Prehabilitation before total knee arthroplasty

Annals of Physical and Rehabilitation Medicine 66 (2023) 101705

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Review

Prehabilitation before total knee arthroplasty: A systematic review on the use and efficacy of stratified care

Sophie Vervullens[a,b,g], Lotte Meert[a,b,g], Isabel Baert[a,g], Rob J.E.M. Smeets[b,c,g], Peter Verdonk[d], Frank Rahusen[e], Mira Meeus[a,f,g,*]

[a] Research Group MOVANT, Department of Rehabilitation Sciences and Physiotherapy (REVAKI), University of Antwerp, Wilrijk, Belgium
[b] Research School CAPHRI, Department of Rehabilitation Medicine, Maastricht University, Maastricht, the Netherlands
[c] CIR Revalidatie, location Eindhoven, the Netherlands
[d] ORTHOCA, Antwerp, Belgium and ASTARC department, Antwerp University, Belgium
[e] Department of Orthopaedics, St Jans Gasthuis Weert, the Netherlands
[f] Department of Rehabilitation Sciences and Physiotherapy, Ghent University, Ghent, Belgium
[g] Pain in Motion International Research Group (PiM), www.paininmotion.be, the Netherlands

ARTICLE INFO

Article History:
Received 29 September 2021
Accepted 9 August 2022

Keywords:
Knee osteoarthritis
Total knee arthroplasty
Preoperative rehabilitation
Phenotype
Subgroup
Stratified care

ABSTRACT

Background: Preoperative rehabilitation (hereafter called "prehabilitation") has been proposed as a potentially effective treatment to target preoperative risk factors to prevent insufficient outcome after total knee arthroplasty (TKA).
Purpose: We aimed to assess whether previous clinical trials of non-surgical, non-pharmacological prehabilitation in individuals with knee osteoarthritis (KOA) awaiting TKA focused on specific clinical phenotypes or specific individual characteristics and whether the content of the prehabilitation was stratified accordingly. Second, we aimed to summarize and compare the long-term effects of stratified and non-stratified care on pain, satisfaction, function and quality of life.
Methods: A systematic literature search of PubMed, Web of Science, Scopus and Embase was performed. All relevant articles published up to April 19, 2021 reporting "(randomized controlled) clinical trials or prospective cohort studies" (S) related to the key words "total knee arthroplasty" (P), "preoperative conservative interventions" (I), "pain, function, quality of life and/or satisfaction" (O) were included.
Results: After screening 3498 potentially eligible records, 18 studies were assessed for risk of bias. Twelve studies had low, 2 moderate, 3 serious, and one high risk of bias. The latter study was excluded, resulting in 17 included studies. Five studies investigated a"stratified prehabilitation care" and 12 "non-stratified prehabilitation care". Stratified prehabilitation in 4 studies meant that the study sample was chosen considering a predefined intervention, and in the fifth study, the prehabilitation was stratified to individuals' needs. No direct comparison between the 2 approaches was possible. We found weak evidence for a positive effect of biopsychosocial prehabilitation compared to no prehabilitation on function (stratified studies) and pain neuroscience education prehabilitation compared to biomedical education on satisfaction (non-stratified studies) at 6 months post-TKA. We found strong evidence for positive effects of exercise prehabilitation compared to no prehabilitation on pain at 6 months and on function at 12 months post-TKA (non-stratified studies).
Conclusion: More research is needed of stratified prehabilitation care focusing on individual characteristics in people with KOA awaiting TKA.
Registration number: This systematic review was prospectively registered at PROSPERO on March 22, 2021 (no. CRD42021221098).

Introduction

Knee osteoarthritis (KOA) is one of the most common forms of osteoarthritis [1], representing a degenerative joint disease known as a frequent cause of pain, disability and loss of quality of life [2,3]. KOA has a huge impact on an individual's personal life but also on society, especially given the high costs related to total knee arthroplasty (TKA) [4].

Abbreviations: BMI, body mass index; CBT, cognitive behavioural therapy; EBRO, Evidence-based Guideline Development; KOA, knee osteoarthritis; OARSI, Osteoarthritis Research Society International; RCTs, randomized controlled trials; RoB, risk of bias; ROBINS-I, The international Cochrane risk of bias checklist for nonrandomized controlled trials; ROB-II, The international Cochrane risk of bias checklist for randomized controlled trials; TKA, total knee arthroplasty

* Corresponding author at: Research Group MOVANT, Department of Rehabilitation Sciences and Physiotherapy (REVAKI), University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium.
E-mail address: mira.meeus@uantwerpen.be (M. Meeus).

https://doi.org/10.1016/j.rehab.2022.101705
1877-0657/

Although TKA appears to be an effective treatment in most people with end-stage KOA [5], 20% to 40% of individuals remain dissatisfied and experience chronic postoperative pain [6–8].

Given the expected increase in TKA surgeries due to the ageing of population and the increasing prevalence of obesity, the outcomes and satisfaction rates after TKA must be optimized [4]. Physiotherapy is traditionally delivered as rehabilitation after surgery to improve the timeline and extent of recovery. However, various preoperative functional, metabolic, as well as psychosocial risk factors and abnormal sensory processing signs for chronic postoperative pain and dissatisfaction have been described [6,9–11]. Therefore, preoperative rehabilitation (hereafter called "prehabilitation") has also been proposed as a potentially effective treatment to target these preoperative risk factors and to prevent insufficient outcome after TKA [12,13].

Results of previous systematic reviews and meta-analyses are contradictory and in general indicate no or only little positive effect of various forms of prehabilitation on postoperative outcomes [12–17]. This observation might be explained by the fact that KOA is a heterogeneous pathology: individuals can present different aetiological backgrounds, prognoses and/or clinical presentations and may respond differently to specific treatment contents [18,19].

Considering the heterogeneous nature of the KOA population, subgroups of individuals may exist [19–23]. In the context of intervention studies, the identification of phenotypes based on clinical signs are assumed necessary for more efficacious and personalized treatments [24]. Therefore, Dell'Isola et al. (most recent review on clinical phenotypes) tried to classify these into 5 clinical phenotypes: chronic pain, inflammatory KOA, metabolic syndrome, bone and cartilage metabolisms, mechanical overload and minimal joint disease [19]. Recognizing relevant clinical phenotypes and adapting the intervention to these phenotypes (stratified care) is considered fundamental to offer individuals the best matching and most effective treatment [24–26]. For example, if treatment focusses on losing weight, likely little or no therapeutic effect will be achieved when everyone with KOA, regardless of their body mass index (BMI), receives this treatment.

To date, we do not know whether previous experimental clinical trials on the effect of prehabilitation identified these clinical phenotypes in people with KOA, gave stratified prehabilitation related to these characteristics, and as a consequence reported different long-term results as compared with studies not accounting for these subgroups. None of the previous systematic reviews studied whether a stratified approach is more effective than a "one-size-fits-all" approach (non-stratified care) [15] (Appendix S1). Hence, more evidence in this field is highly necessary [27]. According to research of people with KOA [28,29] and back pain [30,31], outcomes might be better when clinical phenotypes are taken into account and prehabilitation is adapted to these phenotypes. The non-stratified approach may have attenuated treatment effects because of the varying number of potential responders and non-responders in this heterogenous population [27].

Therefore, the first aim of this systematic review was to investigate whether prehabilitation in previous clinical trials focused on specific clinical phenotypes (or other more specific individual characteristics beyond the KOA diagnosis) in people with KOA scheduled for TKA and whether the content of the prehabilitation was stratified accordingly. The second aim was to synthesise and compare the long-term results on postoperative pain, satisfaction, function and/or quality of life of the clinical trials with a more tailored approach (stratified care) in relation to clinical trials with a "one-size-fits-all" approach (non-stratified care).

Methods

This systematic review followed the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines [32], and the protocol was prospectively registered on PROSPERO (CRD42021221098; March 22, 2021). The Participant, Intervention, Comparison, Outcomes and Study (PICOS) design was used to define the eligibility criteria and key words of search strategy [33].

Eligibility criteria

To be included in this systematic review, articles had to describe results of studies that evaluated the effect of preoperative conservative (non-pharmacological, non-surgical) interventions (prehabilitation) (I) on postoperative pain, satisfaction (main outcomes), function or quality of life (additional outcomes) (O) in individuals diagnosed with KOA scheduled for TKA (P). Only (randomized controlled) clinical trials, single-case experimental designs and prospective cohort studies were allowed (S). The search results had to be in accordance with the criteria presented in Table 1.

Information sources and search strategy

Two reviewers (SV, LM) searched 4 electronic databases, including PubMed (MELDINE) [34], Web of Science [35], Embase [36] and Scopus [37], up to April 19, 2021. Four groups of key words were used,

Table 1
Eligibility criteria.

	Inclusion	Exclusion
P	Human adults diagnosed with KOA scheduled for TKA > 18 years of age	Scheduled for partial, unicompartimental or revision knee arthroplasty Statistical analyses of mixed population (e.g. KOA participants plus other indications for TKA, or TKA and THA participants)
I	Prehabilitation includes preoperative conservative (non-pharmacological and non-surgical) intervention A follow-up period of at least 6 months after TKA	
C	/	
O	Pain (primary) Participant satisfaction (primary) Function, e.g., muscle strength; functional ability, range of motion etc. (secondary) Quality of life (secondary)	Other outcomes
S	Articles written in English, Dutch or French Experimental designs or prospective cohort studies	Other languages Other study designs

KOA, knee osteoarthritis; THA, total hip arthroplasty; TKA, total knee arthroplasty

Table 2
Search query (PubMed).

	Key words
Group 1 (P)	(('Knee Prosthesis'[Mesh]) OR 'Arthroplasty, Replacement, Knee'[Mesh]) OR (knee arthroplasty OR knee prosthesis OR knee replacement OR knee surgery)
Group 2 (I)	(('Preoperative Period'[Mesh] OR 'Preoperative Care'[Mesh]) OR (preoperative OR pre-operative OR presurgical OR pre-surgical OR pre-surgery OR preadmission)) AND ((((((('Physical Therapy Specialty'[Mesh] OR 'Physical Therapy Modalities'[Mesh] OR 'Cognitive Behavioral Therapy'[Mesh] OR 'Acupuncture Therapy'[Mesh] OR 'Exercise Therapy'[Mesh] OR 'Behavior Therapy'[Mesh] OR 'Cryotherapy'[Mesh] OR 'Therapy, Soft Tissue'[Mesh] OR 'Acceptance and Commitment Therapy'[Mesh]) OR ('Exercise Movement Techniques'[Mesh] OR 'Resistance Training'[Mesh] OR 'Exercise'[Mesh])) OR ('Rehabilitation'[Mesh] OR 'rehabilitation' [Subheading] OR 'Telerehabilitation'[Mesh])) OR ('Manipulation, Orthopedic'[Mesh] OR 'Musculoskeletal Manipulations'[Mesh])) OR 'Dry Needling'[Mesh]) OR (physical therapy OR physiotherapy OR cognitive behavioral therapy OR cognitive therapy OR acupuncture OR exercise therapy OR manual therapy OR mobilization OR mobilisation OR behavior therapy OR behaviour therapy OR cryotherapy OR soft tissue therapy OR 'acceptance and commitment' OR resistance training OR strength training OR conservative therapy OR graded activity OR graded exposure OR graded exercise OR pain education OR participant education))
Group 3 (O)	(((((('Pain'[Mesh] OR 'Musculoskeletal Pain'[Mesh] OR 'Chronic Pain'[Mesh]) OR 'Disability Evaluation'[Mesh]) OR 'Activities of Daily Living'[Mesh]) OR 'Quality of Life'[Mesh]) OR ('Personal Satisfaction'[Mesh] OR 'Participant Satisfaction'[Mesh])) OR (pain OR functioning OR 'activities of daily living' OR activities OR participation OR quality of life OR satisfaction OR disability)
Group 4 (S)	(('Pragmatic Clinical Trial' [Publication Type] OR 'Controlled Clinical Trial' [Publication Type] OR 'Randomized Controlled Trial' [Publication Type] OR 'Clinical Trial' [Publication Type] OR 'Cross-Over Studies'[Mesh]) OR ('Cross-Sectional Studies'[Mesh] OR 'Cohort Studies'[Mesh] OR 'Longitudinal Studies'[Mesh] OR 'Follow-Up Studies'[Mesh] OR 'Case-Control Studies'[Mesh] OR 'Prospective Studies'[Mesh])) OR (clinical trial OR randomized controlled trial OR randomised controlled trial OR cohort studies OR prospective studies OR longitudinal studies OR follow-up studies OR case-control studies OR cross-sectional studies)

related to "Total Knee Arthroplasty" (P), "Preoperative conservative Interventions" (I), "Pain, Satisfaction, Function, and Quality of life" (O) and "randomized controlled trials (RCTs), clinical trials or prospective cohort studies" (S). More details can be found in Table 2, Table S1 and Table S2.

