systematically missing in one study (Yim *et al.*). All primary analyses were performed on the imputed data. Detailed information is provided in Additional file 2.

We used both a one-stage and a two-stage approach to analyse the data[37]. In the one-stage approach, the combined IPD was simultaneously analysed using a linear mixed-effects regression model that fully accounts for heterogeneity across studies whilst accounting for the clustering of participants within studies. The mixed-effects regression analysis included all common predictors (e.g., age, gender, BMI etc) and baseline values of the evaluated outcome (e.g., knee pain, overall knee function, health-related quality of life or mental health score) as fixed effects, while patient number, trial number and time were added as random effects. Continuous variables that were known for having a non-linear functional form (e.g., age, BMI, baseline score) were analysed using restricted cubic splines with five knots[31]. In the two-stage approach, we performed the same mixed-effect regression analyses for each study separately to obtain study-specific treatment effect estimates. Thereafter, we pooled the outcomes in a random-effects meta-analysis To reflect the variation of the treatment effect in a different setting, 95% prediction intervals were reported[38].

Effect modification was investigated by testing the interaction between APM and predefined patient characteristics in a multivariable linear mixed-effects model similar to the one-stage approach[25]. The patient characteristics tested for effect modification were described in Table I.

The effect modifiers were tested as overall, within-study, and across-study interactions to avoid ecological bias[39]. Although not described in the protocol, we also performed exploratory generalized linear mixed-effects model trees (GLMM trees) to detect potential complex variable interactions (two or three-way interactions).

All analyses were performed using R (version 4.0.2, The R Foundation for Statistical Computing, Vienna, Austria), using packages mice (version 3.10.0), lme4 (version 1.1–23), glmertree (version 0.2–0) and data.table (version 1.12.8)[40–44].

Sensitivity analyses

To avoid data availability bias, the aggregated main study effects of the six excluded studies were analysed separately, and additionally combined with IPD data (if the study had 2-year follow-up) in the two-stage meta-analysis. Moreover, we performed an as-treated and per-protocol analysis to analyse the effect of treatment crossover. The patients that did crossover from non-surgical or sham surgery to APM were also analysed separately to check if this subgroup improved after crossing over. These latter two analyses were not described in the protocol.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study as this study is a secondary analysis of existing data. There are plans to disseminate the results of the research to the relevant patient communities.

Results

Search strategy

The initial database searches identified 4195 records and additionally 239 trials were identified through trial registries. After the full-text screening, ten eligible trials remained with 1306 patients in total. Of the ten trials, five shared their IPD[12,13,16–18]. Of the five studies for which no IPD was obtained, two studies did not respond to our (repeated) inquiries[9,15], one study declined participation[11], one study no longer had the IPD available[10], and one study was unable to share the IPD due to a stringent informed consent limiting the ability to share the IPD with another research group[14].

Eventually, after the exclusion of one study with limited follow-up[13], four studies remained resulting in a total set of 605 patients, depicted in Fig. 1[12,16–18].

IPD

No issues were identified when checking the IPD. The study populations ranged from 44 to 319 patients. The mean age of the patients was 54.6 (SD: 7.5), 317 (52%) were female and the mean BMI was 26.5 (SD: 3.7), see also Table II and Additional file 3. All four studies excluded patients with acute locked knees that required surgery. Patients had no prior comorbidity and the right knee was most commonly affected (right: 276 (46%), left: 226 (37%), unknown: 103 (17%)). All patients in the intervention group were assigned to receive APM. In two studies, these patients additionally received a postoperative home exercise program[16,17].

The control treatment was either exercise therapy ($n = 3$)[12,16,17] or sham surgery ($n = 1$)[18], with variations in the length and duration of the exercise therapy. With respect to the primary outcome, two studies used the KOOS scale[12,18], one study used the Lysholm knee score scale[16], and one study used the IKDC[17]. In the intention-to-treat (ITT) analysis, 24 months follow-up was on average completed in 94.6% (range: 89–100) in the intervention group and 93.6% (range: 87–100) in the control group. No information on adverse events of both the APM and control group was available in the datasets.

