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Review

A high physical activity level after total knee arthroplasty does not increase the risk of revision surgery during the first twelve years: A systematic review with meta-analysis and GRADE

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ABSTRACT

Background: High physical activity (HPA) levels after total knee arthroplasty (TKA) might be related to increased wear and subsequent aseptic loosening, negatively affecting TKA survival. This systematic review studied the association between activity levels and risk of revision surgery at medium (3–10 years) and long term (>10 years) follow up in patients with TKA.

Methods: Databases (PubMed, Embase) were searched up to 12 October 2021. Studies comparing low physical activity (LPA) and HPA levels in TKA patients and related risk of revision surgery were eligible for inclusion. After data extraction and evaluation of methodological quality, a meta-analysis was performed. Quality of evidence was assessed using the GRADE framework. PROSPERO registration: CRD42020194284.

Results: Five cohort studies and one case–control study met the inclusion criteria, involving 4811 TKA procedures in 4263 patients (mean follow up 4–12 years). Five studies were of moderate methodological quality and one of low quality. Meta-analysis demonstrated no association between HPA level and an increased risk of all-cause revision surgery (risk ratio (RR) 0.62, 95 % confidence interval (CI) 0.24–1.63, level of certainty: very low) or revision surgery due to aseptic loosening (RR 1.33, 95 % CI 0.34–5.24, level of certainty: moderate). Only one study reported on survivorship, with an improved survivorship for the HPA group (odds ratio of 2.4, 95 % CI 1.2–4.7, level of certainty: low).

Conclusion: During the first 12 postoperative years after TKA, there seems to be no increased risk for revision surgery for patients with a HPA level compared with patients with an LPA level.

Abbreviations: ADL, Activities of Daily Living; BMI, Body Mass Index; CI, Confidence Interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HPA, High Physical Activity; IADL, Instrumental Activities of Daily Living; LPA, Low Physical Activity; LEAS, Lower-Extremity Activity Scale; MAQ, Modifiable Activity Questionnaire; MET, Metabolic Equivalent of Task; OR, Odds Ratio; PAS, Physical Activity Survey; PE, Polyethylene; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analysis; RR, Risk Ratio; TKA, Total Knee Arthroplasty; TKRAQ, Total Knee Replacement Activity Questionnaire; UCLA, University of California Los Angeles (activity questionnaire).

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Contents

1. Introduction

Implant survival of total knee arthroplasty (TKA) at medium (3–10 years) and long term (>10 years) is influenced by surgical factors (e.g., alignment [1], fixation technique [2], design [3]) and patient factors (e.g., weight [4]). High physical activity (HPA) levels, often associated with younger patients or with increasing functional demands from older patients [5,6], is also thought to be an important, patient-related factor influencing implant survival [7–10]. HPA levels can result in increased wear, inducing foreign body responses leading to aseptic loosening [10,11], which is the most common reason for revision surgery at medium and long term [12,13]. TKA patients with aseptic loosening are in need of revision surgery, often associated with less satisfactory outcomes. To date, the association between activity levels and implant failure in TKA remains unclear.

Following the primary procedure, the orthopaedic surgeon provides advice on physical activities to the patient [14]. Unfortunately, current guidelines on activity recommendation after TKA are based on expert opinion and surveys only [7,8,15]. Recently, Straat et al. [16] applied the Delphi method to reach consensus regarding recommendations for 27 physical activities following TKA for patients with an average, quick or slow recovery rate. Based on the statement by the Knee Society (2005), sports such as swimming, golf and normal walking are allowed, but doubles tennis is only recommended for experienced players and jogging is not recommended [7].

Two TKA retrieval studies showed a relation between activity levels and wear of polyethylene (PE) inserts [17,18]. In contrast, a recent clinical study showed no increased risk of revision surgery in active patients after TKA [19]. To our knowledge, the risk of revision surgery related to activity level after TKA was not the primary focus of previous systematic reviews or relevant studies on this topic were excluded following their inclusion criteria. Therefore, this systematic review was conducted to study the association between activity levels and the risk of revision surgery at medium (3–10 years) and long term (>10 years) follow up in patients with primary TKA.

2. Material and methods

This systematic review was conducted according to the PRISMA statement of Preferred Reporting Items for Systematic reviews and Meta-Analysis [20]. The protocol for this systematic review was registered in PROSPERO (Identification number: CRD42020194284).

2.1. Search strategy

The electronic databases PubMed and Embase were searched for publications from their start date through to 12 October 2021, with the help of a clinical librarian. In addition, reference lists of selected studies were hand searched to identify additional records. In the databases the following keywords (and related synonyms) were used to build a sensitive, systematic search strategy: “Arthroplasty, Replacement, Knee” [MeSH]; activity; sports [MeSH]; loosening; wear; survival. Within each category (domain, determinant and outcome), the synonyms were combined with “OR.” The three categories were combined with “AND”. The search strategy for each electronic database is presented in the Appendix.