Study selection

Results of the searches were imported into Endnote and duplicates were removed [38]. Eligibility criteria were checked by 2 reviewers (SV, LM) using the Rayyan screening tool [39]. The first screening was conducted on the title and abstract, and if the study was considered potentially relevant, the full text was retrieved. A second selection was based on the full text, and after both screening phases, all disagreements on inclusion or exclusion were discussed and resolved by consensus.

Data items and collection

Relevant information from every included article was extracted and reported in an evidence table (Table 3). The following data (if available) were extracted from every article: 1) author and year of publication, 2) study design and setting, 3) participant characteristics (sample size, age, number of women, inclusion and exclusion criteria, study criteria related to clinical phenotype according to Dell'Isola et al. [19]), 4) prehabilitation (content, modalities and provider in intervention and control groups and whether the intervention was related to phenotype or study criteria of the study), 5) continuation in the postoperative period (yes/no + content), 6) follow-up times (6-month minimum), 7) lost to follow-up, 8) outcome measure, and 9) results (mean difference [increase or decrease] + effect size). The evidence table was completed by the first author (SV) and independently checked by the second author (LM).

Risk of bias in individual studies

The risk of bias (RoB) within the different articles was assessed by using the international Cochrane Risk of Bias checklist (ROB-II) for RCTs [40] and non-RCTs (ROBINS-I) [41]. The ROB-II checklist contains 5 domains, which can be rated as high, moderate or low RoB. The 7 domains of the ROBINS-I checklist can be rated as critical, serious, moderate or low RoB. Studies were considered to have an overall high RoB if one domain was judged as high or serious RoB and as having an overall moderate RoB if one domain was considered moderate; all others were rated as low RoB. Only when all domains were judged as low RoB was the overall RoB of the study considered low (Table 4). Interpretation of the guidelines regarding the scoring items was harmonised beforehand to improve consensus. We excluded studies with an overall RoB score of high or critical in order to guarantee conclusions of a bundle of high-quality research.

The Evidence-Based Guideline Development (EBRO) was used to evaluate the overall level of evidence per study. In accordance with the methodology, a classification of the selected studies was based on following criteria: A2, a double-blind RCT of good quality and substantial size and B, a controlled trial not satisfying the conditions of A2 (Table 4). In addition, the EBRO method was used to determine the level of conclusions per outcome. A level-one conclusion was based on at least two A2 studies and converted into strong evidence. A level-two conclusion was determine if one A2 study or at least two B studies agreed on the results, called moderate evidence. A level-three conclusion was based on one B study and converted to weak evidence. Finally, the term "conflicting evidence" was used if results were contradictory. Conclusions were established per outcome measure and targeted approach (Table 5 and Table 6) [42].

Two reviewers (SV, LM) assessed the RoB independently and with blinding to each other's assessment. Results were compared and in case of disagreement, the article was analysed again. Conflicts were resolved by consensus.

Results

Study selection and characteristics

Fig. 1 provides an overview of the study selection process. A first literature search was conducted on November 9, 2020 and updated on April 19, 2021. After removing duplicates, the search strategies led to 3578 studies based on previous described inclusion and exclusion criteria. After the first screening phase, 65 studies were considered eligible for the second screening phase, which resulted in 18 studies to score for RoB [43–60]. The main reasons for exclusion were wrong timing (e.g., follow-up less than 6 months or no postoperative outcomes described) or wrong population (e.g., no separate data reports for people with KOA undergoing TKA). With a high RoB, the study of Jahic et al. [51] was additionally excluded. This resulted in 17 eligible studies. Conflicts in the first (1.37%) and second (15.38%) screening phase were resolved by consensus of the 2 reviewers (SV, LM). Fourteen studies [45–50,52,54–60] were RCTs and 3 [43,44,53] were non-RCTs. Details and characteristics of the included studies are in Table 3.

Table 3
Evidence table

Author and year	-Study design -Setting -Aim	Subject characteristics			Prehabilitation			Continuation in postop period	Postop follow-up time (≥6m)	Loss to follow-up + ITT or PPA analysis	Outcome measurements at all follow-up moments	Results (compared to baseline) Effect size (if mentioned)
		Sample size Mean age (SD) Number of K&L scale	Inclusion and exclusion criteria	Suggested clinical phenotype	Intervention group (IG) -Content -Modalities -Provider	Control group (CG) -Content -Modalities -Provider (if mentioned)	Intervention related to phenotype or specific study criteria					
Aytekin et al. (2019) [43]	-Prospective non-randomized controlled study -Home-based -To detect difference in IG and CG in improving pain and functional ability	Total: n = 44 IG: n = 21, 68y [6] 18 K&L scale 3 : n = 8 K&L scale 4: n= 13 CG: n = 23, 70y [6] 18 K&L scale 3 : n = 12 K&L scale 4: n= 11	Inclusion: -Severe KOA with pain not responsive to conservative treatment scheduled for TKA Exclusion: -Inflammatory arthritis -Dermatological conditions affecting the thigh -Neurological disorders -Implanted pacemakers -History of uncontrolled angina -Severe cardiomyopathy -Contraindications for exercise -Revision surgery	/	-Training program: Exercise (mobility, strength and stretching of lower extremity) and education (general, joint protection, home safety and TKA + manual booklet) -12w before surgery, 5x/w, 60 sessions -Physiatrist	No information given	No	/	6m	IG: n = 10 CG: n = 0 ITT	-Pain intensity: VASrest & during activities KOOSpain -Function KOOStotal, stiffness, daily living activities & sports -QoL KOOSQoL	No interaction effect (p>0.05) Within-group scores: All results decreased in both groups (p<0.01)
Barral et al. (2020) [44]	-Prospective non-randomized controlled study -Setting not given - To detect difference in IG and CG in improving pain and opioid consumption	Total: n = 81 IG: n = 41, 74y [8] 23 CG: n = 40, 75y [7] 24 K&L scale not reported	Inclusion: -KOA scheduled for primary TKA Exclusion: -History of surgery on the operated knee -Bilateral TKA in same operation -Participant refusal	/	-Osteopathic manipulative therapy (rhythmic mobilization and myofascial relaxation) -3w and 1w before surgery, 2 sessions -Osteopath	Traditional preoperative management	No	/	6m 12m	Total 6m: n = 19 (IKS) n = 33 (WOMAC) Total 12m: n = 45 (IKS & WOMAC) PPA	-Pain intensity WOMACpain -Funtion: IKSknee & function WOMACstiffness & function	No between-group differences at 6 and 12m (p>0.05) (results of both groups compared at 6 and 12m, not compared to baseline)
Beaupre et al. (2004) [45]	-RCT -Community physical therapy clinic - To detect difference in IG and CG in improving functional recovery, QoL, health service utilization and costs	Total: n = 131 IG: n = 65, 67y [7] 39 CG: n = 66, 67y [6] 33 K&L scale not reported	Inclusion: -Non-inflammatory arthritis -Scheduled for primary TKA -Between 40 and 75y -Willing to take intervention and follow-up visits -Understand English or have a translator	/	-Education (crutch walking, mobility and transfers, postop ROM routine) + exercise (mobility and strength exercises of lower extremity) -4w before surgery, 3x/w, 12 sessions -Not specified who	Usual care: same treatment routinely received (as if they not entered the study)	No	/	6m 12m	6m IG: n = 21 CG: n = 10 12m IG: n = 14 CG: n = 8 ITT	-Pain intensity WOMACpain SF-36bodiliy pain -Function WOMACstiffness & function Active knee ROM Strength Quadriceps & Hamstrings SF-36 function, role physical & PCS	No interaction effect at 6m and 12m (p>0.05) Within-group scores: All results decreased in both groups at 6m and 12m (p<0.05)
Birch et al. (2020) [46]	-RCT -Setting not given - To detect difference in IG and CG in improving pain coping, physical function, QoL, self-efficacy and pain catastrophizing	Total: n = 67 IG: n = 31, 66y [9] 22 CG: n = 29, 66y [10] 18 K&L scale not reported	Inclusion: -Primary KOA scheduled for primary TKA -Age ≥ 18y **- >22 on the PCS** -Proficiency in written and spoken Danish -Informed consent Exclusion: **-Severe depression diagnosed with Major Depression Inventory** -Contralateral TKA within 1y postop	Chronic pain	-CG intervention + education based on CBT -2w before surgery, 3 (or 2) sessions -2 physiotherapists	Usual care: multidisciplinary information meeting	Yes: phenotype	IG: -education based on CBT -until 3m after surgery, 4 sessions CG: /	12m	IG: n = 4 CG: n = 3 ITT	-Pain intensity VASrest & during activities OKS KOOSpain -Function OKS 6min walk test Sit to stand -QoL EQ-5D	No interaction effect (p>0.05). Within-group scores: -Pain intensity: VASduring activities decreased and OKS increased in both groups (p<0.05) -Function: OKS increased in both groups (p<0.05) -No significant results for all the other outcomes (p>0.05)
Culliton et al. (2018) [47]	-RCT -Home - To detect difference in IG and CG in fulfilling expectations and improving satisfaction	Total: n = 345 IG: n = 167, 64y [8] 98 CG: n = 178, 63y [9] 123 K&L scale not reported	Inclusion: -KOA scheduled for elective primary TKA - >20y -Cognitive capacity to give consent Exclusion: -Revision TKA -Patellar resurfacing -Hemi- or unicondylar TKA -High tibial osteotomy -Knee surgery to address a tumour	/	-CG intervention + an online e-learning tool (TKA animation, expectations about pain, function, limitations; demonstrations of participants after TKA) -Before surgery, 1 session -Videos of therapists, surgeons and previous TKA recipients	Hard copy of 'my guide to TKA'	No	IG: Online e-learning tool -6w, 3 m and 1y after surgery, 3 sessions CG: /	12m	IG: n = 13 CG: n = 13 ITT	-Pain intensity KOOSpain -Satisfaction KSSsatisfaction PASS -Function KSSsymptoms, functional activities, activities of daily living & sports -Quality of life KOOSquality of life	Between-group differences: -Function: KSSSsymptoms and functional was higher in CG (p=0.04) -No significant results for all the other outcomes (p>0.05) (results of both groups compared at 12m, not compared to baseline) Interaction effects and within-group scores not given