Overall improvement at 24 months follow-up

All primary analyses were performed according to the ITT principle. At 24 months of follow-up, knee pain had improved in both treatment groups; 24 points (95% confidence interval (CI): 21–27) for APM and 21 points (95% CI: 18–24) for control. Overall knee function also improved in both groups; 24 points (95% CI: 22–26) for APM and 20 points (95% CI: 18–22) for control. The health-related quality of life improved with 11 points (95% CI: 10–12) for APM and 9 points (95% CI: 7–10) for control. The mental health outcome was stable from baseline to 24 months in both

Name	Description
Age	Age of the patient at inclusion
Gender	Gender of the patient
BMI	Body mass index at baseline
Affected knee side	Knee side (left or right leg) with meniscus tear
Meniscus tear location, medial	Location of meniscus tear (medial or lateral)
KL grade	Kellgren Lawrence grade, classifying the severity of osteoarthritis using five grades (0 – no radiological findings; 4 – severe cartilage loss)
Tegner Activity Scale	Self-reported Tegner Activity Scale, grading work and sporting activities on 0–10 scale (low to high activity level)
Mechanical knee symptoms	Self-reported mechanical knee symptoms, ranges from 0 to 1 on a continuous scale, with 0 being always knee symptoms and severely limited function and 1 being no symptoms or limited function.
Walking ability	Self-reported walking ability, on 1–5 scale from "no problems walking about" to "unable to walk about"
Baseline pain score	Pain score at baseline on 0–100 scale
Baseline overall knee function score	Overall knee function at baseline on 0–100 scale
Baseline HRQoL score	Health-related quality of life score at baseline on 0–100 scale
Baseline Mental health score	Mental health score at baseline on 0–100 scale

Table I

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Patient characteristics that were evaluated as potential modifying factors for the treatment effect of APM

groups (APM: 2 points (95% CI: 0–3), control: 1 point (95% CI: 0–3)) (Table III).

Treatment effect APM

At 24 months of follow-up, patients that received APM scored 2.5 points (95% CI: 0.8–4.2) and 2.2 points (95% CI: 0.9–3.6, I^2: 0%, τ^2: 0) better on the knee pain outcome compared to the control group (non-surgical or sham surgery), for the one- and two-stage analysis, respectively. No statistically significant differences were detected on overall knee function at 24 months between APM and control group (1.3 points (95% CI: −0.1 to 2.6) and 1.7 (95% CI: −0.4 to 3.8, I^2: 0%, τ^2: 0.4), for the one- and two-stage analysis, respectively).

Three of the four studies measured the health-related quality of life and mental health[12,17,18]. In these three studies, no statistically significant differences between APM and control group were found on health-related quality of life (0.4 points (95% CI: −0.6 to 1.4) and 0.3 (95% CI: −0.5 to 1.1, I^2: 0%, τ^2: 0), for the one- and two-stage analysis, respectively) and mental health (−0.2 points (95% CI: −1.6 to 1.3) and 0.0 (95% CI: −0.6 to 0.5, I^2: 0%, τ^2: 0), for the one- and two-stage analysis, respectively). The forest plots of the one- and two-stage meta-analysis are displayed in Additional file 4.

Effect modification

All measured factors that could modify the treatment effect were evaluated (Table III). No interaction effects (i.e., differences between subgroups) were detected for the four outcomes on the total, within-study and across-study interactions (Fig. 2 & Additional file 5). Only the baseline mental health score had a statistically significant treatment–covariate interaction on the health-related quality of life outcome score (7.2 points (95% CI: 0.1–14.4)), however, this effect was not detected in either the within or across study interaction and not considered clinically relevant. The GLMM trees showed that the baseline outcome scores (knee pain, overall knee function, health-related quality of life and mental health) and the KL grade at baseline were the most important split variables to determine the outcome differences between the two treatment groups for all four outcomes (Additional file 6). However, the largest detected treatment effect in favour of APM was 5.4 points (95% CI 0.7–10.2) in a small subgroup of patients with severe knee pain (<34 points) at baseline. The other subgroups showed no statistically significant differences between APM and control.