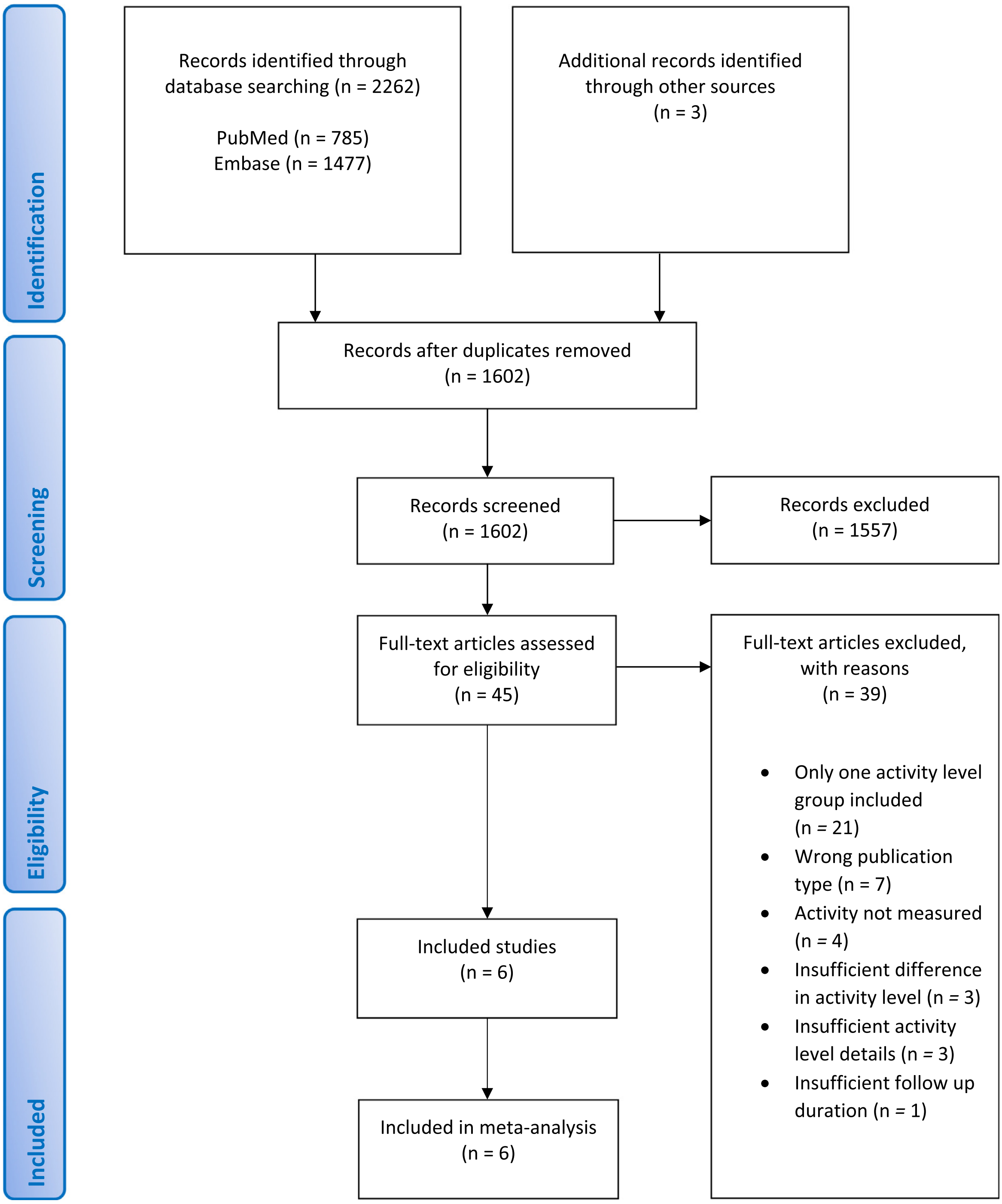

Fig. 1. Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) flow diagram for study inclusion.

2.2. Study eligibility criteria

Studies were included if: (1) patients received primary TKA surgery; (2) recreational and sports activity levels were measured postoperatively with a well-defined activity instrument; (3) the study described at least two distinctly different activity levels; (4) activity levels were compared related to the risk of revision surgery; (5) revision rate at medium- (3–10 years) or long-term follow up (>10 years) was presented, with a minimum mean follow up of 3 years; and (6) the association between physical activity level and revision rate was presented in detail (i.e., number of revisions instead of correlation only). In addition, (7) included study designs were cohort or case–control studies written in English, Dutch or German. Studies were excluded if: (1) a constrained or high-flexion knee prosthesis was implanted; (2) the TKA procedure followed an osteotomy or intra-articular knee fracture; (3) TKA procedures were simultaneously bilateral; (4) measured activity levels were restricted to activities of daily living (ADL) only (i.e., walking, stair climbing); and (5) the publication concerned a retrieval study.

The primary outcome was the rate of revision surgery of TKA at medium- (3–10 years) or long-term follow up (>10 years) in patients with an HPA level compared with patients with a low physical activity (LPA) level. Secondary outcomes were the rate of aseptic loosening and implant survivorship related to the measured physical activity level.

2.3. Study selection

After removal of duplicates all titles and abstracts were screened independently by two authors (AK, WvdW) for eligibility. Disagreements were resolved by discussion. Next, the full-text manuscripts of the selected records were screened independently by these two authors. In case of doubt, consensus was reached by discussion. If full-text manuscripts were not available, authors were contacted via email and a request was placed on ResearchGate. The web application Rayyan QCRI was used for study management. A flow diagram of the selection of studies [20] is presented in Fig. 1.

2.4. Data extraction and risk of bias assessment

The following characteristics of the included studies were extracted by one author (AK) and independently checked by a second author (WvdW): (1) study information: author, year and country; (2) study design with follow up duration; (3) patient inclusion and exclusion criteria; (4) activity instrument and cut-off for at least HPA and LPA groups; (5) details on the study population: size, sex, age, body mass index (BMI) and diagnosis; (6) type of HPA; (7) TKA details: design, method of fixation (with or without cement) and PE insert; (8) risk of revision with calculations of risk ratio (RR) or odds ratio (OR) with 95 % confidence interval (CI); (9) reasons for revision; and (10) implant survival. Disagreements between both authors were resolved by discussion. Relevant authors were contacted via email to obtain missing data.

The risk of bias in each study was evaluated independently by two authors (AK, WvdW) and differing opinions for item scores were resolved by discussion. The Critical Appraisal Skills Programme (2018) CASP Cohort Study Checklist or Case Control Study Checklist was used, depending on study design [21]. This quality assessment method consists of 11 (case–control) or 12 (cohort) items divided into three sections: (a) validity of study results; (b) specific results; and (c) application and implications. Items were assessed with 'yes' (+, good quality), 'can't tell' (?) or 'no' (−, deficiency in methodology). The criteria for defining a study as low, moderate or high quality were arbitrarily defined (see Tables 1 and 2), because to the best of our knowledge cut-off values for CASP checklists are not mentioned in the literature.

2.5. Synthesis of results

A narrative synthesis was used for description of data from the selected studies. Feasibility of a meta-analysis was explored by comparing included studies on homogeneity regarding their exposure – at least HPA versus LPA – and outcome measures, for instance all-cause revision, revision surgery due to aseptic loosening and survivorship. If a meta-analysis was appropriate, an overall estimate of the RR with a 95 % CI was calculated, including I^2 as measure of consistency, using a random effects model in Cochrane's Review Manager 5.3. The results are presented as forest plots including the contribution of each study (weight) to the overall effect (Mantel–Haenszel).