(*continued on next page*)

Table 3 (*Continued*)

Author and year	-Study design -Setting -Aim	Subject characteristics			Prehabilitation			Continuation in postop period	Postop follow-up time (≥6m)	Loss to follow-up + ITT or PPA analysis	Outcome measurements at all follow-up moments	Results (compared to baseline) Effect size (if mentioned)
		Sample size Mean age (SD) Number of K&L scale	Inclusion and exclusion criteria	Suggested clinical phenotype	Intervention group (IG) -Content -Modalities -Provider	Control group (CG) -Content -Modalities -Provider (if mentioned)	Intervention related to phenotype or specific study criteria					
das Nair et al. (2018) [48]	-RCT -Home or hospital (as preferred by participants) - To detect difference in IG and CG in improving pain, function and mood	Total: n = 50 IG: n = 25, >18y 14 CG: n = 25, >18y 9 K&L scale not reported	Inclusion: -KOA scheduled for TKA - >18y **- >7 on either Hospital Anxiety and Depression subscale** Exclusion: -Severe psychiatric conditions -Inflammatory arthritis -Currently receiving any psychological interventions	Chronic pain	-Psychological intervention based on CBT for anxiety depression and pain management -18w before surgery, 10 sessions -Psychologists	Usual care: standard care delivered by each clinical service (no focus on participants' psychological state)	Yes: phenotype	/	6m	IG: n = 12 CG: n= 13 ITT	-Pain intensity IPOC WOMACpain -Function WOMACstiffness & physical function -QoL EQ-5D	Between-group differences: -Function: WOMACphysical function was higher in IG (p=0.009, ES= 1.16) - No significant results for all the other outcomes (p>0.05) (results of both groups compared at 12m, not compared to baseline) Interaction effects and within-group scores not given.
Domínguez-Navarro et al. (2021) [49]	-RCT -Setting not given - To detect difference in IG and CG in improving balance and functional outcomes	Total: n = 82 IG1: n = 20, 70y [6] 13 IG2: n = 24, 71y [5] 14 CG: n = 21, 70y [6] 14 K&L scale > 3: n = 82 (whole group)	Inclusion: -Idiopathic KOA with >3 on K&L scale scheduled for TKA -Scheduled sufficient time until surgery (5-8 weeks) Exclusion: -Contraindications physical activity - < 21 in the Berg Balance Scale - < 20 Mini-Mental State test -Systemic illness	/	IG1: -Strength training, balance- and proprioception training of lower extremity -4w before surgery, 3x/w, 12 sessions IG2: -Strength training of lower extremity -4w before surgery, 3x/w, 12 sessions -Not specified who	No experimental preoperative intervention	No	/	12m	IG1: n = 5 IG2: n = 5 CG: n = 5 ITT	-Pain intensity KOOSpain -Function Berg Balance Scale KOOS-ADL ROM flexion & extension Strength Quadriceps TUG Functional reach test Single leg standing -QoL KOOSQoL	Interaction effect: -Function: Single leg standing increased in favour of IG1 and IG2 compared to CG (p=0.043) - No significant results for all the other outcomes (p>0.05) Within-group scores not given
Huber et al. (2015) [50]	-RCT -Setting not given - To detect difference in IG and CG in improving lower extremity function	Total: n = 45 IG: n = 22, 69y [8] 11 CG: n = 23, 72y [8] 10 K&L scale not reported	Inclusion: -KOA scheduled for primary TKA -Aged between 55y and 90y -Scheduled sufficient time until surgery (to take 8 sessions) -Understood German Exclusion: -Revision surgery -Inflammatory arthritis -Cognitive impairments -inability to walk at least 3m	/	-CG intervention + neuromuscular and biomechanical training (stability, functional alignment, strength of lower extremity and functional exercises) -4 to 12w before surgery, 4 to 12 sessions -Physiotherapist	-Knee school (information on anatomy, activities, postoperative pain management and rehabilitation) -4w before surgery, 1x/w, 3 sessions -Physiotherapist	No	/	12m	IG: n = 5 CG: n = 4 ITT	-Pain intensity KOOSpain SF36pain EQ-5Dpain & VAS -Function KOOSfunction, symptoms & sports SF- function & role physical -QoL KOOSQoL EQ-5Dmobility & activities	No interaction effect (p>0.05). Within-group scores: -Pain intensity: KOOSpain increased in both groups (p≤0.001) SF36pain increased in IG (p≤0.05) -No significant results for all the other outcomes (p>0.05) (all results are compared to three months after surgery)
Liljensoe et al. (2021) [52]	-RCT -Home - To detect difference in IG and CG in improving QoL, function, mobility and body composition	Total: n = 76 IG: n = 38, 65y [46-81] 27 CG: n = 38, 65y [46-85] 27 K&L scale not reported	Inclusion: -KOA scheduled for primary TKA **- BMI ≥30** -Motivated for weight loss Exclusion: -Rheumatoid arthritis -Planned bariatric surgery	Metabolic syndrome or mechanical overload	-Low-energy liquid diet (810 kcal/day) and nutritional education -61.6 to 8w before surgery, 1x/w -Dietitian	-Standard care with no benefit of losing weight before TKA	Yes: phenotype	IG: Low-energy liquid diet + nutritional education -until 1y postop, 1x/w -Dietitian	12m	IG: n = 0 CG: n = 0 ITT and PPA (focus on ITT)	-Pain intensity KOOSpain -Function SF36 PCS KOOSsymptoms, activities of daily living & sports 6min walk test -QoL KOOSQoL	ITT: No interaction effects (p>0.05). Within-group differences: -Function: SF36 PCS improved in all participants (CI: 5 to 10) KOOSsymptoms improved in all participants (CI : 16.0 to 25.0) 6min walk test improved in all participants (CI: 56 to 100) -QoL: KOOSQoL improved in all participants (CI: 26.4 to 37.7) No significant results for pain intensity (p>0.05)
Louw et al. (2019) [53]	-Prospective controlled clinical trial -Hospital - To detect difference in IG and CG in improving function, pain, pain medication use, fear, catastrophizing and satisfaction	Total : n = 103 IG : n = 49, 74y [10] 32 CG : n = 54, 70y [11] 28 K&L scale not reported	Inclusion: -KOA scheduled for TKA and standard preoperative TKA education program -Willingness to participate -Ability to read and understand English Exclusion: -Previous or bilateral TKA	/	-CG intervention + pain neuroscience education - 2 to 12 days before surgery, one session - Physiotherapist	-Preoperative TKA education class (anatomy, expectations, information surgery, pain medication and rehabilitation) - 2 to 12 days before surgery, one session - Not specified who	/	/	6m	IG: n = 18 CG: n = 18 ITT and PPA (focus on PPA)	-Pain intensity NPRS -Satisfaction Statement: 'the surgery met my expectations' -Function WOMACfunction	PPA: Interaction effects: -Satisfaction: The 'met expectations statement' improved in favour of IG (p=0.03) Within-group differences: -Pain intensity and function: NPRS and WOMACfunction improved over time for all participants (p<0.001) (compared to 3m postop)

(*continued on next page*)

Table 3 (*Continued*)

Author and year	-Study design -Setting -Aim	Subject characteristics			Prehabilitation			Continuation in postop period	Postop follow-up time (≥6m)	Loss to follow-up + ITT or PPA analysis	Outcome measurements at all follow-up moments	Results (compared to baseline) Effect size (if mentioned)
		Sample size Mean age (SD) Number of K&L scale	Inclusion and exclusion criteria	Suggested clinical phenotype	Intervention group (IG) -Content -Modalities -Provider	Control group (CG) -Content -Modalities -Provider (if mentioned)	Intervention related to phenotype or specific study criteria					
Matassi et al. (2012) [54]	-RCT -Home - To detect difference in IG and CG in improving ROM and functional recovery	Total : n = 122 IG : n = 61, 66y [7] 33 CG : n = 61, 67y [8] 26 K&L scale not reported	Inclusion: -Non-inflammatory OA scheduled for unilateral TKA -Moderate to severe knee pain -Aged between 18y and 90y -Willing to participate -Stable health Exclusion: **-BMI >35 + physical activity needs less than moderate** -TKA or THA or knee physiotherapy in last 6m -Failed TKA or unicondylar KA or high tibial osteotomy -Active local/systemic infection or contraindicated conditions -Grade 3 collateral ligament insufficiency **- < 80° knee flexion, >20° fixed flexion deformity, >10° varus/valgus** -Immunosuppressive disorder or therapy, autoimmune disease or pregnancy -Recent fracture (3m) or steroid infiltration (6weeks) -Inability to understand the study	/	-Exercises for lower extremity muscle strength and flexibility (individual explanation + written information) - 6w before surgery, 5x/w, 30 sessions - Individual explanation by physiotherapist	-To continue with regular activities	Yes: exclusion criteria (BMI, physical activity, joint motion)	/	6m 12m	IG: n = 0 CG: n = 0 ITT	-Function ROM active, passive knee flexion & knee extension Knee Society Clinical Rating System Knee score Function score	Between-group differences: -Function: The evolution (baseline to 12m postop) of the extension was different between groups ($p = 0.032$), but not the absolute score (as in other studies) -No significant results for all the other outcomes ($p>0.05$) Within-group scores not given.
Mayoral et al. (2013) [55]	-RCT -Hospital - To detect difference in IG and CG in improving pain	Total : n = 40, 29 IG : n = 20, 72y [6] CG : n = 20, 73y [8] K&L scale not reported	Inclusion: -KOA scheduled for TKA -Presence of active or latent MTrPs in at least one muscle Exclusion: -Any other condition that could cause myofascial or neuropathic pain in lower limb -Any condition considered a perpetuating factor of MTrPs	/	-Dry needling -Right before surgery during anaesthesia, one session -Physical therapist	-No needling (simulated needling without any application)	Yes: in- and exclusion criteria (MTrPs)	/	6m	IG: n = 4 CG: n = 5 ITT	-Pain intensity VAS WOMACpain -Function WOMACstiffness & function ROM Strength Quadriceps & Hamstrings	-No between- and within-group significant results for all the outcomes ($p>0.05$)
Rooks et al. (2006) [56]	-RCT -Setting not given - To detect difference in IG and CG in improving functional status, pain and muscle strength	Total: n = 45 IG: n = 22, 65y [8] 11 CG: n = 23, 69y [8] 13 K&L scale not reported	Inclusion: -Advanced KOA scheduled for THA or TKA -Ability to answer in English -Scheduled sufficient time until surgery (8-12 weeks) Exclusion: -Inflammatory arthritis -Parkinson's disease -Any condition in which exercise was contraindicated	/	-Water and land-based exercise (mobility, strength, flexibility and cardiovascular exercises of lower extremity and total body) -6w before surgery, 3x/w, 18 sessions -Physical therapist	-Education in accessibility, reduce falling and injury and preparing for surgery -6w before surgery, 1x/w, 4 sessions -Mail and telephone, not specified who	No	/	6m	IG: n = 8 CG: n = 8 ITT	-Pain intensity: WOMACpain SF-36bodily pain -Function: WOMACfunction SF-36function &role physical 1RM leg press test Functional reach test TUG	Interaction effect: -Pain intensity: decrease in SF-bodily pain ($p<0.05$) in favour of IG -No significant results for all the other outcomes ($p>0.05$) Within-group scores not given.