Sensitivity analyses

The six excluded studies with aggregated data ($n = 694$) were analysed separately (Additional file 7-a), but no statistically significant effect of APM was detected on the overall knee function score (standardized mean difference (SMD): 0.04 (95% CI −0.2 to 0.28, I^2: 50%, τ^2: 0.03)). Similar to our main analysis, combining the IPD with aggregated data at 24 months of follow-up (IPD: $n = 605$, aggregated data: $n = 593$) showed that APM did not affect overall knee function score (SMD: 0.08 (95% CI: −0.09 to 0.26, I^2: 51%, τ^2: 0.03) as shown in Additional file 7-b).

In the as-treated analysis (analysing all patients according to the received treatment), no statistically significant treatment effect for APM was detected for all four outcomes in both the one- and two-stage analysis. Similarly, no statistically significant treatment effect for APM was detected on any of the four outcomes when crossover patients were excluded from the analyses. Therefore, no additional subgroup analyses were performed.

Patients in the control group (exercise therapy or sham surgery) that crossed over to APM (68 patients (22% of patients in the control group)) were analysed separately to check if this group improved after crossover. No statistically significant differences were found in recovery between crossover patients and patients that stayed in the control group on the pain outcome (MD: 2 points, 95% CI: −4.6 to 1.6) after 2 years. Patients that did crossover had more pain at baseline (MD: −4 points (95% CI: −0.1 to −6.8)) and worse overall knee function scores at baseline (MD: −11 points (95% CI: −8.9 to −12.8)) compared to patients that did not.

Risk of bias across studies

The risk of bias was assessed using the Cochrane risk-of-bias tool for randomised trials (Additional file 8). The overall bias showed