2.6. Grade

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework for prognostic studies was used to assess the quality of evidence for included studies regarding the association between HPA level and three outcomes: all-cause revision, revision surgery due to aseptic loosening and survivorship [22]. The framework was drafted by one author (AK) and independently checked by a second author (PK). Four levels of quality were used: high, moderate, low and very low, with high meaning 'we are very confident that the true effect lies close to that of the estimate of the effect' [23]. Very low means 'we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect' [23]. The starting point for the quality of evidence of the studies was 'high', given the inclusion of studies aimed to investigate the association between physical activity and revision surgery [22]. Next, downgrading the quality of evidence was based on the following five factors: (1) study limitations (majority of studies having a high risk of

Table 1
Methodological quality cohort studies [21]. (See below-mentioned references for further information.)

Cohort studies	**A)** Valid study results		**B)** Specific results									**C)** Application and implications		
	1. Clearly focused issue	2. Cohort recruitment	3. Measurement exposure	4. Measurement outcome	5a. Identification confounders	5b. Accounting for confounders	6a. Follow-up complete	6b. Follow-up duration	7. Results	8. Accuracy of results	9. Belief in results	10. Application to local population	11. Fit with other evidence	12. Implications for practice
Bercovy 2015 [25]	+	+	+	+	+	–	+	+	+	?	?	+	+	+
Crawford 2020 [19]	+	?	?	+	+	+	+	+	+	+	+	?	+	+
Mont 2007 [6]	+	?	+	?	+	+	+	+	+	+	?	+	+	+
Ponzio 2018 [27]	+	?	+	+	+	?	–	+	+	+	?	+	–	+
Valle 2017 [26]	+	?	?	–	–	–	–	+	+	?	?	?	+	?

Classification was based on sections A and B. High quality (low risk of bias): section A two positive (+) scores, section B maximum of two 'can't tell (?)'-items; low quality (high risk of bias): section A $\leq$ 1 positive score, section B $\geq$ 4 items rated as 'no' (–) or 'can't tell'; studies scoring in between these two categories were rated as moderate quality.

Table 2
Methodological quality case–control study [21]. (See below-mentioned references for further information.)

Case-control study	**A)** Valid study results									**B)** Specific results	**C)** Application	
	1. Clearly focused issue	2. Appropriate method	3. Recruitment of cases	4. Selection of controls	5. Measurement exposure	6a. Equal treatment groups	6b. Accounting for confounders	7. Results	8. Accuracy of results	9. Belief in results	10. Application to local population	11. Fit with other evidence
Jones 2004 [24]	+	+	?	+	+	?	+	+	+	?	?	+

Classification was based on section A. High quality (low risk of bias): ≤ 1 'can't tell (?)'-item; low quality (high risk of bias): ≥ 4 items rated as 'no' (−) or 'can't tell'; studies scoring in between these two categories were rated as moderate quality.

bias or the minority of studies having a prospective study design); (2) inconsistency (I^2 > 50 %); (3) indirectness (not fully representative population, not specifically aseptic loosening as outcome); (4) imprecision (less than 10 revision surgeries per study; or 95 % CI of the effect size includes 1, unless the boundaries of the lower and upper limit of the 95 % CI are smaller than 0.8–1.2, indicating high certainty of no effect of HPA on the outcome measure; or the range of the 95 % CI is larger than 0.5 (effect size < 1) or larger than 2 (effect size > 1), indicating uncertainty regarding the effect of HPA); and (5) publication bias present (yes). Finally, study findings with moderate or large effect sizes (i.e., upper limit of 95 % CI risk estimate < 0.5 or lower limit 95 % CI risk estimate > 2) and the presence of an exposure–response relationship in the majority of studies (yes) resulted in upgrading the quality of evidence [22].

3. Results

3.1. Study selection

The electronic and hand searches combined yielded 2265 articles. After removing 663 duplicates, 1602 articles remained for screening on title and abstract. Forty-five full-text articles were reviewed of which 39 were excluded. Six studies [6,19,24–27] met all inclusion criteria and were eligible for meta-analysis. See Fig. 1 for a flow diagram of the study selection process.

3.2. Study characteristics

The six included studies [6,19,24–27] involved a total of 4263 patients (min–max: 52 [24] – 2016 [27]) with 4811 TKA procedures, and follow up varied from a mean of 4 [24] to 12 years [26]. Six distinct activity questionnaires were used to measure activity levels. In addition, the HPA characteristics showed some variation between studies. One study included patients mostly involved in low-impact activities with low or moderate intensity, such as walking (65 %) and gardening (77 %) [24]. A second study reported low- to moderate-impact activities (walking 89 %, swimming 53 %, and training with strength-training equipment 46 %) in the HPA group with a very high frequency (average of 11 times a week) [6]. A third study reported low- to moderate-impact activities such as walking (42.5 %), cycling (37.5 %) and downhill skiing (10.0 %) with a minimum of three times a week [26]. In the fourth study the HPA group had a mean postoperative Lower-Extremity Activity Scale (LEAS, 1–18) score of 13.7 (standard deviation (SD) ± 2.7) with 5.6 % of these patients reporting the highest possible LEAS outcome of 18 (vigorous sports participation) [27]. In the remaining two studies [19,25] HPA patients participated in high-impact sports such as jogging or running, tennis, water-skiing and martial arts, but different cut-offs were used to define the HPA group (University of California Los Angeles (UCLA, 1–10) activity questionnaire score ≥ 6 [19] versus UCLA score ≥ 8 [25]). All study characteristics, including reported implant characteristics, are presented in Table 3.

3.3. Methodological quality

The methodological quality of five studies was rated as moderate [6,19,24,25,27] and for one study as low [26]. The quality assessment for each study is presented in Table 1 (cohort studies) and Table 2 (case–control study).

3.4. Results of individual studies

3.4.1. All-cause revision surgery

Five studies [19,24–27] presented results regarding HPA level in relation to the risk of all-cause revision surgery. Two studies indicated a protective effect (RR 0.09 and 0.42) of HPA levels at medium- (mean 7.5 years) [25] and long-term (mean 11.4 years) [19] follow up. In both studies a small proportion of patients, 1.7 % (34 knees [19]) and 9.9 % (49 knees [25]), participated in high-impact sports such as jogging and tennis. Bercovy et al. [25] reported no revisions (0 %) in the HPA group and 12 all-cause revisions (3.5 %, $P = 0.022$) in the LPA group. In the study by Crawford et al. [19] the all-cause revision in the HPA group was 1.7 % compared with 4.0 % in the LPA group ($P = 0.003$), while the revision for aseptic failure was 1.3 % in the HPA group compared to 3.0 % in the LPA group ($P = 0.015$).