(*continued on next page*)

Table 3 (*Continued*)

Author and year	-Study design -Setting -Aim	Subject characteristics			Prehabilitation			Continuation in postop period	Postop follow-up time (≥6m)	Loss to follow-up + ITT or PPA analysis	Outcome measurements at all follow-up moments	Results (compared to baseline) Effect size (if mentioned)
		Sample size Mean age (SD) Number of K&L scale	Inclusion and exclusion criteria	Suggested clinical phenotype	Intervention group (IG) -Content -Modalities -Provider	Control group (CG) -Content -Modalities -Provider (if mentioned)	Intervention related to phenotype or specific study criteria					
Skoffer et al. (2020) [57]	-RCT -University Hospital -To detect difference in IG and CG in improving functional performance, muscle strength, pain, function and QoL	Total : n = 59 IG : n = 30, 71y [7] 19 CG : n = 29, 70y [6] 17 K&L scale not reported	Inclusion: -KOA scheduled for primary unilateral TKA -Residents in the Aarhus municipality -Able to transport themselves Exclusion: -Aged < 18y -Heart disease or uncontrolled hypertension -Neuromuscular or neurodegenerative disorders -Unable to comprehend the protocol instructions	/	-Exercises for lower extremity muscle strength and flexibility -4w before surgery, 3x/w, 12 sessions -Physiotherapist	Usual care (live as usual)	No	IG: -Exercises for lower extremity muscle strength and flexibility -4 w after surgery, 3x/w, 12 sessions -Physiotherapist	12m	IG: n = 6 CG: n = 9 ITT	-Pain intensity KOOSpain Current, worst & average pain score -Function KOOSsymptoms, activities of daily living & sports 30s time chair stand test TUG 10min & 6min walk test Strength Quadriceps & Hamstrings (both legs) ROM active and passive flexion & extension -QoL KOOSQoL Health-related QOL	Interaction effect: -Function: Strength of the Quadriceps (p=0.002) and Hamstrings (p=0.042) of the operated leg increased in favour of IG. -No significant results for all the other outcomes (p>0.05) Within-group scores not given.
Sun et al. (2020) [58]	-RCT -Outparticipant clinic -To detect difference in IG and CG in improving pain, function, QoL and pain catastrophizing	Total: n = 80 IG: n = 42, 58y [9] 19 K&L scale 2: n = 22 K&L scale 3: n= 17 K&L scale 4: n= 3 CG: n = 38, 60y [8] 21 K&L scale 2: n = 18 K&L scale 3: n= 16 K&L scale 4: n= 4	Inclusion: -Understand/speak Chinese -Primary KOA scheduled for primary TKA -Aged > 18y -Provide informed consent Exclusion: -Cognitive disorders -Trigeminal neuralgia, neuritis, migraine, and other similar reasons for pain -Long-term use of sleeping pills or addiction to opioids -Renal insufficiency -History of knee ligament, meniscus injury, or surgery	/	-CG intervention + education based on CBT -2w before surgery, 3 sessions -Physiotherapist	-Usual care (nursing procedure and education, meeting about operation method, risk and postop rehabilitation) -Nurses, orthopaedists, physiotherapists and anaesthesiologists	No	IG: -Usual care + education based on CBT -2w after surgery, 3 sessions Physiotherapist CG: - Active exercise and CPM exercise	12m	IG : n = 8 CG : n = 12 PPA	-Pain intensity VASrest & during activities -Function Knee ROM OKS HSS Knee rating scale -QoL EQ-5D	No interaction effects (p>0.05) Within-group differences: -Pain intensity and Function: Knee ROM, EQ-5D and HSS increased over time, while OKS and VAS scores decreased over time in both groups (p<0.001) -No significant results for all the other outcomes (p>0.05)
Tolk et al. (2021) [60]	-RCT -Setting not given -To detect difference in IG and CG in fulfilling expectations and improving satisfaction	Total: n = 204 IG: n = 101, 68y [9] 60 CG: n = 103, 69y [10] 62 K&L scale not reported	Inclusion: -Symptomatic KOA scheduled for primary TKA Exclusion: -Medical illness that results in life expectancy shorter than 1y -Previous contralateral TKA -Unicompartmental KA -Staged or bilateral TKA -Insufficient command of the Dutch language	/	-CG intervention + 30-minute joint-specific educational module aimed at achieving realistic expectations on long-term recovery after TKA -Before surgery, 1 session -Not specified who	-Standard 90-minute multidisciplinary education program (what to expect from perioperative period) -Before surgery, 1 session -Not specified who	No	/	12m	IG: n = 8 CG: n = 9 ITT and PPA (focus on ITT)	-Pain intensity NRS pain -Satisfaction NRS satisfaction, HSS-KRES -Function KOOSfunction -QoL EQ-5D	Interaction effect: ITT: No interaction effects (p>0.05), PPA: Higher NRS satisfaction in favour of IG 12m postop (p= 0.012) Within-group differences: -Satisfaction: Subscale kneel (p=<0.001), squat (p=0.015) and walk long distance (p=0.006) more fulfilled in IG 12m -No significant results for all the other outcomes (p>0.05) (Within-group differences compared at 12m, not to baseline)

(*continued on next page*)

Table 3 (*Continued*)

Author and year	-Study design -Setting -Aim	Subject characteristics			Prehabilitation			Continuation in postop period	Postop follow-up time (≥6m)	Loss to follow-up + ITT or PPA analysis	Outcome measurements at all follow-up moments	Results (compared to baseline) Effect size (if mentioned)
		Sample size Mean age† (SD) Number of K&L scale	Inclusion and exclusion criteria	Suggested clinical phenotype	Intervention group (IG) -Content -Modalities -Provider	Control group (CG) -Content -Modalities -Provider (if mentioned)	Intervention related to phenotype or specific study criteria					
Tungtrongjit et al. (2012) [59]	-RCT -Home -To detect difference in IG and CG in improving pain, ROM, quadriceps strength and QoL	Total: n = 60 IG: n = 30, 63y [8] 26 K&L scale 2: n = 1 K&L scale 3: n= 5 K&L scale 4: n= 24 CG: n = 30, 66y [7] 24 K&L scale 3: n= 10 K&L scale 4: n= 20	Inclusion: -Idiopathic/secondary KOA grade ≥2 on K&L scale scheduled for primary TKA - ≥50y Exclusion: -History of old cerebrovascular accident -Knee joint or postop wound infection, dehiscent or trauma	/	-Quadriceps exercises -3w before surgery, daily sessions -Not specified who	-Usual care (to continue normal activities)	No	/	6m	Total: n = 4 PPA	-Pain intensity VAS WOMACpain -Function Total WOMAC WOMACstiffness & function Strength Quadriceps ROM flexion, extension & total	Interaction effect: -Pain intensity: WOMACpain score decreased in favour of IG (p=0.029) -No significant results for all the other outcomes (p>0.05) Within-group differences not given

Abbreviations: 1RM= one repetition maximum, CBT = Cognitive Behavioural Therapy, CG= control group, CPM= continuous passive motion, EQ-5D= Euro Quality of Life – 5D, EQ-5Dmobility= EQ-5D – subscale mobility, EQ-5Dpain= EQ-5D – subscale pain, EQ-5Dusualactivities= EQ-5D – subscale usual acitivites, EQ-5DVAS= EQ-5D – subscale VAS, HSS-KRES= Hospital for Special Surgery Knee Replacement Expectations Survey, IG= intervention group, IKSfunction= IKS – subscale function, IKSknee= International Knee Society score – subscale knee, ITT= intention to treat analysis, K&L= Kellgrenn and Lawrence, KOOSdaily living activities= KOOS – subscale daily living activities, KOOSpain = Knee Injury and Osteoarthritis Outcome Score – subscale pain, KOOSquality of life= KOOS – subscale quality of life, KOOSsports= KOOS – subscale sports, KOOSstiffness = KOOS – subscale stiffness, KOOStotal= KOOS total, KSSfunctional activies= KSS – subscale functional activities, KSS-satisfaction= KSS – subscale satisfaction, KSSsymptoms= Knee Society Score System – subscale symptoms, m= month, min= minutes, n = number, NPRS= Numeric Pain Rating Scale, OKS= Oxford Knee Score, PASS = Participant Acceptable Symptom State, PCS= Pain Catastrophizing Scale, postop= postoperative KOA= knee osteoarthritis, PPA= per protocol analysis, QoL= Quality of life, RCT = randomized controlled trial, ROM = Range of motion, s= seconds,SD = standard deviation, SF PCS= SF – subscale physical component score, SF- role physical= SF – subscale role physical, SF-bodily pain: 36-item Short Form Survey – subscale bodily pain, SF-physical function= SF- subscale physical function, TKA = Total Knee Arthroplasty, TUG= Timed Up and Go, VASduring activities = VAS during activities, VASrest = Visual Analogue Scale in rest, w= week, WOMACfunction= WOMAC- subscale function, WOMACpain = Western Ontario and McMaster Universities Osteoarthritis Index – subscale pain, x/w= times weekly, y = year

Risk of bias

The RoB assessment and levels of evidence results are presented in Table 4. Almost excellent agreement of 94.22% and 98.48% was achieved between both assessors, before consensus, for the ROB-II and ROBINS-I, respectively. Twelve studies had low [45,47,49,50,52,54–60], 2 moderate [46,48], 3 serious [43,44,53], and one high RoB [51]. RoB due to confounding or missing data was the main reason for increased RoB. The study with the highest RoB [51] was excluded from this systematic review. Because all studies were comparative, the 12 studies with an overall low RoB score received a level of evidence of A2 (good evidence) [45,47,49,50,52,54–60] and the other 5 studies a level of evidence of B (moderate evidence).

Study population and intervention

Study population

None of the studies described subgroups or focused on a specific clinical phenotype explicitly. However, the study population in 3 studies could be classified as a specific KOA phenotype. Birch et al. [46] and das Naïr et al. [48] focused on KOA individuals with specific psychological features, consistent with the chronic pain phenotype, and Liljensoe et al. [52] on KOA individuals with increased BMI, consistent with the metabolic syndrome or mechanical overload phenotype. Two other studies described more specific inclusion and exclusion criteria than only KOA diagnosis but could not be classified as a specific clinical phenotype [54,55]. Matassi et al. [54] excluded OA individuals with high BMI, less than moderate physical needs and limited joint motion, and Mayoral et al. [55] included KOA individuals with myofascial trigger points. In 4 of 5 studies [46,52,54,55], a predefined prehabilitation was set up, and only participants with a certain matching phenotype or more specific inclusion and exclusion criteria were included. Only in the das Naïr et al. [48] study was the intervention stratified to the individuals' needs. The other 12 studies [43–45,47,49,50,53,56–59] used a "one-size-fits-all" approach and described general inclusion criteria such as signs related to KOA diagnosis.

When a study used more stringent eligibility criteria than the KOA diagnosis itself and when the intervention was tailored to these criteria (or visa versa, e.g., if individuals were chosen according to a predefined intervention), studies were classified as the stratified care approach. Otherwise, studies were classifed as the non-stratified care approach.

The sample size ranged from 40 [55] to 122 [54] individuals for the stratified care approach studies, and 44 [43] to 345 [47] for the non-stratified care approach studies.

All details are presented in Table 3.