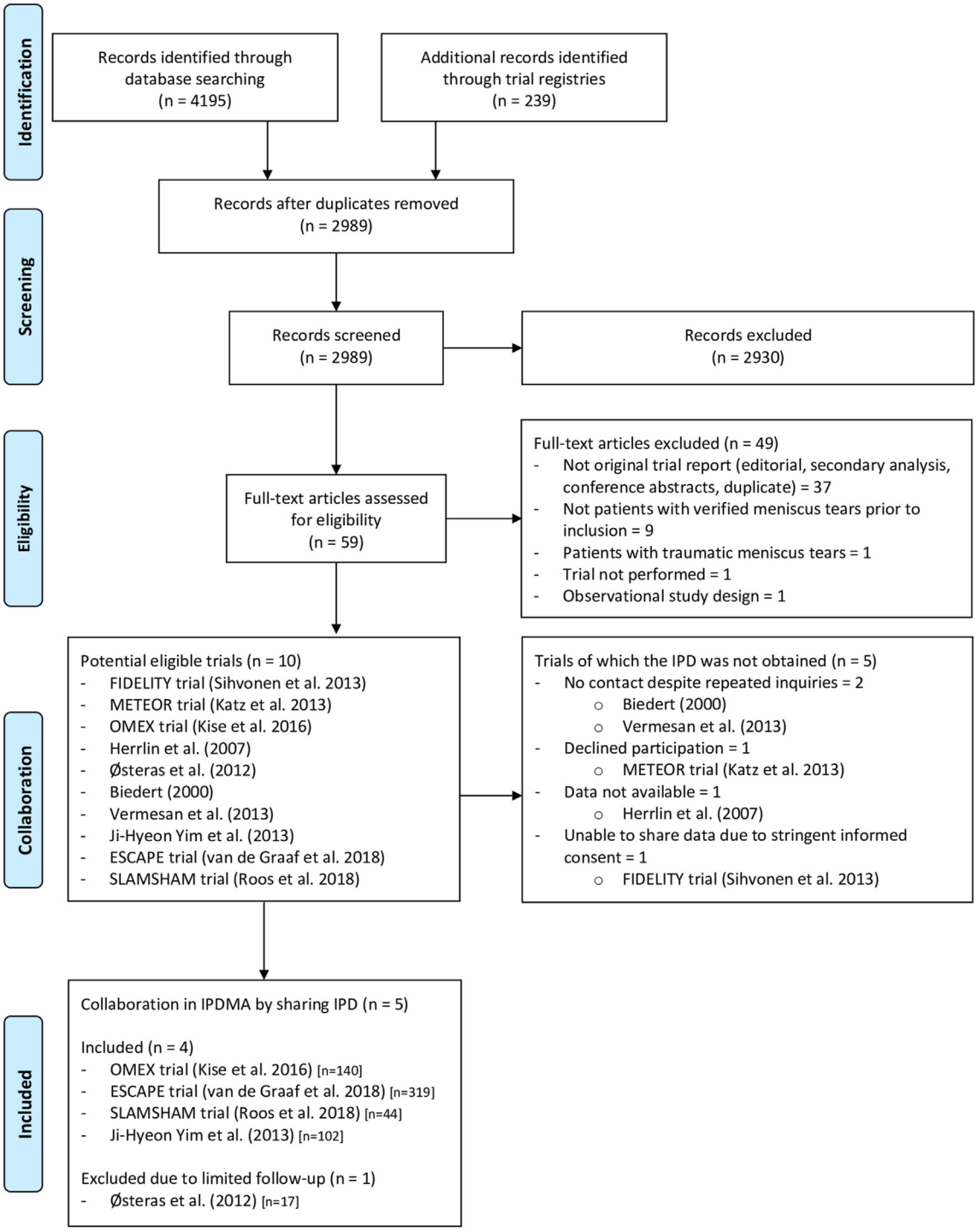

Fig. 1

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PRISMA flow chart of the systematic review detailing studies that shared IPD and were included. IPD, individual participant data.

	Control ($n = 305$)	APM ($n = 300$)
Age, mean (SD)	55.0 (7.7)	54.2 (7.4)
Gender, *n* (%)		
Female	160 (52.5)	157 (52.3)
Male	145 (47.5)	143 (47.7)
BMI, mean (SD)	26.8 (3.8)	26.3 (3.6)
Affected knee side, *n* (%)		
Left	117 (38.4)	109 (36.3)
Right	135 (44.3)	141 (47.0)
Missing	53 (17.4)	50 (16.7)
Location of meniscus tear		
Medial	280 (91.8)	268 (89.3)
Lateral	25 (8.2)	30 (10.0)
Missing	0 (0.0)	2 (0.01)
Maximal flexion, degree (SD)	132.5 (12.8)	133.0 (10.5)
Kellgren Lawrence grade, *n* (%)		
0	94 (30.8)	99 (33.0)
1	58 (19.0)	54 (18.0)
2	80 (26.2)	88 (29.3)
3	56 (18.4)	45 (15.0)
4	5 (1.6)	6 (2.0)
Missing	12 (3.9)	8 (2.7)
Tegner activity scale, mean (SD)	2.9 (1.9)	3.0 (2.0)
Self-reported mechanical knee symptoms, mean (SD)[a]	0.6 (0.2)	0.6 (0.2)
Self-reported mobility (%)		
No problem walking	38 (12.5)	39 (13.0)
Slight problems walking	65 (21.3)	56 (18.7)
Moderate problems walking	63 (20.7)	59 (19.7)
Severe problems walking	15 (4.9)	25 (8.3)
Unable to walk	0 (0)	0 (0)
Missing	124 (40.7)	121 (40.3)

APM, arthroscopic partial meniscectomy; SD, standard deviation; BMI, body mass index.
[a] Ranges from 0 to 1, with 0 being always knee symptoms and severely limited function and 1 being no symptoms or limited function.

Table II

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Patient characteristics at baseline of the four studies of which IPD was available

some concerns, mainly due to the 'deviations from intended interventions'-domain due to lack of blinding of participants, which is common in surgical trials[45]. The funnel plot of the main study outcome showed some asymmetry, but the total number of studies was regarded too small to confirm potential publication bias (shown in Additional file 9).

Discussion

Our IPD meta-analysis showed that APM has a marginal effect on perceived knee pain levels compared to sham surgery or exercise therapy in patients with MRI-confirmed degenerative meniscus tears. No clinically relevant effect of APM was detected for overall knee function, health-related quality of life or mental health outcomes. Furthermore, although we performed extensive subgroup analyses, we did not identify any relevant subgroup of patients that benefitted from APM compared to sham surgery or exercise therapy, including patients with mechanical symptoms.

