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Do pre-operative therapeutic interventions affect outcome in people undergoing hip and knee joint replacement? A systematic analysis of systematic reviews

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ABSTRACT

Background: THR and TKR patients represent one of the largest groups of surgical patients globally, yet we do not know how to optimise pre-operative care to improve post-operative outcomes.

Objective: To clarify the effect of pre-operative prehabilitation interventions such as exercise, neuromuscular stimulation, and psychological therapies on outcomes for hip (THR) and knee (TKR) replacement patients.

Methods: We used PRISMA guidelines and guidelines by Smith and colleagues on conducting reviews of reviews. Searches were conducted on Medline, the Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects (DARE). Additional hand searches were also conducted. Articles were selected based on inclusion criteria and we report meta-analyses of data by outcome measures.

Major Findings: 6848 articles were screened and the full text of 33 reviews were obtained. Twenty systematic reviews were included, containing 67 unique randomised controlled trials. In 70% of the reviews (14/20), intervention fidelity was not reported. The components of prehabilitation that were tested were: exercise, education, nutrition, acupuncture and neuromuscular stimulation. Exercise alone did not affect functional outcome for TKR patients, but it did affect activity levels prior to THR, and pain prior to THR and TKR. Exercise alone may reduce Length of Stay (by between 0.8 and 4 days). Education when combined with exercise can reduce Length of Stay for TKR patients. Relaxation did not affect function or length of stay but gave a modest reduction of pain.

Conclusions: Providing education alongside exercise as a pre-operative intervention may reduce Length of Stay. One small RCT combined all three elements of exercise, education and dietary advice and there is no robust evidence to determine whether combining these elements can influence functional outcome.

Osteoarthritis (OA) is a leading cause of global disability with an age standardised point prevalence of 3754.2 per 100,000 [1]. The management of hip and knee OA has been revolutionised by the advent of joint replacement (arthroplasty), which improves pain and quality of life [2]. Arthroplasty is one of the most common surgical procedures in the UK, with 95,677 hip and 103,617 knee primary procedures carried out in England, Wales, and Northern Ireland in 2019 [3]. This number reduced to 54,858 hip and 50,904 knee procedures in 2020 representing a massive under-provision [4]. In 2020, waiting lists for elective orthopaedic surgery became 3 times longer than they were in 2019 largely due to the COVID pandemic [5]. The situation has improved with 84,998 THR's and 77,830 TKRs carried out in 2021 [6] but the 2021 rates still represent a significant under provision and patients are still waiting longer [7]. This heightens the need to improve outcomes and fully explain what high quality care should look like for orthopaedic patients who are waiting a long time for surgery so that we can maintain well-functioning health systems.

Prehabilitation refers to a series of structured interventions delivered before an operation which are designed to optimise patients' holistic fitness prior to surgery with the aim of improving outcomes [8]. First studied and introduced in colorectal surgery [8], interest has now turned to evaluating prehabilitative interventions for patients undergoing

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elective orthopaedic procedures such as total knee replacements (TKRs) and total hip arthroplasties (THRs) [9]. Within the context of orthopaedic surgery these are often exercise programmes, weightloss programmes, and psychological counselling, though numerous interventions have been studied [10–12].

Whilst individual studies have shown how exercise or physiotherapy programmes may be associated with lower post-operative pain, and a reduced length of hospital stay [13–16], a dose-response relationship has not always been conclusive [17]. Educational and psychological interventions have also been explored with papers reporting efficacy in outcomes for depression, quality of life, and function after elective TKR and THR surgeries [17–19].

Providing a range of prehabilitation interventions prior to elective surgery may improve outcomes due to better management of patient expectations [19, 20] (*via* education and counselling) and improved post-operative function, pain and muscle mass (*via* exercise.) [18] Lower body-mass index (BMI) has also been shown to help outcomes from TKR and THR surgery [21, 22].

The National Institute for Health and Care Excellence (NICE) guidelines on joint replacements for hip, knee and shoulder [23] also emphasised the value of pre-operative care, However, NICE [23] has prioritised establishing the clinical and cost effectiveness of prehabilitation for arthroplasty patients, before publishing full guidance on what should be included in the orthopaedic prehabilitation intervention. Given the number of interventions studied, numerous systematic reviews have been published aiming to evaluate the effectiveness of prehabilitative interventions on surgical outcomes. Often these have focussed on one set of interventions such as exercise-alone and have rarely sought to evaluate multiple types of interventions. Smith et al. [24] have published on the need to provide robust evidence from these systematic reviews using new methodologies such as a review of reviews.