Intervention and control groups

All studies were comparative experimental designs consisting of 14 RCTs and 3 controlled clinical trials and had at least one intervention group and one control group. As mentioned, the phenotype [46,48,52] or specific individual characteristics [54,55] of almost all the stratified care studies were chosen to match the intervention (except for das Naïr et al. [48]). The interventions could be divided into 4 domains: interventions based on a more biopsychosocial approach for individuals with the chronic pain phenotype [46,48]; weight loss intervention for individuals with the metabolic syndrome or mechanical overload phenotype [52]; exercise (lower limb strength and flexibility) for individuals with lower BMI, more than moderate physical needs and normal joint motion [54]; and dry needling for individuals with myofascial trigger points [55]. The biopsychosocial approach of the das Naïr et al. study was based on cognitive behavioural therapy (CBT) focusing on anxiety, depression and pain management, and was tailored to each individual's needs [48]. The biopsychosocial approach of Birch et al. was also based on CBT but focused on standardized pain education, pain coping skills training and ways to apply these skills into real life and as such, less tailored

Table 4
Risk of bias.

Study	Study-design	RoB tool	1	2	3	4	5	6	7	Overall	LoE
Aytekin et al. [43]	Non-RCT	ROBINS-I	Serious	Low	Low	Moderate	Serious	Low	Low	**Serious**	B
Barral et al. [44]	Non-RCT	ROBINS-I	Serious	Low	Low	Low	Moderate	Low	Low	**Serious**	B
Beaupre et al. [45]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Birch et al. [46]	RCT	ROB-II	Low	Some concerns	Low	Low	Low			**Some concerns**	B
Culliton et al. [47]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
das Naïr et al. [48]	RCT	ROB-II	Low	Some concerns	Some concerns	Low	Low			**Some concerns**	B
Dominquez-Navarro et al. [49]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Huber et al. [50]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Jahic et al. [51]	RCT	ROB-II	Some concerns	Low	Low	High	Some concerns			**High**	N/A
Liljensoe et al. [52]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Louw et al. [53]	Non-RCT	ROBINS-I	Serious	Low	Low	Low	Moderate	Low	Low	**Serious**	B
Matassi et al. [54]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Mayoral et al. [55]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Rooks et al. [56]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Skoffer et al. [57]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Sun et al. [58]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Tolk et al. [60]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2
Tungtrongjit et al. [59]	RCT	ROB-II	Low	Low	Low	Low	Low			**Low**	A2

LoE, level of evidence; N/A, not applicable due to exclusion; RCT, randomized controlled trial; ROB-II, Revised Cochrane Risk of Bias tool for randomized trials; ROBINS-I, Risk of Bias In Non-randomized Studies of Interventions
Articles scored with ROBINS-I: bias due to 1 = confounding, 2 = selection of participants in the study, 3 = classification of interventions, 4 = deviations from intended interventions, 5 = missing data, 6 = measurement of outcomes.
Articles scored with ROB-II: bias due to 1 = randomization process, 2 = deviations from intended interventions, 3 = missing outcome data, 4 = measurement of outcome, 5 = selection of the reported result.

Table 5
Level of conclusion of the 'stratified care' approach : interaction-effects and between-group differences

Outcome measure	Intervention	Effect	Studies	Follow-up time	Level of evidence	RoB	Level of conclusion
Pain	Biopsychosocial approach	-	Das Naïr et al. [48]	6m	B	Some concerns	Weak
	Weight loss intervention	-	Birch et al. [46]	12m	B	Some concerns	Weak
	Dry needling	-	Liljensoe et al. [52]	12m	A2	Low	Moderate
		-	Mayoral et al. [55]	6m	A2	Low	Moderate
Function	Biopsychosocial approach	+	Das Naïr et al. [48]	6m	B	Some concerns	Weak
		-	Birch et al. [46]	12m	B	Some concerns	Weak
	Weight loss intervention	-	Liljensoe et al. [52]	12m	A2	Low	Moderate
	Dry needling	-	Mayoral et al. [55]	6m	A2	Low	Moderate
	Exercise	-	Matassi et al. [54]	6m/12m	A2	Low	Moderate
QoL	Biopsychosocial approach	-	Das Naïr et al. [48]	6m	B	Some concerns	Weak
		-	Birch et al. [46]	12m	B	Some concerns	Weak
	Weight loss intervention	-	Liljensoe et al. [52]	12m	A2	Low	Moderate

Abbreviations: m= months, QoL= Quality of Life, RoB= Risk of Bias

to individuals' needs [46]. Nevertheless, the study was still considered stratified because more stringent inclusion criteria (related to the chronic pain phenotype) were used.

Interventions in other studies were given to a general group of people with KOA and could be divided into 5 domains: exercise (strength, balance, neuromuscular or cardiovascular) [49,56,57,59], biomedical education alone [47], exercise + biomedical education [43,45,50], osteopathic manipulative interventions [44] and interventions based on a more biopsychosocial approach [53,58,60]. As biopsychosocial interventions, a standardized pain neuroscience education was used in Louw et al. [53] and a realistic expectation program in Tolk et al. [60]. The same CBT program as in Birch et al. [46] was used in Sun et al. as a biopsychosocial intervention [58].

Most control groups received no specific prehabilitation intervention and were asked to continue their activities as if they had not entered the study [43–46,48,49,52,54,55,57,59]. Individuals in the control group of 6 studies received a preoperative biomedical-oriented education [47,50,53,56,58,60]. None of the studies compared a non-stratified care approach with a stratified care approach to prehabilitation but only compared the approaches with a control intervention.

The mean starting time before surgery ranged from 61 weeks before surgery [52] to the day of surgery [55]. The prehabilitation interventions ended before surgery, except for in 5 studies [46,47,52,57,58] in which the content of the prehabilitation continued in the postoperative phase. As such, the intervention phase of the study continued postoperatively (ranging from 3 weeks to 1 year post-TKA). All other studies involved standard postoperative rehabilitation (as if participants had not entered the study).

Table 6
Level of conclusion of 'non-stratified care' approach : interaction-effects and between-group differences

Outcome measure	Intervention	Effect	Studies	Follow-up time	Level of evidence	RoB	Level of conclusion
Pain	Exercise	+	Rooks et al. [56]	6m	A2	Low	Strong
		+	Tungtrongjit et al. [59]	6m	A2	Low	
		-	Domínguez-Navarro et al. [49]	12m	A2	Low	Strong
		-	Skoffer et al. [57]	12m	A2	Low	
	Exercise + biomedical education	-	Aytekin et al. [43]	6m	B	Serious	Moderate
		-	Beaupre et al. [45]	6m	A2	Low	
		-	Beaupre et al. [45]	12m	A2	Low	Moderate
		-	Huber et al. [50]	12m	A2	Low	
	Biopsychosocial approach	-	Louw et al. [53]	6m	B	Serious	Weak
		-	Sun et al. [58]	12m	A2	Low	Strong
		-	Tolk et al. [60]	12m	A2	Low	
	Biomedical education	-	Culliton et al. [47]	12m	A2	Low	Moderate
	Osteopathic manipulation	-	Barral et al. [44]	6m/12m	B	Serious	Weak
Satisfaction	Biopsychosocial approach	+	Louw et al. [53]	6m	B	Serious	Weak
		-	Tolk et al. [60]	12m	A2	Low	Moderate
	Biomedical education	-	Culliton et al. [47]	12m	A2	Low	Moderate
Function	Exercise	-	Tungtrongjit et al. [59]	6m	A2	Low	Moderate
		+	Domínguez-Navarro et al. [49]	12m	A2	Low	Strong
		+	Skoffer et al. [57]	12m	A2	Low	
	Exercise + biomedical education	-	Aytekin et al. [43]	6m	B	Serious	Moderate
		-	Beaupre et al. [45]	6m	A2	Low	
		-	Beaupre et al. [45]	12m	A2	Low	Strong
		-	Huber et al. [50]	12m	A2	Low	
	Biopsychosocial approach	-	Louw et al. [53]	6m	B	Serious	Weak
		-	Sun et al. [58]	12m	A2	Low	Strong
		-	Tolk et al. [60]	12m	A2	Low	
	Biomedical education	-	Culliton et al. [47]	12m	A2	Low	Moderate
	Osteopathic manipulation	-	Barral et al. [44]	6m/12m	B	Low	Weak
QoL	Exercise	-	Domínguez-Navarro et al. [49]	12m	A2	Low	Strong
		-	Skoffer et al. [57]	12m	A2	Low	
	Exercise + biomedical education	-	Aytekin et al. [43]	6m	B	Serious	Weak
		-	Huber et al. [50]	12m	A2	Low	Moderate
	Biopsychosocial approach	-	Tolk et al.[60]	12m	A2	Low	Moderate
	Biomedical education	-	Culliton et al. [47]	12m	A2	Low	Moderate

Abbreviations: m= months, QoL= Quality of Life, RoB= Risk of Bias

All details about follow-up time, loss to follow-up, content, modalities and provider of intervention are in Table 3.

Long-term outcome after a stratified care approach (Table 5)

The effects of the studies of Birch et al. [46] and Liljensoe et al. [52] are presented as interaction effects (group x time), and the effects of das Naïr et al. [48], Matassi et al. [54] and Mayoral et al. [55] are only presented as between-group differences at a given time (no interaction effect).

Pain. Four of 5 studies investigated the effect on pain. Dry needling in individuals with myofascial trigger points [55] and a biopsychological approach (based on tailored CBT) in individuals with the chronic pain phenotype [48] as prehabilitation resulted in no improvement

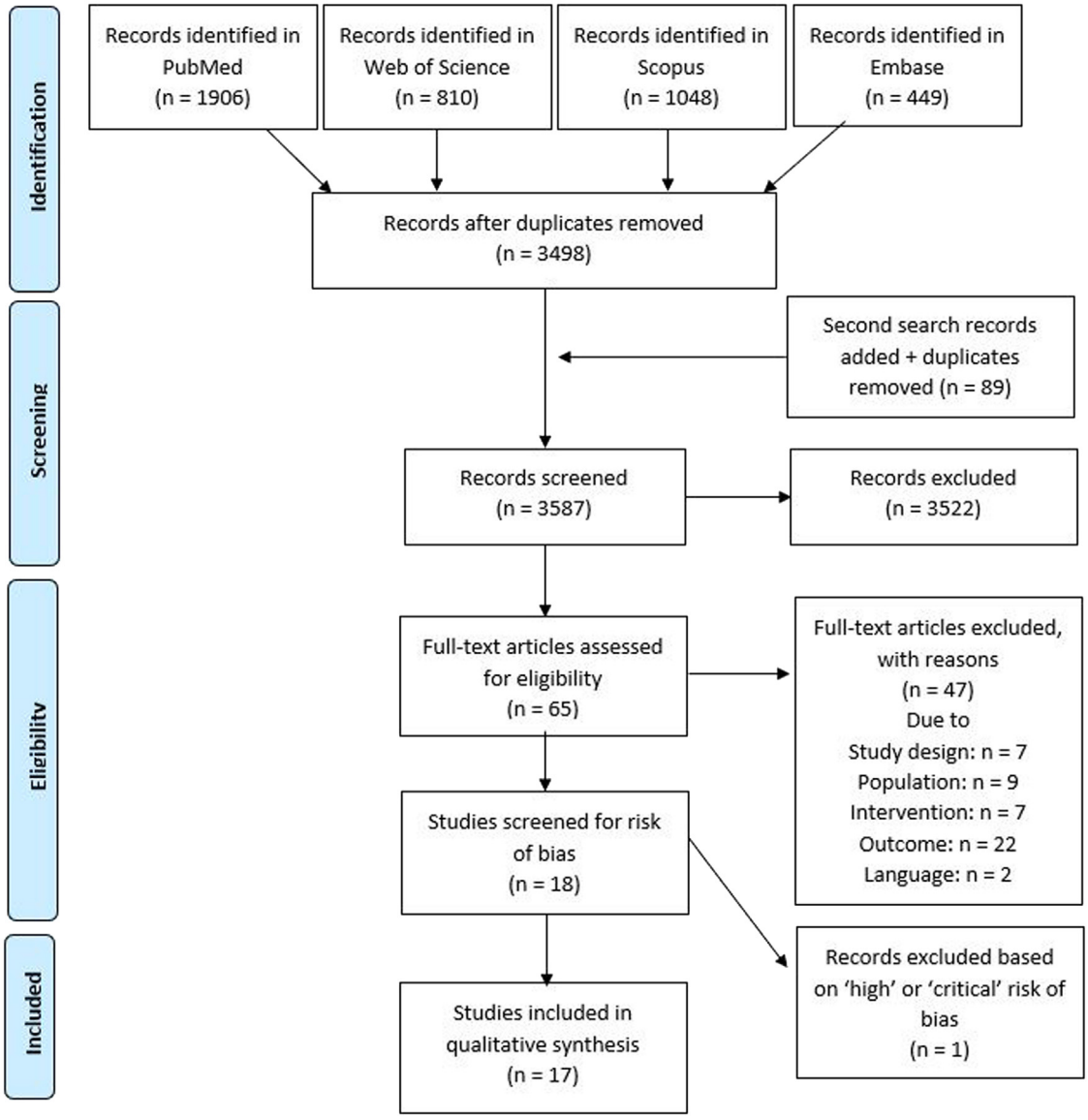

Fig. 1. Flowchart of study selection.