Our results are in line with Katz *et al.*, van de Graaf *et al.* and Sihvonen *et al.* whom also reported no between-group difference in functional improvement according to Kellgren–Lawrence grades[11,14,17]. We also confirmed the findings of the secondary analysis of the FIDELITY trial that concluded that patients with mechanical symptoms do not report better effects after APM compared to sham surgery[46]. We were, however, not able to confirm a potential subgroup that modifies the effect of APM based on baseline pain score and BMI such as detected by van de Graaf *et al.*[17].

Strengths and limitations

In this meta-analysis, we used individual participant data to increase the flexibility of our analyses as we were able to extensively check the data and reproduce previously published results. 605 patients were included from four different RCTs executed in different countries, which enabled us to perform extensive subgroup analyses on all the available and heterogeneous evidence, increasing our ability to detect potential subgroups of patients that benefit from APM. Due to the international collaboration, our team consisted of orthopaedic surgeons, physical therapists, and methodological experts that provided useful and relevant feedback on our analyses and helped to define potential subgroups of patients that might benefit from APM. The international collaboration also enabled us to identify national and cultural differences, which can improve the generalisability of our results.

Some limitations should also be discussed. First, of the 10 eligible trials, the IPD from five studies was not available either because the investigators declined to share the data[11], were unable to share data[14], the data was unavailable[10], or because the authors did not respond to our (repeated) requests[9,15]. However, the studies

	Control ($n = 305$)	APM ($n = 300$)
Baseline		
Knee pain	62 (24)	60 (23)
Overall knee function	51 (17)	52 (17)
Health-related quality of life	38 (11)	39 (11)
Mental health	51 (14)	50 (14)
3 months		
Knee pain	76 (21)	81 (18)
Overall knee function	65 (19)	67 (19)
Health-related quality of life	44 (11)	44 (11)
Mental health	52 (13)	49 (13)
6 months		
Knee pain	79 (23)	83 (20)
Overall knee function	67 (19)	69 (19)
Health-related quality of life	44 (11)	46 (11)
Mental health	51 (13)	50 (14)
12 months		
Knee pain	83 (19)	85 (18)
Overall knee function	70 (19)	75 (19)
Health-related quality of life	46 (11)	48 (11)
Mental health	50 (14)	51 (13)
24 months		
Knee pain	83 (21)	84 (20)
Overall knee function	72 (19)	76 (17)
Health-related quality of life	48 (10)	51 (9)
Mental health	52 (11)	52 (12)

Values represent mean (SD). Outcomes are presented on a uniform scale from 0 to 100, with 0 being the worst score and 100 the best score. APM, arthroscopic partial meniscectomy.

Table III Osteoarthritis and Cartilage

Knee pain, overall knee function, health-related quality of life and mental health outcome of the IPD for the intervention and control group at baseline, 3 months, 6 months, 12 months, and 24 months follow-up of four studies for which IPD was available