Two studies reported a comparable risk of revision in the HPA and LPA groups at mid-term follow up (mean 4 years [24], OR of 0.99; OR of 0.18 and RR of 0.32) and long-term follow up (mean 12 years [26], RR of 0.64). The study of Valle et al. [26] observed a lower risk of revision in the HPA group (15.2 %) than in the LPA group (23.8 %, $P = 0.495$), without reaching statistical significance. Reasons for revision were not reported. The case–control study by Jones et al. [24] found no association between leisure activity (OR 0.99, 95 % CI 0.99–1.02), occupational activity (OR 0.99, 95 % CI 0.99–1.01) or instrumental activities of daily living (IADL that allow an individual to live independently, such as cooking, cleaning and laundry; OR 1.00, 95 % CI 1.00–1.01) and the risk of revision surgery. The same result was seen for total historical physical activity (past leisure and occupational activity combined) in their adjusted multivariate model. The corresponding OR was 0.99 (95 % CI 0.99–1.01) with no association with the risk of revision surgery. Basically, for the cases a median of 44.5 Metabolic Equivalent of Task (MET)-hours of total historical physical activity per week (average number of hours per week for each activity, multiplied by

Table 3
Study characteristics.

Study	Study design	Inclusion and exclusion criteria	Activity instrument and cut-off	Study population	HPA details	TKA details
Bercovy et al. [25] (2015) France	Prospective cohort Mean 7.5 years FU (min–max 5–13 years; 123 knees with >10 years FU)	Inclusion: Unilateral or staged bilateral TKA Complete assessment at ≥5 years FU Exclusion: Severe psychiatric, neurologic or locomotor disability	UCLA activity score (1–10) LPA: UCLA ≤7 HPA: UCLA ≥8	Included: 584 knees (482 patients) Age: 70.6 (min–max 40.1–91.2) Female: 65.9 % BMI: 29.6 (19.8–47.6) Diagnosis: OA 91.8 %/ON 2.9 %/RA 2.7 %/post-traumatic 2.6 % Analysed: 494 knees (403 patients): LPA: 347 knees/HPA: 147 knees No separate characteristics presented for LPA and HPA groups	UCLA 8 (97 knees): golf, backpacking, dancing UCLA 9 (31 knees): tennis, water-skiing, downhill skiing, etc. UCLA 10: (18 knees): marathon running, parasailing, martial arts 1 knee: unknown	ROCC with sacrificing PCL 38 (6.6 %) cemented femoral components 391 (66.9 %) cemented tibial components PE: compression moulded
Crawford et al. [19] (2020) USA	Prospective cohort Mean 11.4 years FU (min–max 5.1–15.9 years, SD: 1.9 years; 1745 knees ≥10 years FU)	Inclusion: ≥5 years FU or earlier revision surgery Exclusion: No postoperative UCLA score	UCLA activity score [a] (1–10) LPA: UCLA ≤5 HPA: UCLA ≥6	LPA: 1210 knees (978 patients) Age *: 64.9 Female *: 72.7 % BMI *: 34.6 Diagnosis: not reported HPA: 828 knees (633 patients) Age *: 62.3 Female *: 53.7 % BMI *: 32.8 Diagnosis: not reported	UCLA 6 (604 knees, 29.6 %) UCLA 7 (114 knees, 5.6 %) UCLA 8 (76 knees, 3.7 %) UCLA 9 (28 knees, 1.4 %) UCLA 10 (6 knees, 0.3 %) No detailed sports participation per patient	Vanguard, no details on exact type 100 % cemented PE: compression moulded
Jones et al. [24] (2004)	Case–control, retrospectively matched Mean 4 years FU of activity (min–max	Inclusion: Unilateral or bilateral TKA Age ≥25 years Cases: revision surgery	Structured telephone interview using MAQ and YALE PAS to assess: (a) Leisure activity (b) Occupational activity (c) IADL	52 knees (52 patients) Age 70.5 (SD: 8.9; min–max 47–85) Cases: 26 knees (26	High-intensity leisure and occupational activities: median 0 % in cases and controls High-impact leisure activities: 0 cases (0 %) and 2 controls (8 %)	Cases: 20 (80 %) PCL-retaining 6 (23 %) cemented femoral components

(continued on next page)

Table 3 (*continued*)

Study	Study design	Inclusion and exclusion criteria	Activity instrument and cut-off	Study population	HPA details	TKA details
USA	1–10 years, SD: 2 years)	Controls: no history of revision TKA Exclusion: Implant failure ≤2 years after TKA History of knee infection, resection arthroplasty, lower extremity arthrodesis or amputation ≥1 revision surgery	Total historical physical activity = (a) + (b) All outcomes in MET-hours per week; high-intensity activities: ≥6 MET	patients) Female: 65 % BMI: 30.3 (SD: 6.4) Diagnosis: OA Total historical physical activity: median 44.5 MET-hours per week (min–max 0–137) Controls: 26 knees (26 patients) Female: 65 % BMI: 30.3 (SD: 8.4) Diagnosis: OA Total historical physical activity: median 55.1 MET-hours per week (min–max 0–278)	Most frequent leisure activity: Cases = walking (65 %) Controls = gardening (77 %) Most frequent occupational activities: Cases = retirement (42 %) and homemaker (39 %) Controls = retirement (54 %) and homemaker (23 %)	15 (58 %) cemented tibial components Controls: 13 (52 %) PCL-retaining 18 (69 %, $P<0.05$) cemented femoral components 26 (100 %) cemented tibial components PE: no details reported
Mont et al. [6] (2007) USA	Prospective, matched cohort Mean 7 years FU (min–max 4–14 years)	Inclusion: Unilateral or bilateral TKA ≥4 years FU Charnley A or B Exclusion: No details provided	Screening question: "rate your usual activity/energy level" Then classification with the use of the self-developed TKRAQ [a] calculation of weighted activity score based on frequency and impact points LPA: very low activity to moderately active on question and TKRAQ <9 HPA: active to extremely active on question and TKRAQ ≥9	144 knees (114 patients) LPA: 72 knees (57 patients) Age: 71 (min–max 41–85) Female: 65.3 % BMI: 28.3 (16–42) Diagnosis: OA 98.2 %/ON 1.8 % Mean weighted activity score: 3.7* (0–8) HPA: 72 knees (57 patients) Age: 69 (min–max 45–86) Female: 65.3 % BMI: 29.5 (23–42) Diagnosis: OA 98.2 %/RA 1.8 % Mean weighted activity score: 14.7* (9–27)	Walking (89 %), swimming (53 %), weight machines (training with strength training equipment, 46 %), gardening activities (44 %), stationary biking (37 %), dancing (32 %), cycling [b] (21 %), hiking [b] (19 %), tennis [b] (18 %), carpentry/construction [b] (16 %), golf [b] (9 %), jogging [b] (7 %), yoga [b] (7 %), bowling [b] (4 %), ice-skating [b] (2 %) and skiing [b] (2 %) Average: 11 times a week	PCL-retaining only Equal distribution of fixation method in HPA and LPA, no further details PE: no details reported