at 6 months after TKA as compared with no prehabilitation (p>0.05). In addition, no effect was found for a biopsychological approach (based on standardized CBT) in individuals with the chronic pain phenotype [46] or weight loss intervention in individuals with the metabolic syndrome or mechanical overload phenotype [52] at 12 months after TKA as compared with no prehabilitation (p>0.05).

Function. All 5 studies investigated the effect on several aspects of function. Only das Naïr et al., in which a biopsychosocial prehabilitation (stratified CBT) in individuals with the chronic pain phenotype was performed [48], reported a significant effect on function at 6 months post-TKA as compared with no prehabilitation (p=0.009). Dry needling in participants with myofascial trigger points [55] and exercise in individuals with specific criteria related to BMI, physical function and joint motion [54] resulted in no difference after 6 months as compared with no prehablitation (p>0.05). In addition, a biopsychosocial prehabilitation approach (standardized CBT) in individuals with the chronic pain phenotype resulted in no significant improvement at 12 months post-TKA as compared with no prehabilitation (p>0.05) [46]. Also, the weight loss intervention in individuals with the metabolic syndrome or mechanical overload phenotype conferred no significant improvement at 12 months post-TKA as compared with no prehabilitation (p>0.05) [52].

Quality of life. Quality of life was assessed in 3 studies. Despite the phenotype or specific study criteria-tailored prehabilitation in the studies, no differences over time were found for the biopsychosocial approaches in individuals with chronic pain phenotype at 6 months [48] and 12 months post-TKA [46] and a weight loss intervention in individuals with the metabolic syndrome or mechanical overload phenotype [52] at 12 months post-TKA as compared with no prehabilitation (p>0.05).

Satisfaction. This outcome measure was not used in the studies with a stratified care approach.

Details can be found in Table 3 and Table 5.

Long-term outcome after a non-stratified care approach (Table 6)

All effects are presented as interaction effects (group x time), except for the studies of Barral et al. [44] and Cullliton et al. [47], in which only the between-group differences at one given time (baseline and postoperative) are described (no interaction effects).

Pain. All 12 studies used pain as an outcome measure. None of the prehabilitation intervention types had an effect on pain at 6 or 12 months after TKA as compared with no or biomedical education prehabilitation, except for the studies of Rooks et al. [56] and

Tungtrongjit et al. [59]. These studies found a significant improvement at 6 months after TKA in favour of their intervention groups receiving exercise ($p<0.05$ and $p=0.029$, respectively) as compared with biomedical education prehabilitation and no prehabilitation, respectively.

Satisfaction. Three studies investigated the effect of prehabilitation on satisfaction; only Louw et al. [53] reported a significant positive effect of a biopsychosocial prehabilitation (standardized pain neuroscience education) approach at 6 months after TKA as compared with biomedical education prehabilitation ($p=0.03$). However, Tolk et al. [60] found no significant improvement in satisfaction at 12 months after TKA for the biopsychosocial prehabilitation (realistic expectations program) approach as compared with the biomedical education prehabilitation using an intention-to-treat analysis ($p>0.05$). The authors also performed a per protocol analysis for this outcome, which did reveal a significant positive effect of the intervention on satisfaction at 12 months post-TKA ($p= 0.012$). However, the intention-to-treat analysis was dominant according to their methodology. Additionally, an online e-learning tool of biomedical education prehabilitation resulted in non-significant improvements at 12 months after TKA as compared with a biomedical education given on paper ($p>0.05$) [47].

Function. All 12 studies investigated the effect on function. None of the interventions had an effect on postoperative function as compared with no prehabilitation or biomedical education prehabilitation, again except for exercise [49,57]. Despite no significant effect found at 6 months post-TKA ($p>0.05$), exercise did result in a significant increase in single leg standing time [$p=0.043$] [49] and increase in strength of quadriceps ($p=0.002$) and hamstrings ($p=0.042$) [57] at 12 months post-TKA as compared with no prehabilitation.

Quality of life. Exercise, exercise + biomedical education, a biopsychosocial approach or biomedical education alone as prehabilitation resulted in no significant effects regarding quality of life at 6 months [43] or 12 months [47,49,50,57,60] post-TKA ($p>0.05$) as compared with no or biomedical education prehabilitation.

Details can be found in Table 3 and Table 6.

Discussion

The first aim of this systematic review was to investigate whether previous prehabilitation studies of people with KOA awaiting TKA included phenotypes or specific individual characteristics as study inclusion or exclusion criteria and whether the content of the prehabilitation was stratified accordingly. The second aim was to synthesise and compare the long-term outcomes after TKA regarding pain, satisfaction, function or quality of life of the studies with non-stratified prehabilitation care in relation to studies with stratified prehabilitation care.

For the first aim, our systematic review found that none of the previous prehabilitation clinical trials explicitly mentioned clinical phenotypes in their study inclusion criteria. The study inclusion criteria of 3 studies [46,48,52] could be related to a specific phenotype, and 2 others [54,55] described more specific criteria beyond the KOA diagnosis. The study inclusion and exclusion criteria of 4 studies [46,52,54,55] were adapted to the intervention accordingly; only in the das Naïr et al. [48] study was the intervention adapted to individuals' needs.

Regarding the second aim, none of the studies compared a non-stratified care approach with a stratified care approach to prehabilitation. Our systematic review found that all studies compared their prehabilitation with a control group, and as such, could only provide a comparison of stratified care versus control and non-stratified care versus control prehabilitation. Evidence was weak for a positive effect of the stratified care approach: biopsychosocial prehabilitation (stratified CBT) resulted in a positive effect at 6 months after TKA on function as compared with no prehabilitation. Accordingly, evidence was weak for a positive effect of the non-stratified care approach of a standardized pain neuroscience education program compared to a biomedical education program but not on satisfaction at 6 months post-TKA. However, evidence was strong for a positive effect of exercise prehabilitation on pain at 6 months after TK and on function at 12 months after TKA in the non-stratified care approach as compared with no prehabilitation. We could not establish other significant results on any outcome and follow-up time regarding other prehabilitation interventions compared to control groups. Details about all levels of conclusions are presented in Table 5 and Table 6.

Despite the acknowledged importance of subgrouping and stratified care in heterogenous diseases such as KOA [61], most of the literature including prehabilitation before TKA completely lacked this approach. In people with back pain, Foster et al. [26] identified 3 approaches for stratified care: stratification based on risk profile, mechanisms and treatment respondents. The third approach was used in 4 stratified studies included in this review [46,52,54,55]. The interventions of these studies already existed, and individuals were selected on the basis of criteria matched to the factors the intervention were thought to address [26]. However, this strategy seemed not ideal. For example, in the study of Mayoral et al. [55] (one of stratified care studies), people with KOA were screened for myofascial trigger points to match their predefined intervention; regardless, every individual screened by the authors fulfilled the criteria and therefore none could be excluded. As such, this seemed no argument for a subgroup of people with KOA. Only the das Naïr et al. study [48] (one of the stratified care studies) implemented biopsychosocial prehabilitation care stratified to individuals' needs, instead of visa versa (such as the other 4 studies). Remarkably, this is also the only stratified care study that showed a significant positive effect. As such, this study probably used a more effective way of stratification.

The treatment-respondents approach is in fact not the most ideal way of individual centered care in research and clinical practice. Current Osteoarthritis Research Society International guidelines still recommend a "stepped care" approach in KOA intervention studies; that is, all people with KOA receive the same intervention, and treatments are modified only if an individual does not benefit sufficiently. Exercise and education are the core elements. However, these guidelines focus on non-surgical management, and clear guidelines for prehabilitation are lacking [62].

All the prehabilitation interventions of the included studies had the aim to improve certain postoperative outcomes more than control interventions. Nevertheless, the goal of prehabilitation itself is to focus on improving risk factors for insufficient postoperative outcome [13]. None of the studies explicitly targeted this, and hence, the aim of prehabilitation was probably missed. More ideally, the most suitable prehabilitation intervention is to probably tailor the intervention based on the phenotype or specific individual's characteristics (including risk factors for insufficient postoperative outcome). This situation creates a sub-clustering of people with KOA in which the intervention needs to be adapted to the modifiable prognostic characteristics of the individual [63,64].

In terms of research, single-case experimental designs or pragmatic trials, with the possibility to stratify the intervention, are a great option to test the hypothesis that stratified rather than non-stratified prehabilitation is more effective [65]. This will be the only way to finally find evidence about whether to use a stratified approach or not and if so, to draw conclusions about the best matched stratified approach. A recent review also indicated the importance of a direct comparison of effective stratified versus non-stratified care because this kind of research in musculoskeletal diseases is extremely lacking [63].

In addition, previous research of people with KOA suggested the importance of identifying a clinical phenotypes based on modifiable factors first, to guarantee optimal individual stratified treatment [24–26]. Hence, the phenotypes chosen in the Dell'Isola et al. study

[19] were based on people with KOA not awaiting TKA and therefore not specifically chosen for prehabilitation purposes. More studies building further on clinical phenotypes are necessary, to find the optimal division of clinical phenotypes that can be used in people with KOA awaiting TKA and to test the prognostic value of identified phenotypes.

In general, we found the strongest evidence for the effect of exercise prehabilitation on pain at 6 months and on function at 12 months post-TKA in the non-stratified care approach as compared with no prehabilitation. This finding is in line with studies focusing on the effect of exercise as treatment in people with KOA or as rehabilitation in individuals with TKA [62]. Exercise therapy seems to have a positive effect on pain and function in many populations; however, most of the time, the positive effects of exercise therapy have been rather small to moderate [66,67]. The extent of the positive effect of exercise in the included studies is unclear because none reported effect sizes. As suggested above, effective matched stratified prehabilitation care might result in even better effects [18,63,64]. This hypothesis is strengthened because in a recent study, a stratified exercise approach in people with KOA (not awaiting TKA) revealed higher improvements regarding pain and functional activity as compared with previous stepped care research [29]. Therefore, ineffective stratified care (matching the individuals to the intervention instead of visa versa) could have resulted in non-significant positive effects of exercise prehabilitation in the stratified care studies of this review.