of which we received IPD were comparable to the studies of which no IPD was received based on comparative treatment, patient inclusion, patient characteristics and study outcomes. Moreover, given that the two largest studies (Katz *et al.* ($n = 330$) & Sihvonen *et al.* ($n = 146$), 69% of aggregated studies) reported no overall treatment effect for APM (when compared to either sham surgery or exercise therapy) and found no exploratory subgroups of patients that benefitted from APM, it is unlikely that additional subgroups will be detected. To avoid data availability bias, we did include the aggregated results in a sensitivity analysis and similar to our main analysis, APM did not improve the overall knee function when compared to sham surgery or non-surgical treatments. Missing values were common in the IPD. To test the robustness of our imputation method, we performed a sensitivity analysis with the original (unimputed) dataset and in a complete case analysis. Both did not alter our conclusions. Second, one-sided crossover was common (22% of patients in the control group) in the included trials. To provide a conservative estimate of the treatment effect we performed all our analyses "as randomised" (intention-to-treat), limiting the effect of crossover in our analyses. However, even in the additional and less conservative "as-treated" analysis, no clinically-relevant treatment effect of APM was detected, indicating the absence of a treatment effect of APM on our main outcomes. We also found no difference between the group that did and did not crossover from control to APM. In addition, we used propensity score matching to match comparable patients but no relevant effect was detected between the patients that did or did not cross over, which suggests that patients who are crossing over have comparable outcomes to patients who do not. However, it is impossible to ascertain how the patients who crossed over would have done without APM. Third, we have analysed over ten potential effect modifying factors in our analyses, but some of these subgroups might be too small for valid subgroup identification due to low power (even though we included 605 patients). However, if we assumed the presence of a true treatment–covariate interaction in a small group of 58 patients (29 APM patients vs 29 control patients), we still had 80% power to detect a moderate to large clinically relevant effect of 15 points for APM (using a standard deviation of 20 points from Table III). Moreover, as no overall relevant treatment effect of APM was detected it is unlikely that other subgroups exist as this would also suggest the presence of a subgroup with a detrimental treatment effect of APM. Fourth, we did not search for subgroups at other time points because even if we were to identify a subgroup at 3- or 6-months follow-up, the potential short-term benefit of this surgical intervention may not outweigh the cost, given that we do not detect a subgroup at 24 months. Moreover, conducting subgroup analysis at multiple time points is likely to result in false positives due to multiplicity, which could be addressed through statistical multiplicity correction, but this would reduce our power to detect a relevant subgroup at 24 months, which was our primary objective. Fifth, we aimed to study the adverse events of both the APM and control group, but unfortunately these were not available in the datasets. From the published reports we found that out of the ten included studies, three studies did not detect a between-group difference in serious adverse events[11,14,17], two studies found more complications in the APM group compared to the comparative treatment[9,18], one did not find any serious adverse events[12], and four studies did not report any adverse events[10,13,15,16]. However, definitions of these (serious) adverse events varied.

Implications

APM resulted in slightly less pain but similar overall knee function, health-related quality of life or mental health, when compared to sham surgery or exercise therapy. There was no evidence for any subgroup of patients with greater benefit from APM compared to non-surgical or sham treatment. This reiterates that APM should not be the first treatment of choice in patients with degenerative meniscus tears because of similar outcomes with non-operative treatment[20]. Given all current evidence, we might conclude that there are no subgroups of patients that benefit from APM. APM might still be indicated for patients with acute or chronically locked knees but this group may represent a minority of patients currently treated with APM, and were not included in this study.

All included trials showed similar improvements on pain, overall knee function score and the health-related quality of life outcome for all patients regardless of the treatment they received, indicating that the symptoms of most degenerative meniscus tears also improve over time without the need for APM[27]. Although not shown in our analyses, this improvement over time on pain- and overall knee function was smaller for overweight patients (BMI over 30) compared to patients with a healthy BMI (18–25), independent of the assigned treatment group. Obese patients generally have a 4.7-fold increased risk of knee osteoarthritis[47] and therefore might show limited improvement compared to patients with a healthy BMI. For this subgroup, it might be beneficial to reduce body weight to improve pain and overall knee functionality[48].