Table 3 (*continued*)

Study	Study design	Inclusion and exclusion criteria	Activity instrument and cut-off	Study population	HPA details	TKA details
Ponzio et al. [27] (2018) USA	Prospective, matched cohort Mean FU not reported (min–max 5–10 years)	Inclusion: Unilateral TKA Complete pre- and 2 years postoperative measurements Exclusion: No OA History of ipsilateral knee surgical procedure LEAS ≤6	LEAS activity score (1–18) LPA: LEAS 7–12 HPA: LEAS 13–18	2016 knees (2016 patients) LPA: 1008 knees (1008 patients) Age: 66.3 (SD: 9.0) Female: 43.5 % BMI: 28.4 (SD: 4.9) Diagnosis: OA Mean LEAS baseline 9.1* (SD: 1.7) Mean LEAS 2 years FU 11.6 (SD: 2.9) with n = 727 HPA: 1008 knees (1008 patients) Age: 66.3 (SD: 9.1) Female: 43.5 % BMI: 28.3 (SD: 5.0) Diagnosis: OA Mean LEAS baseline 14.6* (SD: 1.2) Mean LEAS 2 years FU 13.7 (SD: 2.7) with n = 772	No details about physical activity of patients with LEAS 13–17 Baseline LEAS 18 (daily vigorous sports participation): LPA 0 %, HPA 3.5 % 2 years FU LEAS 18 (daily vigorous sports participation): LPA 0.83 %, HPA 5.6 %	Design: not reported Fixation method and PE: no details reported
Valle et al. [26] (2017) Germany	Prospective cohort Mean 12 years FU	Inclusion: No details provided Exclusion: Persistent pain NRS >2 Reoperation between index surgery and study inclusion Extension deficiency <100° knee flexion	Unspecified standardized questionnaire: practising sports yes/no LPA: no sports activity HPA: sports participation ≥3 times a week	130 patients (LPA: 42, HPA: 88) Age: 69.2 Female: 47.7 % BMI: not reported Diagnosis: not reported 7 years FU, LPA: 27, HPA: 60 12 years FU, LPA: 21, HPA: 46, total 67 patients, no characteristics presented for LPA/HPA	7 years FU: walking (42.5 %), cycling (37.5 %), swimming (35.0 %), golf (15.0 %), Nordic walking (12.5 %), cross-country skiing (15.0 %) and downhill skiing (10.0 %) 12 years FU: not presented	Design: not reported 100 % cemented PE: no details reported

BMI, body mass index in kg/m^2; FU, follow up; HPA, high-physical-activity group; IADL, instrumental activities of daily living; LPA, low-physical-activity group; LEAS, Lower-Extremity Activity Scale; MAC, Modifiable Activity Questionnaire; MET, metabolic equivalent; NRS, Numeric Rating Scale; OA, osteoarthritis; ON, osteonecrosis; PAS, Physical Activity Survey; PCL, posterior cruciate ligament; PE, polyethylene; RA, rheumatoid arthritis; ROCC, Rotating Concave–Convex; SD, standard deviation; TKA, total knee arthroplasty; TKRAQ, Total Knee Replacement Activity Questionnaire; UCLA, University of California Los Angeles activity score.

[*] Significant difference, $P < 0.001$.

[a] Questionnaire presented in article.

[b] Estimation from figure in article.

Table 4
Study results.

Study	Risk of revision	Reasons for revision	Survivorship
Bercovy et al. [25]	RR[a] all-cause, HPA group: 0.09 95 % CI 0.01–1.58 [b], P^+=0.022 * RR[a] aseptic loosening, HPA group: 0.34 95 % CI 0.02–6.46 [b], P^+=0.558	All-cause: 12 knees (all in LPA) due to aseptic loosening (n = 2)/ early fixation failure (n = 1)/late sepsis (n = 7)/fracture with implant revision (n = 2) No details provided: 3 knees	All cases mean 13 years survivorship All-cause: 97.5 % (95 % CI, 96.3–98.8) Aseptic loosening: 99.4 % (95 % CI, 98.8–100)
Crawford et al. [19]	RR[a] all-cause, HPA group: 0.42 95 % CI 0.23–0.75, P=0.003 RR[a] aseptic failure, HPA group: 0.45 95 % CI 0.23–0.87, P=0.015 RR[a] aseptic loosening, HPA group: 0.73 95 % CI 0.13–3.98, P^+=1.00	Infection: LPA n = 13, HPA n = 3 Aseptic failure: LPA n = 36, HPA n = 11 Aseptic loosening: LPA n = 4, HPA n = 2	HPA: OR 2.4 (95 % CI 1.2–4.7, P=0.011) All-cause 12-year survivorship: LPA: 95.3 % (95 % CI 94.6–96) HPA: 98 % (95 % CI 97.4–98.6, P=0.003) Aseptic loosening 12-year survivorship: LPA: 96.3 % (95 % CI 95.6–97) HPA: 98.4 % (95 % CI 97.9–98.9, P=0.02)
Jones et al. [24]	Total historical physical activity: OR 0.99 (95 % CI 0.99–1.01) Leisure: OR 0.99 (95 % CI 0.99–1.02) Occupational: OR 0.99 (95 % CI 0.99–1.01) IADL: OR 1.00 (95 % CI 1.00–1.01) RR[a] all-cause, HPA group: 0.32 95 % CI 0.03–4.08 [b], P^+=0.49	Cases: PE failure (42 %); component loosening (38 %); patellar instability (12 %); arthrofibrosis (4 %); oversized components (4 %). Controls: no revisions	Not applicable
Mont et al. [6]	RR[a] aseptic loosening, HPA group: 1.00 95 % CI 0.06–15.69 [c], P^+=1.00	HPA and LPA groups: no revisions	100 % at mean FU of 7 years (min–max. 4–14)
Ponzio et al. [27]	RR[a] all-cause, HPA group: 2.00 95 % CI 1.10–3.62, P=0.019 RR[a] aseptic loosening, HPA group: 8.00 95 % CI 1.00–63.85, P^+=0.039**	All-cause: LPA n = 16, HPA n = 32 Aseptic loosening: LPA n = 1, HPA n = 8	–
Valle et al. [26]	RR[a] all-cause, HPA group: 0.64 95 % CI 0.23–1.78, P^+=0.495	Reasons not reported	–