Another important observation is that none of the studies included a process evaluation of the given prehabilitation, except for Birch et al. [46], in which physiotherapists regularly met to align their given treatment. Only in Beaupre et al. [45] and Matassi et al. [54] were individuals instructed to complete a log book to have an idea about their therapy compliance, which was in both studies about 80%. No other control factor to guarantee the quality of the intervention was mentioned in these and other studies.

The lack of effect of other prehabilitation strategies, apart from exercise, is in line with a recent systematic review and meta-analysis of Dennis et al. [15], which found low to moderate evidence that prehabilitation before TKA resulted in no benefit on long-term pain outcomes, and also other recent systematic reviews reported only a benefit on short-term outcomes [68,69]. This situation might be related to the aforementioned theories of effective stratified care [29]. Likely, the included studies in the reviews did not perform personalized stratified care, or none of the reviews intended to compare studies with a stratified care approach to studies with a non-stratified care approach.

Moreover, in 2 studies of the non-stratified care approach as well as in more than the half of the studies using the stratified care approach [44,47,48,54,55], statistical analyses did not measure interaction effects. Therefore, the difference in results was only measured and compared at a specific time and so the analyses were cross-sectional. This situation may have resulted in indecisive changes over time. Additionally, 2 stratified care studies exhibited only medium RoB; therefore, conclusions could only be made with moderate or weak evidence [46,48]. Both reasons again might not have revealed potentially positive results of prehabilitation.

In general, to date, there are not enough high-quality studies to draw hard conclusions. Scientific research is the basis for our education and clinical practice, so this field of research must be brought to a higher level. First, an adequate assessment of the individual taking into account all modifiable risk factors for insufficient postoperative outcome with the prognostic value is necessary for sub-clustering individuals in scientific research and clinical practice. Second, an individual–characteristics stratified intervention with a sufficient process evaluation including all qualitative (adherence to intervention protocol, control whether the changes are as expected) and quantitative (number of sessions, frequency per week etc.) elements, including the clear aim of the prehabilitation must follow.

Strengths and limitations of the review

A huge strength of this systematic review is that this is the first review of people with KOA that tried to investigate the difference in effectiveness between studies with a stratified care approach and those with a non-stratified care approach. We were not able to make a direct comparison, but the comparison of stratified care versus control and non-stratified care versus control was possible to a certain level.

A limitation is that studies that used a follow-up period of < 6 months were excluded. Perhaps if other studies with a shorter follow-up were included, the short-term differences could also be investigated. One of the 2 approaches could have resulted in better outcomes sooner as compared with the other approach, but the difference in treatment effect faded away at a longer follow-up. This study could also be interesting, because in this population, apart from the influence of other factors, the sooner individuals get better, the fewer treatment sessions they might need. However, our focus, and thus main outcomes, were persistent pain and satisfaction. Because previous research on the effect of TKA in people with KOA has shown that most of the improvement was seen at 3 to 6 months after surgery (a normal expected healing process) [70–73], this strengthened our decision to opt for a minimum follow-up time of 6 months.

A second limitation is that we used the clinical phenotypes described by Dell-Isola et al. [19]. We do not know whether all study characteristics included in the different phenotypes were modifiable factors with a sufficient prognostic value as the studies, on which the division of Dell-Isola et al. was based, were cross-sectional. The characteristics of the described phenotypes have never been tested in an intervention study, and therefore, no definite conclusion about the “modifiability” and “prognostic value” can be drawn. Nevertheless, this is the first review that described such clinical division, and in a later study, Dell-Isola et al. found that 84% of their 600 participants with KOA could be divided into these phenotypes [74]. This finding strengthens our choice to analyse the included studies based on their identified phenotypes, as this is currently the only available “more clinically based stratification”. More research on stratifying and its treatment efficacy is certainly warranted.

Conclusion

To date, only 5 existing clinical prehabilitation intervention trials in people with KOA awaiting TKA focused on a specific sample, which was based on a KOA phenotype or more stringent inclusion or exclusion study criteria and thus used a kind of stratified prehabilitation care. However, in 4 of the 5 studies, this stratification was not that efficient because the intervention was set up first and the study participants were matched to the intervention instead of visa versa. This systematic review found strong evidence for a positive effect of exercise prehabilitation versus no prehabilitation on pain at 6 months post-TKA and function at 12 months post-TKA and weak evidence for a positive effect of a pain neuroscience education prehabilitation versus biomedical education on satisfaction at 6 months post-TKA regarding the non-stratified care studies. Evidence was weak for a positive effect of a biopsychosocial approach prehabilitation on function at 6 months after TKA as compared with no intervention regarding the stratified care studies. This was also the only study that used stratification based on individual characteristics instead of visa versa. No direct comparison of stratified compared to non-stratified studies was possible. More matched stratified care studies using a pragmatic trial or single-case experimental design in people with KOA are highly needed.

Conflict of interest

None declared.

Funding

The study was not financially supported by any study sponsor. SV is a predoctoral research fellow of BOF UAntwerp and L.M. is a predoctoral research fellow of the FWO-Flanders.

Acknowledgements

The authors thank Emily Evans, Elise Vermeiren and Jolien Hoydonckx for their contribution.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.rehab.2022.101705.

References

[1] Pereira D, Ramos E, Osteoarthritis BJ. Acta Med Port 2015 Jan;28(1):99–106 2015/03/31 ed.
[2] Lluch E, Nijs J, Courtney CA, Rebbeck T, Wylde V, Baert I, et al. Clinical descriptors for the recognition of central sensitization pain in patients with knee osteoarthritis. Disabil Rehabil 2018 Nov;40(23):2836–45 2017/08/05 ed.
[3] Reginster JY. The prevalence and burden of arthritis. Rheumatol Oxf 2002 Apr;41 (Supp 1):3–6 2002/08/14 ed.
[4] Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Jt Surg Am 2007 Apr;89(4):780–5 2007/04/04 ed.
[5] Ethgen O, Bruyère O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. J Bone Jt Surg Am 2004 May;86(5):963–74 2004/05/01 ed.
[6] Baert IA, Lluch E, Mulder T, Nijs J, Noten S, Meeus M. Does pre-surgical central modulation of pain influence outcome after total knee replacement? A systematic review. Osteoarthr Cartil 2016 Feb;24(2):213–23 2015/09/19 ed.
[7] Sakellariou VI, Poultsides LA, Ma Y, Bae J, Liu S, Sculco TP. Risk assessment for chronic pain and patient satisfaction after total knee arthroplasty. Orthopedics 2016 Jan;39(1):55–62 2016/01/06 ed.
[8] Scott CE, Howie CR, MacDonald D, Biant LC. Predicting dissatisfaction following total knee replacement: a prospective study of 1217 patients. J Bone Jt Surg Br 2010 Sep;92(9):1253–8 2010/08/28 ed.
[9] Rice DA, Kluger MT, McNair PJ, Lewis GN, Somogyi AA, Borotkanics R, et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. Br J Anaesth 2018 Oct;121(4):804–12 2018/09/22 ed.
[10] Chesham RA, Shanmugam S. Does preoperative physiotherapy improve postoperative, patient-based outcomes in older adults who have undergone total knee arthroplasty? A systematic review. Physiother Theory Pr 2017 Jan;33(1):9–30 2016/10/14 ed.
[11] Mizner RL, Petterson SC, Snyder-Mackler L. Quadriceps strength and the time course of functional recovery after total knee arthroplasty. J Orthop Sports Phys Ther 2005 Jul;35(7):424–36 2005/08/20 ed.
[12] Wang L, Lee M, Zhang Z, Moodie J, Cheng D, Martin J. Does preoperative rehabilitation for patients planning to undergo joint replacement surgery improve outcomes? A systematic review and meta-analysis of randomised controlled trials. BMJ Open 2016 Feb 1;6:e009857.
[13] Cabilan CJ, Hines S, Munday J. The effectiveness of prehabilitation or preoperative exercise for surgical patients: a systematic review. JBI Database Syst Rev Implement Rep 2015 Jan;13(1):146–87 2015/10/09 ed.
[14] Wallis JA, Taylor NF. Pre-operative interventions (non-surgical and non-pharmacological) for patients with hip or knee osteoarthritis awaiting joint replacement surgery—a systematic review and meta-analysis. Osteoarthr Cartil 2011 Dec;19 (12):1381–95 2011/10/01 ed.
[15] Dennis J, Wylde V, Gooberman-Hill R, Blom AW, Beswick AD. Effects of presurgical interventions on chronic pain after total knee replacement: a systematic review and meta-analysis of randomised controlled trials. BMJ Open 2020 Jan 20;10(1):e033248 2020/01/23 ed..
[16] Gill SD, McBurney H. Does exercise reduce pain and improve physical function before hip or knee replacement surgery? A systematic review and meta-analysis of randomized controlled trials. Arch Phys Med Rehabil 2013 Jan;94(1):164–76 2012/09/11 ed.
[17] Moyer R, Ikert K, Long K, Marsh J. The value of preoperative exercise and education for patients undergoing total hip and knee arthroplasty: a systematic review and meta-analysis. JBJS Rev 2017 Dec;5(12):e2. 2017/12/13 ed..
[18] Bierma-Zeinstra SMA, Verhagen AP. Osteoarthritis subpopulations and implications for clinical trial design. Arthr Res Ther 2011 Apr 5;13(2):213.
[19] Dell'Isola A, Allan R, Smith SL, Marreiros SS, Steultjens M. Identification of clinical phenotypes in knee osteoarthritis: a systematic review of the literature. BMC Musculoskelet Disord 2016 Oct 12;17(1):425. 2016/10/14 ed.
[20] Bierma-Zeinstra SM, van Middelkoop M. Osteoarthritis: in search of phenotypes. Nat Rev Rheumatol 2017 Dec;13(12):705–6 2017/11/04 ed.
[21] Deveza LA, Melo L, Yamato TP, Mills K, Ravi V, Hunter DJ. Knee osteoarthritis phenotypes and their relevance for outcomes: a systematic review. Osteoarthr Cartil 2017 Dec;25(12):1926–41 2017/08/30 ed.
[22] Knoop J, van der Leeden M, Thorstensson CA, Roorda LD, Lems WF, Knol DL, et al. Identification of phenotypes with different clinical outcomes in knee osteoarthritis: data from the osteoarthritis Initiative. Arthr Care Res 2011 Nov;63(11):1535–42.
[23] van der Esch M, Knoop J, van der Leeden M, Roorda LD, Lems WF, Knol DL, et al. Clinical phenotypes in patients with knee osteoarthritis: a study in the Amsterdam osteoarthritis cohort. Osteoarthrs Cartil 2015 Apr;23(4):544–9.
[24] Felson DT. Identifying different osteoarthritis phenotypes through epidemiology. Osteoarthr Cartil OARS Osteoarthr Res Soc 2010 May;18(5):601–4.
[25] Driban JB, Sitler MR, Barbe MF, Balasubramanian E. Is osteoarthritis a heterogeneous disease that can be stratified into subsets? Clin Rheumatol 2010 Feb;29 (2):123–31.
[26] Foster NE, Hill JC, O'Sullivan P, Hancock M. Stratified models of care. Best Pract Res Clin Rheumatol 2013 Oct 1;27(5):649–61.
[27] Bennell KL, Hall M, Hinman RS. Osteoarthritis year in review 2015: rehabilitation and outcomes. Osteoarthr Cartil 2016 Jan;24(1):58–70.
[28] Knoop J, Dekker J, van der Leeden M, de Rooij M, Peter WFH, van Bodegom-Vos L, et al. Stratified exercise therapy compared with usual care by physical therapists in patients with knee osteoarthritis: a randomized controlled trial protocol (OCTOPuS study). Physiother Res Int [Internet] 2020;25(2) Apr [cited 2021 Jun 3] Available from: ncbi.nlm.nih.gov/pmc/articles/PMC7187154/.
[29] Knoop J, van der Leeden M, van der Esch M, de Rooij M, Peter WF, Bennell KL, et al. Is a model of stratified exercise therapy by physical therapists in primary care feasible in patients with knee osteoarthritis? : a mixed methods study. Physiotherapy 2020 Mar 1;106:101–10.
[30] Hill JC, Whitehurst DGT, Lewis M, Bryan S, Dunn KM, Foster NE, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial. Lancet Lond Engl 2011 Oct 29;378(9802):1560–71.
[31] Brennan GP, Fritz JM, Hunter SJ, Thackeray A, Delitto A, Erhard RE. Identifying subgroups of patients with acute/subacute 'nonspecific' low back pain: results of a randomized clinical trial. Spine 2006 Mar 15;31(6):623–31.
[32] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62 (10):1006–12 oktober.
[33] Eriksen MB, Frandsen TF. The impact of patient, intervention, comparison, outcome (PICO) as a search strategy tool on literature search quality: a systematic review. J Med Libr Assoc JMLA 2018 Oct;106(4):420–31.
[34] PubMed [Internet]. PubMed. [cited 2021 Mar 11]. Available from: pubmed.ncbi.nlm.nih.gov/
[35] Trusted publisher-independent citation database [Internet]. Web of Science Group. [cited 2021 Mar 11]. Available from: clarivate.com/webofsciencegroup/solutions/web-of-science/.
[36] Embase - Login [Internet]. [cited 2021 Mar 11]. Available from: embase.com/login
[37] Scopus - Document search [Internet]. [cited 2021 Mar 11]. Available from: scopus.com/search/form.uri?display=basic#basic.
[38] Bramer WM, Giustini D, de Jonge GB, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. J Med Libr Assoc JMLA 2016 Jul;104(3):240–3.
[39] Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016/12/07 ed. 2016 Dec 5;5(1):210.
[40] RoB 2: A revised Cochrane risk-of-bias tool for randomized trials [Internet]. [cited 2021 Mar 11]. Available from: rob-2-revised-cochrane-risk-bias-tool-randomized-trials.
[41] ROBINS-I [Internet]. [cited 2021 Mar 11]. Available from: risk-bias-non-randomized-studies-interventions.
[42] Meeus M (viaf)161462844068153320 91, Gebruers N. Health literacy : from reference to review [Internet]. Leuven : Acco; 2016. Available from: lib.ugent.be/catalog/rug01:002320186.
[43] Aytekin E, Sukur E, Oz N, Telatar A, Eroglu Demir S, Sayiner Caglar N, et al. The effect of a 12 week prehabilitation program on pain and function for patients undergoing total knee arthroplasty: a prospective controlled study. J Clin Orthop Trauma 2019 Apr;10(2):345–9.
[44] Barral P, Klouche S, Barral N, Lemoulec Y-P, Thés A, Bauer T. Preoperative osteopathic manipulative therapy improves postoperative pain and reduces opioid consumption after total knee arthroplasty: a prospective comparative study. J Am Osteopath Assoc 2020 Jul 1;120(7):436–45.
[45] Beaupre LA, Lier D, Davies DM, Johnston DBC. The effect of a preoperative exercise and education program on functional recovery, health related quality of life, and health service utilization following primary total knee arthroplasty. J Rheumatol 2004 Jun;31(6):1166–73.
[46] Birch S, Stilling M, Mechlenburg I, Hansen TB. No effect of cognitive behavioral patient education for patients with pain catastrophizing before total knee arthroplasty: a randomized controlled trial. Acta Orthop 2020 Feb;91(1):98–103 2019/11/26 ed.
[47] Culliton SE, Bryant DM, MacDonald SJ, Hibbert KM, Chesworth BM. Effect of an e-learning tool on expectations and satisfaction following total knee arthroplasty: a randomized controlled trial. J Arthroplasty 2018 Jul;33(7):2153–8.