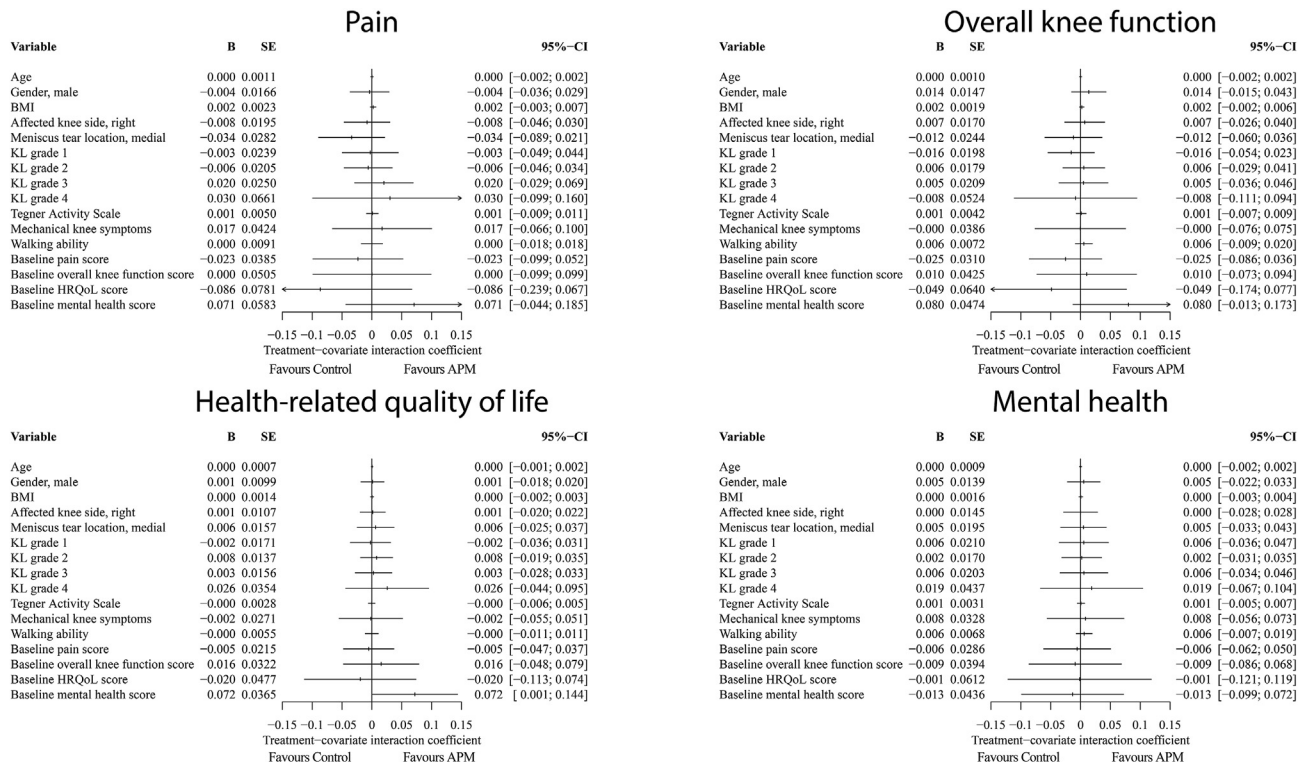

Fig. 2

Osteoarthritis and Cartilage

Forest plot for each outcome (knee pain, overall knee function, health-related quality of life and mental health) displaying the treatment−covariate interaction coefficient of each potential effect modifier (patient characteristics) derived from the multivariable linear mixed-effects model.

Conclusions

We did not identify a relevant subgroup of patients that benefitted from APM with respect to knee pain, overall knee function and health-related quality of life compared to non-surgical or sham treatment. We recommend that physicians minimize the use of APM to treat patients with degenerative meniscus tears because there is no significant advantage over non-surgical treatment.

Ethics approval and consent to participate

All principal investigators provided written confirmation that all participants included in the original trials had given informed consent.

Availability of data and materials

Following the ICMJE's data sharing statement policy, de-identified individual participant data will be made available at the end of the research project, including the study protocol, beginning 9 months and ending 36 months following article publication. The data will be shared with investigators whose proposed use of the data has been approved by a review committee to be identified for this purpose. Proposals may be submitted up to 36 months following article publication. After 36 months the data will be available in our university's data warehouse without investigator support other than deposited metadata.

Authors' contributions

SW, GH, ME and MMR have contributed to the conception and design of the study. SW, MMR, and GH drafted the manuscript. Data was collected by HØ, MAR, EMR, KBH, VAvdG, RWP, HA and JKS. Statistical analyses were performed by SW and GH. All authors have made contributions to the drafting and revising of the article. All authors have read, reviewed and approved the final version of the manuscript before submission. MMR is the manuscript's guarantor.

Conflict of interest

All authors have completed the Unified Competing Interest form (available on request from the corresponding author). Dr. Risberg reports grants from South-Eastern Norway Health Authorities, during the conduct of the study; Dr. van de Graaf reports grants from The Netherlands Organisation for Health Research and Development (in Dutch: ZonMw), grants from Achmea Healthcare Foundation (in Dutch Stichting Achmea Gezonheidszorg fonds), grants from Foundation of medical research OLVG, Amsterdam, the Netherlands, during the conduct of the study; Dr. Englund reports personal fees from Pfizer outside the submitted work. All other authors declared that they received no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, no other relationships or activities that could appear to have influenced the submitted work.

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Supplementary data

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