CI, confidence interval; FU, follow up; HPA, high-physical-activity group; IADL, instrumental activities of daily living; LPA, low-physical-activity group; OR, odds ratio; PE, polyethylene; RR, relative risk.
P^+ = P-value calculated from original data and Fisher's exact test instead of Chi-squared in case a cell has an expected count < 5.
* Although the P-value is significant on an $\alpha = 0.05$ level, the 95 % CI is not significant due to the applied zero-cell correction technique.
** This P-value is different from the P-value of 0.238 reported by the authors, who did a within-group comparison using n = 48 patients with a revision.
[a] Calculated using raw data extracted from article.
[b] Zero-cell correction by adding a fixed value (0.5) to all cells of study results table, in accordance with the meta-analysis.
[c] Zero-cell correction by adding a fixed value (1.0) to all cells of study results table, in accordance with the meta-analysis.

the activity's metabolic equivalent, min–max: 0–137) was reported. This is less compared with the controls (median 55.1, min–max: 0–278). No case (0 %) and only two controls (7.7 %) engaged in high-impact leisure activities, resulting in an OR of 0.18 (95 % CI 0.01–4.05) and a RR of 0.32 (*P* = 0.49) [24].

In contrast, one study showed a higher risk (RR 2.00) of revision in the HPA group, at 5–10 years following TKA (mean follow up not presented) [27]. The all-cause revision risk in the HPA group was 3.2 % compared with 1.6 % in the LPA group, *P* = 0.019 [27]. However, in the multivariable model, LEAS level and activity level (HPA compared to LPA) were no risk factors for revision surgery and only age > 64 years at the time of TKA remained significant (OR = 2.51, *P* = 0.014) [27].

3.4.2. Revision surgery due to aseptic loosening

Four studies [6,19,25,27] reported on results regarding HPA level and the risk of revision surgery due to aseptic loosening. Two studies [19,25] reported a lower (although not statistically significant) risk for the HPA group (RR 0.34, 95 % CI 0.02–6.46 [25] and RR 0.73, 95 % CI 0.13 –3.98 [19]). Bercovy et al. [25] had no revisions (0 %) in the HPA group and three revisions (0.9 %) in the LPA group for aseptic loosening (*P* = 0.558). In the study of Crawford et al. [19], this outcome was 0.24 % in the HPA group compared with 0.33 % in the LPA group (*P* = 1.00). One study showed no difference (RR 1.00) between HPA and LPA groups, because Mont et al. [6] recorded no revision for aseptic loosening in either the HPA or LPA patient cohorts (*P* = 1.00). The fourth study showed a significant, opposite effect of an eight-times higher risk of aseptic loosening for the HPA group [27]. This study by Ponzio et al. [27] reported 0.8 % (n = 8) revisions due to aseptic loosening in the HPA group versus 0.1 % (n = 1) in the LPA group (*P* = 0.039).

3.4.3. Survivorship

Two studies examined survivorship [19,25], of which one compared survivorship between the HPA and LPA groups [19]. Crawford et al. [19], after controlling for age, sex, preoperative pain, Knee Society clinical and functional scores and BMI, reported an OR of 2.4 (95 % CI 1.2–4.7) for improved survivorship in the HPA group. This study also reported a better 12-year survivorship for aseptic loosening in the HPA group compared with the LPA group (98.4 % vs 96.3 %, respectively, *P* = 0.02) [19]. All study results are presented in Table 4.

3.5. Synthesis of results

The meta-analysis, based on one low- [26] and three moderate-quality [19,25,27] cohort studies, and on one moderate-quality case–control study [24], showed that an HPA level was not a risk factor for all-cause revision surgery (RR 0.62, 95 % CI 0.24–1.63, Fig. 2).

The meta-analysis regarding the risk of revision surgery due to aseptic loosening, based on four moderate-quality cohort studies [6,19,25,27], showed no association between HPA and an increased risk of revision surgery (RR 1.33, 95 % CI 0.34–5.24, Fig. 3).

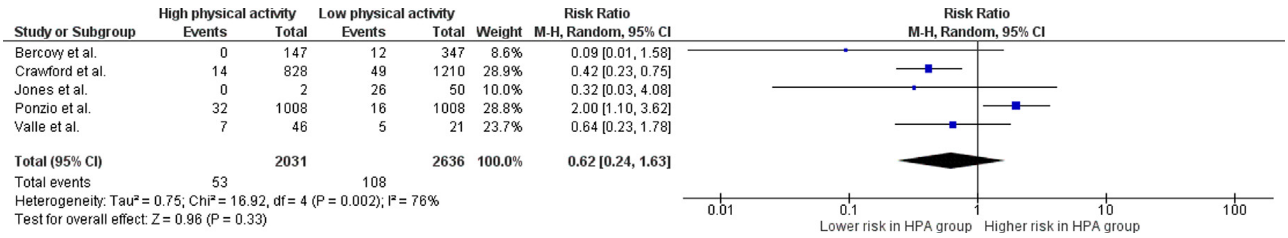

Fig. 2. Forest plot of the association between high physical activity level and the risk of all-cause revision surgery, expressed as a risk ratio. CI, confidence interval; HPA, high physical activity; M–H, Mantel–Haenszel.

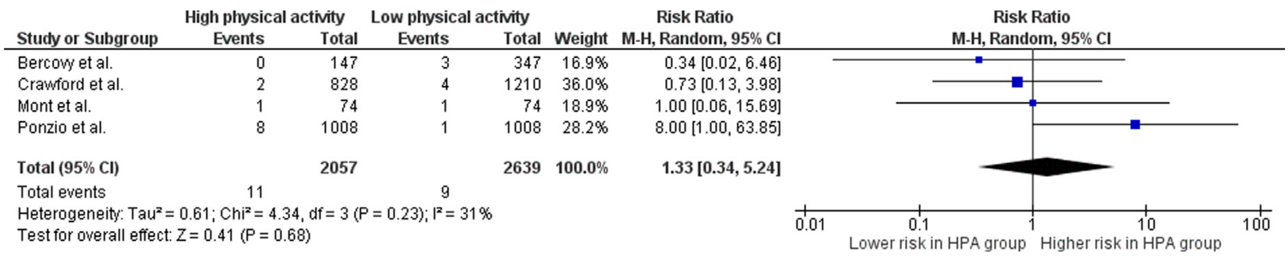

Fig. 3. Forest plot of the association between high physical activity level and the risk of revision surgery due to aseptic loosening, expressed in a risk ratio. CI, confidence interval; HPA, high physical activity; M–H, Mantel–Haenszel. Due to the reporting of no events in both arms in the study of Mont et al. [6], zero-cell correction has been applied in this study by adding a fixed value of 1.0 to all cells of the study results table.