[48] das Nair R, Mhizha-Murira JR, Anderson P, Carpenter H, Clarke S, Groves S, et al. Home-based pre-surgical psychological intervention for knee osteoarthritis (HAPPiKNEES): a feasibility randomized controlled trial. Clin Rehabil 2018 Jun;32(6):777–89.
[49] Domínguez-Navarro F, Silvestre-Muñoz A, Igual-Camacho C, Díaz-Díaz B, Torrella JV, Rodrigo J, et al. A randomized controlled trial assessing the effects of preoperative strengthening plus balance training on balance and functional outcome up to 1 year following total knee replacement. Knee Surg Sports Traumatol Arthrosc Off J ESSKA 2021 Mar;29(3):838–48.
[50] Huber EO, Roos EM, Meichtry A, de Bie RA, HA Bischoff-Ferrari. Effect of preoperative neuromuscular training (NEMEX-TJR) on functional outcome after total knee replacement: an assessor-blinded randomized controlled trial. BMC Musculoskelet Disord 2015 Apr 25;16:101.
[51] Jahic D, Omerovic D, Tanovic AT, Dzankovic F, Campara MT. The effect of prehabilitation on postoperative outcome in patients following primary total knee arthroplasty. Med Arch Sarajevo Bosnia Herzeg 2018 Dec;72(6):439–43.
[52] Liljensøe A, Laursen JO, Bliddal H, Søballe K, Mechlenburg I. Weight loss intervention before total knee replacement: a 12-month randomized controlled trial. Scand J Surg SJS Off Organ Finn Surg Soc Scand Surg Soc 2021 Mar;110(1):3–12.
[53] Louw A, Puentedura EJ, Reed J, Zimney K, Grimm D, Landers MR. A controlled clinical trial of preoperative pain neuroscience education for patients about to undergo total knee arthroplasty. Clin Rehabil 2019 Nov;33(11):1722–31 2019/06/20 ed.
[54] Matassi F, Duerinckx J, Vandenneucker H, Bellemans J. Range of motion after total knee arthroplasty: the effect of a preoperative home exercise program. Knee Surg Sports Traumatol Arthrosc Off J ESSKA 2012 Dec 28;22.
[55] Mayoral O, Salvat I, Martín MT, Martín S, Santiago J, Cotarelo J, et al. Efficacy of myofascial trigger point dry needling in the prevention of pain after total knee arthroplasty: a randomized, double-blinded, placebo-controlled trial. Evid Based Complement Altern Med. 2013/04/23 ed. 2013;2013:694941.
[56] Rooks DS, Huang J, Bierbaum BE, Bolus SA, Rubano J, Connolly CE, et al. Effect of preoperative exercise on measures of functional status in men and women undergoing total hip and knee arthroplasty. Arthritis Rheum 2006 Oct 15;55(5):700–8.
[57] Skoffer B, Maribo T, Mechlenburg I, Korsgaard CG, Søballe K, Dalgas U. Efficacy of preoperative progressive resistance training in patients undergoing total knee arthroplasty: 12-month follow-up data from a randomized controlled trial. Clin Rehabil 2020 Jan;34(1):82–90.
[58] Sun J-N, Chen W, Zhang Y, Zhang Y, Feng S, Chen X-Y. Does cognitive behavioral education reduce pain and improve joint function in patients after total knee arthroplasty? A randomized controlled trial. Int Orthop 2020 Oct;44(10):2027–35.
[59] Tungtrongjit Y, Weingkum P, Saunkool P. The effect of preoperative quadriceps exercise on functional outcome after total knee arthroplasty. 2012;95:9.
[60] Tolk JJ, Janssen RPA, Haanstra TM, van der Steen MC, Bierma-Zeinstra SMA, Reijman M. The influence of expectation modification in knee arthroplasty on satisfaction of patients: a randomized controlled trial. Bone Jt J 2021 Apr 1;103-B(4):619–26.
[61] Anonymous. Investigation of Subgroups in Confirmatory Clinical Trials [Internet]. European Medicines Agency; 2018 [cited 2021 June 2]. Available from: ema.europa.eu/en/investigation-subgroups-confirmatory-clinical-trials.
[62] Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthr Cartil 2019 Nov 1;27(11):1578–89.
[63] Kongsted A, Kent P, Quicke JG, Skou ST, Hill JC. Risk-stratified and stepped models of care for back pain and osteoarthritis: are we heading towards a common model? PAIN Rep 2020 Oct;5(5):e843.
[64] Smeets RJEM. How to sustain and improve client centred (matched) care in chronic musculoskeletal pain? Start by changing the way policy makers select and judge the large amount of available data, and get rid of the dogma of stepped care. Eur J Physiother 2021 Mar 4;23(2):66–7.
[65] Krasny-Pacini A, Evans J. Single-case experimental designs to assess intervention effectiveness in rehabilitation: a practical guide. Ann Phys Rehabil Med 2018 May;61(3):164–79 2017/12/19 ed.
[66] Karlsson M, Bergenheim A, Larsson MEH, Nordeman L, van Tulder M, Bernhardsson S. Effects of exercise therapy in patients with acute low back pain: a systematic review of systematic reviews. Syst Rev 2020 Aug 14;9(1):182.
[67] Bricca A, Harris LK, Jäger M, Smith SM, Juhl CB, Skou ST. Benefits and harms of exercise therapy in people with multimorbidity: a systematic review and meta-analysis of randomised controlled trials. Ageing Res Rev 2020 Nov 1;63:101166.
[68] Chen H, Li S, Ruan T, Liu L, Fang L. Is it necessary to perform prehabilitation exercise for patients undergoing total knee arthroplasty: meta-analysis of randomized controlled trials. Phys Sportsmed 2018 Feb;46(1):36–43.
[69] Ma J-X, Zhang L-K, Kuang M-J, Zhao J, Wang Y, Lu B, et al. The effect of preoperative training on functional recovery in patients undergoing total knee arthroplasty: a systematic review and meta-analysis. Int J Surg Lond Engl 2018 Mar;51:205–12.
[70] Lenguerrand E, Wylde V, Gooberman-Hill R, Sayers A, Brunton L, Beswick AD, et al. Trajectories of pain and function after primary hip and knee arthroplasty: the ADAPT cohort study. PLOS One 2016 Feb 12;11(2):e0149306.
[71] Davis AM, Perruccio AV, Ibrahim S, Hogg-Johnson S, Wong R, Streiner DL, et al. The trajectory of recovery and the inter-relationships of symptoms, activity and participation in the first year following total hip and knee replacement. Osteoarthr Cartil 2011 Dec 1;19(12):1413–21.
[72] Halket A, Stratford PW, Kennedy DM, Woodhouse LJ. Using hierarchical linear modeling to explore predictors of pain after total hip and knee arthroplasty as a consequence of osteoarthritis. J Arthroplasty 2010 Feb;25(2):254–62.
[73] 5 Year Outcomes and Survivorship of the Triathlon Total Knee Replacement: a Cohort Study. [Internet]. PubFacts. [cited 2021 Jan 26]. Available from: pubfacts.com/detail/30399989/5-Year-Outcomes-and-Survivorship-of-the-Triathlon-Total-Knee-Replacement-a-Cohort-Study.
[74] Dell'Isola A, Steultjens M. Classification of patients with knee osteoarthritis in clinical phenotypes: data from the osteoarthritis initiative. PLoS One 2018;13(1):e0191045 2018/01/13 ed.