The aim of this review is to collate evidence from systematic reviews studying prehabilitation to summarise the effects, optimal mode of delivery, and clinical outcomes prior to hip and knee arthroplasty.

Methods

We use guidance published by Smith et al. and the PRISMA statement, which whilst pertaining to synthesis of individual trials, can also be used to categorise sub-sections of a review of reviews [24, 25].

This review was registered with PROSPERO (CRD42019120886) at the University of York [26].

Inclusion criteria

Systematic reviews that assess any aspect of prehabilitation (education, exercise, nutrition, relaxation and/or psychological interventions) for people undergoing hip or knee arthroplasty were eligible.

Exclusion criteria

Non-English Language systematic reviews.

Search strategy

Our search strategy (Appendix 1) was designed by two reviewers, AR (an orthopaedic surgeon) and ELS (an orthopaedic physiotherapist). MeSH terms were used where applicable. The terms 'prehabilitation' (search strategy adapted from Perry et al. [27]); 'joint replacement' (adapted from Jordan et al. [28]) and 'systematic reviews' (adapted from White et al. [29]) were combined using Boolean operators following initial scoping searches.

Searches were conducted on 5-2-2019 (after an initial round of pilot searches) using Medline, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects (DARE) and the related articles function of PubMed from inception of databases. Hand searches from included papers and Google Scholar were conducted to maximise capture of literature. Searches were repeated on 15-4-2020, which identified Vasta et al. [30] and on 25-8-2021, which identified Dennis et al. [31].

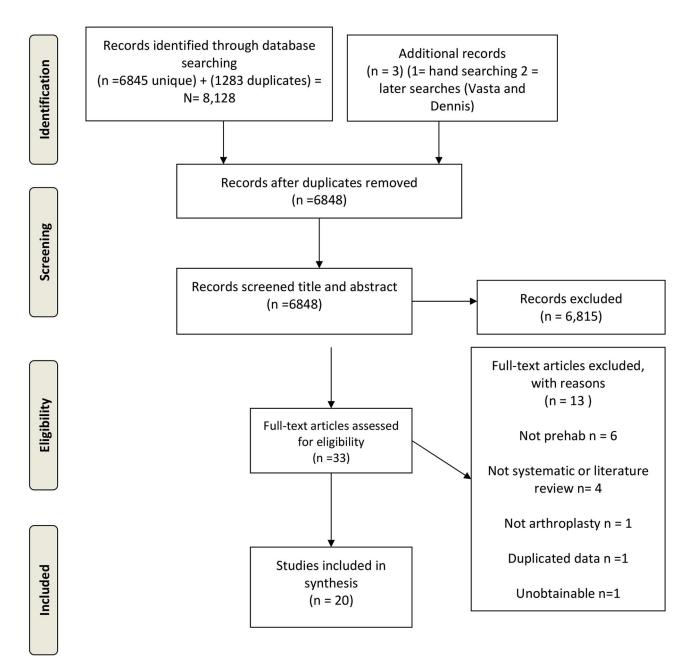
Article selection and data extraction

Titles and abstracts were screened using Rayyan (Rayyan, USA) with two authors selecting papers based on the inclusion criteria. Deadlock was resolved through discussion with a senior author. A single author extracted data using Excel (Microsoft, USA). A second reviewer verified data extraction with disagreements resolved with the same senior author.

Interventions were grouped to facilitate reporting of outcomes. Two reviews (n = 2) [32, 33], included non-orthopaedic populations, which were not included in the analysis. Given that this paper aimed to synthesise evidence from papers with different study designs and inclusion criteria the I² statistic to determine heterogeneity was not used, and metaanalysis could not be employed.

Quality measurement

The AMSTAR 2 (Measurement Tool to Assess Systematic Reviews) [34] score was used to evaluate quality of each aspect of the review process as has



Evaluating the effect of pre-habilitation on outcome in orthopaedic surgery

Figure 1. PRISMA Flow diagram. Evaluating the effect of pre-habilitation on outcome in orthopaedic surgery. PRISMA Flow diagram showing the number of studies initially identified through database searches as 6,845 with duplicates removed. A further three studies were identified using hand searches leaving a total of 6,848 studies to be screened. 33 articles remained after screening and 20 studies were selected for inclusion in the research.

been recommended when conducting a review of reviews. Risk of bias of each RCT was not assessed.