Table 5
GRADE framework [22] regarding the association between a high physical activity level and three outcomes.

Outcome	Possible downgrades							Possible upgrades		Overall quality
	Risk of bias		Inconsistency	Indirectness		Imprecision	Publication bias strongly suspected	Moderate/ large effect size present	Dose–response present	
	# Studies with high risk of bias	# Prospective cohort studies	Heterogeneity (I^2>50 %)	Outcome	Patients	#Total cases; #studies with cases <10 Significant effect (risk estimate, 95 % CI)				
All-cause revision [19,24–27]	1/5	4/5	76 % ↓	Yes ↓	No	161; 0/5 RR 0.62 (0.24–1.63) ↓	No	0.62	NR	Very low
Revision surgery due to aseptic loosening [6,19,25,27]	0/4	4/4	31 %	No	No	18; 4/4 RR 1.33 (0.34–5.24) ↓	No	1.33	NR	Moderate
Survivorship [19]	0/1	1/1	NA	Yes ↓	No	63; 0/1 OR 2.4 (1.2– 4.7, range 3.5) ↓	No	2.4	NR	Low

CI, confidence interval; NA, not applicable; NR, not reported; ↓ downgrade; #, number.

Implant survivorship was reported by one study only [19]. Therefore, no meta-analysis was possible. As reported above, this study reported an improved survivorship for the HPA group with an OR of 2.4 (95 % CI 1.2–4.7).

3.6. Grade

The evidence for the prognostic factor HPA level on the risk of all-cause revision surgery was rated as of very low quality, based on three downgrades and no upgrades (Table 5). This means that 'We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect' [23].

In contrast, the rating of the evidence for HPA level on the risk of revision surgery due to aseptic loosening was of moderate quality, based on one downgrade (due to imprecision) and no upgrades. In GRADE terminology, this means 'We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different' [23].

The level of certainty for HPA on implant survivorship was rated as 'low', based on two downgrades and no upgrades. This means that 'Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect' [23].

4. Discussion

The most important finding of this systematic review was that meta-analysis showed no association between an HPA level and an increased risk of all-cause revision surgery or revision surgery due to aseptic loosening. The single study reporting implant survivorship even showed an improved survivorship with HPA level. The evidence for HPA level on the risk of all-cause revision surgery was of very low quality according to GRADE, but of moderate quality regarding the risk of revision surgery due to aseptic loosening and of low quality for implant survivorship.

Two previously published systematic reviews also had an interest in the association between activity levels and the risk of revision surgery. Jassim et al. [28] explored whether patients were able to return to athletic activity after TKA, with a secondary aim to evaluate implant survival. They found no increased risk of implant failure in active patients, based on a retrieval study [17] (not included in this review) and a case–control study by Jones et al. [24] (included in this review). The second systematic review focused on which host factors (e.g., sex, BMI and activity levels) affect aseptic loosening after TKA. With respect to activity levels, they were unable to include studies due to strict eligibility criteria [29]. After completion of both reviews [28,29] more studies on this topic were published, of which four were included in this systematic review.

Besides patient studies, there are implant retrieval studies which examined the relation between activity levels and wear of PE inserts. Lavernia et al. [17] reported on 28 TKA implants retrieved during autopsy in which patients with higher activity levels (UCLA activity score 5–6) had more wear of PE inserts than those with less activity (UCLA activity score 1–4). In this retrieval study no patients with UCLA > 6 were included. Rather surprisingly, increased wear was associated with the preoperative UCLA score but not with the postoperative UCLA score [17]. Rohrbach et al. [18] found substantial wear in PE inserts in both autopsy and revision retrievals (n = 49), and a higher activity level was associated with increased wear ($P = 0.025$). They concluded that wear was promoted by activity over time [18]. Although these retrieval studies show that insert PE wear is increased with HPA levels, the majority of the clinical patient studies included in this review [6,19,24–26] do not show higher revision rates with higher activity.

The included studies of this review provided limited information [19,25] or no details at all [6,24,26,27] on PE insert characteristics. Cross-linking and additives such as vitamin E have improved wear and ageing properties [30,31]. In addition to materials used, the studies contain little information about technical aspects of the TKA procedure and these have an unquestionable influence on the result. This might explain, to a certain extent, the observed differences in revision rates which ranged from 0 % to 23.8 %. Specifically, the study of Valle et al. [26] reported high revision rates in both the HPA (15.2 %) and LPA groups (23.8 %), without providing any clarification. Although this study had the longest follow up (mean 12 years), the revision percentages were much higher compared with the study by Crawford et al. (0.24–4.0 %) [19] who had an almost similar follow up duration (mean 11.4 years).

A strength of the present review is the extensive search with the help of a clinical librarian. A second strength is that the association between HPA level and three outcomes (all-cause revision, revision surgery due to aseptic loosening and survivorship) was studied. The results were evaluated using both meta-analysis and GRADE. Some limitations must be considered. First, the variety of questionnaires that was used in the included studies to measure activity level. These studies reported use of reliable, validated questionnaires [32–37] and a self-developed questionnaire with unknown psychometric properties [6]. Valle et al. [26] presented no details on the questionnaire used. It is important to realize that even validated activity questionnaires do not encompass all dimensions of activity. For example, the UCLA scores highest activity but without measuring duration and intensity. Secondly, the definition of high-level activity was heterogeneously defined throughout all studies. Patients in the HPA group participated in sports with clearly varying impact, from both low-impact sports (e.g., walking, swimming) to high-impact sports (e.g., running, tennis). Thirdly, confounding factors may influence TKA implant survival. Several prognostic factors are associated with an increased risk for revision surgery following TKA, such as younger age, uncemented components and implant malalignment [38], and taking this into account is important. Four [6,19,24,27] of six studies reported confounding factors (e.g., age, sex and BMI) used for matching of study groups and/or adjusting risk calculations. However, confounding factors related to the implant, such as type of PE, TKA design (retaining or sacrificing the posterior cruciate ligament) and method of fixation were scarcely [6] or not used for this purpose. Also, meta-analysis takes into account study population size, but not confounders.

According to our results, there should be a reconsideration of activity recommendations after TKA. In contrast to current consensus, TKA patients who want to participate in more intense recreational and sports activities should not be deterred from doing so. Patients can be encouraged to remain physically active after TKA, even at a higher level, in which physical activity can contribute to improvements of physical and mental health [7,39,40]. In counselling patients on postoperative physical activities, it is the authors opinion that if patients want to undertake technically demanding activities, such as downhill skiing or singles tennis, preoperative experience in these activities is advised [41].

More long-term, high-quality studies assessing the relationship between activity levels and revision surgery are needed to corroborate our results. Future studies related to physical activity after TKA should report activities in more detail. Activity type, frequency, duration and intensity are of more interest, than solely use of self-reported activity questionnaires. Alternatives might be patient-reported highest exercise-related activity, which can be expressed as a rate of energy expenditure using MET values [42]. Also, use of unobtrusive wearable sensors might provide more objective data related to quantify activity levels [43]. Furthermore, a distinction could be made between occupational physical activity and leisure time physical activity, because evidence suggests a contrast in health effects in these different domains of physical activity [44].

5. Conclusion

Most studies showed an equal or lower risk for all-cause revision surgery and for revision surgery due to aseptic loosening, and improved survivorship in highly active patients during the first 12 years after TKA. Meta-analysis demonstrated no association between HPA level and an increased risk of all-cause revision surgery (level of certainty: very low) or revision surgery due to aseptic loosening (level of certainty: moderate). This was based on a total of 4811 TKAs within a modest number of studies, all of moderate to low methodological quality, with a heterogeneous combination of activity measurement tools and definitions of HPA.

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Declaration of Competing Interest

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Appendix

Search strategy electronic databases

I PubMed (12 October 2021).

Number	Search	Results
1	“Arthroplasty, Replacement, Knee”[MeSH Terms] OR “Knee replacement”[Title/Abstract] OR “Knee replacements”[Title/Abstract] OR “Knee arthroplasty”[Title/Abstract] OR “Knee arthroplasties”[Title/Abstract] OR “Knee prosthesis”[Title/Abstract] OR “Knee prostheses”[Title/Abstract] OR “Knee implant”[Title/Abstract] OR “Knee implants”[Title/Abstract] OR “Total knee” [Title/Abstract] OR “TKA”[Title/Abstract] OR “TKR”[Title/Abstract]	41,952
2	“Sports”[MeSH Terms] OR “Sports”[Title/Abstract] OR “Sport”[Title/Abstract] OR “Activity”[Title/Abstract] OR “Activities”[Title/Abstract] OR “Cycling”[Title/Abstract] OR “Walking”[Title/Ab stract] OR “Running”[Title/Abstract] OR “Swimming”[Title/Abstract]	3,613,546

Appendix (*continued*)

Number	Search	Results
3	"Prosthesis Failure"[MeSH Terms] OR "Prosthesis failure"[Title/Abstract] OR "Prosthesis failures"[Title/Abstract] OR "Prostheses failure"[Title/Abstract] OR "Prostheses failures"[Title/Abstract] OR "Aseptic failure"[Title/Abstract] OR "Aseptic failures"[Title/Abstract] OR "Prosthesis survival"[Title/Abstract] OR "Prostheses survival"[Title/Abstract] OR "Mechanical failure"[Title/Abstract] OR "Mechanical failures"[Title/Abstract] OR "Wear"[Title/Abstract] OR "Osteolysis"[Title/Ab stract] OR "Loosening"[Title/Abstract] OR "Loosenings"[Title/Abstract] OR "Survival"[Title/Abstr act] OR "Survivalship"[Title/Abstract] OR "Survivorship"[Title/Abstract] OR "Bone resorption"[Title/Abstract] OR "Longevity"[Title/Abstract] OR "Failure"[Title] OR "Revision"[Title]	1,361,696
4	1 AND 2 AND 3	785

MeSH, Medical Subject Headings.

II Embase (12 October 2021).

Number	Search	Results
1	exp knee arthroplasty/ OR 'Knee replacement'.ab,kf,ti. OR 'Knee replacements'.ab,kf,ti. OR 'Knee arthroplasty'.ab,kf,ti. OR 'Knee arthroplasties'.ab,kf,ti. OR 'Knee prosthesis'.ab,kf,ti. OR 'Knee prostheses'.ab,kf,ti. OR 'Knee implant'.ab,kf,ti. OR 'Knee implants'.ab,kf,ti. OR 'Total knee'.ab,kf,ti. OR 'TKA'.ab,kf,ti. OR 'TKR'.ab,kf,ti.	55,669
2	exp sport/ OR 'Sport'.ab,kf,ti. OR 'Sports'.ab,kf,ti. OR exp physical activity/ OR 'Activity'.ab,kf,ti. OR 'Activities'.ab,kf,ti. OR 'Cycling'.ab,kf,ti. OR 'Walking'.ab,kf,ti. OR 'Running'.ab,kf,ti. OR 'Swimming'.ab,kf,ti.	4,828,127
3	'Prosthesis failure'.ab,kf,ti. OR 'Prosthesis failures'.ab,kf,ti. OR 'Prostheses failure'.ab,kf,ti. OR 'Prostheses failures'.ab,kf,ti. OR 'Aseptic failure'.ab,kf,ti. OR 'Aseptic failures'.ab,kf,ti. OR 'Prosthesis survival'.ab,kf,ti. OR 'Prostheses survival'.ab,kf,ti. OR 'Mechanical failure'.ab,kf,ti. OR 'Mechanical failures'.ab,kf,ti. OR 'Wear'.ab,kf,ti. OR 'Osteolysis'.ab,kf,ti. OR 'Loosening'.ab,kf,ti. OR 'Loosenings'.ab,kf,ti. OR 'Survival'.ab,kf,ti. OR 'Survivalship'.ab,kf,ti. OR 'Survivorship'.ab,kf,ti. OR 'Bone resorption'.ab,kf,ti. OR 'Longevity'.ab,kf,ti. OR 'Failure'.ti. OR 'Revision'.ti.	1,993,042
4	1 AND 2 AND 3	1477

ab, abstract, exp, Emtree-term; kf, author keyword; ti, title.

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