Results

The PRISMA flow chart is given in Figure 1. After removal of duplicates, we identified 6,848 titles and abstracts. Using inclusion and exclusion criteria this was reduced to 33 full text articles. Of these, 20 were included in the final analysis. We excluded 13 papers: not the right intervention or population (n=7);

duplicated paper (n = 1); not a systematic review (n = 4); and article could not be obtained (n = 1). The included papers were written in the United Kingdom (n = 6), Australia (n = 4), United States (n = 4), Denmark (n = 2), China (n = 1), Canada (n = 1), Italy (n = 1) and the Netherland's (n = 1).

Design of individual studies within the included reviews

The 20 systematic reviews included 67 unique clinical trials including 64 RCTs and 3 non-randomised

Table 1. AMSTAR 2 scores of included studies.

		AMSTAR	AMSTAR Domain															
Study		Quality Score	1	2	3	4	5	6	7	8	9	10	11*	12*	13	14	15*	16
RCTs	Dennis 2020	Low	Y	Y	Y	PY	Y	Y	Ν	Y	Y	Ν	Y	Y	Y	Y	Y	Y
	Peer 2017	Low	Y	PY	Y	PY	Ν	Ν	PY	PY	PY	Ν	Ν	Y	Y	Y	Ν	Ν
	Cabilan 2016	High	Y	Y	Y	PY	Y	Y	Y	PY	PY	Ν	Y	Y	Y	Y	Y	Y
	Chesham 2016	Moderate	Y	PY	Y	PY	Y	Y	PY	Y	PY	Ν	х	х	Y	Y	х	Y
	Aydin 2015	Moderate	Y	PY	Y	PY	Y	Y	PY	PY	PY	Ν	х	х	Y	Y	х	Y
	Kwok 2015	Moderate	Y	PY	Y	PY	Ν	Ν	PY	Y	PY	Ν	х	х	Y	Y	х	Y
	Wang 2015	High	Y	Y	Y	Y	Y	Y	Y	Y	Y	Ν	Y	Y	Y	Y	Y	Y
	Jordan 2014	Low	Y	PY	Y	PY	Y	Y	Y	PY	Y	Y	х	х	Ν	Y	х	Y
	McDonald 2014	High	Y	Y	Y	Y	Y	Y	Y	Y	Y	Ν	Y	Y	Y	Y	Y	Y
	Skoffer 2014	Moderate	Y	PY	Y	PY	Y	Y	PY	PY	PY	Ν	х	х	Y	Y	х	Y
	Baker 2012	Moderate	Y	PY	Y	PY	Y	Y	Ν	PY	PY	Ν	х	х	Y	Y	х	Y
	Hoogeboom 2012	High	Y	PY	Y	Y	Y	Y	PY	Y	Y	Ν	Y	Y	Y	Y	Y	Y
	Louw 2012	Critically low	Y	PY	Y	PY	Y	Y	Ν	Y	Ν	Ν	х	х	Ν	Y	х	Y
	Wallis 2011	Moderate	Y	PY	Y	Y	Y	Y	Y	PY	Y	Ν	Y	Y	Y	Y	Ν	Y
NRS + RTs	Vasta 2020	Moderate	Y	PY	Y	PY	Y	Ν	PY	PY	PY	Ν	х	х	Y	Ν	х	Y
	Chen 2018	Low	Y	PY	Y	PY	Y	Y	Ν	Y	Y	Ν	Ν	Y	Y	Ν	Ν	Y
	Milder 2018	Critically Low	Y	PY	Y	PY	Y	Ν	Ν	PY	Ν	Ν	х	х	Y	Ν	х	Y
	Shoemaker 2013	Critically Low	Y	Ν	Y	PY	Y	Y	Ν	PY	PY	Ν	х	х	Ν	Ν	х	Y
	Simmons 2013	Critically Low	Y	Y	Y	Y	Y	Y	Ν	Ν	PY	Ν	Ν	Ν	Ν	Y	Ν	Ν
	Barbay 2009	Moderate	Y	PY	Y	PY	Ν	Ν	Y	PY	PY	Ν	х	х	Y	Ν	х	Ν

This is a table showing the included 20 studies being screened via AMSTAR 2 tool for quality. Four studies were deemed of high quality, eight of moderate quality, four of low quality, and four of critically low quality.

RCTs, Randomised Control Trials (including quasi-randomised trials); NRS + RTs, Non-Randomised Studies and Randomised Trials; Y, yes; N, No; PY, Partial Yes; x, No meta-analysis performed; *, Could only be scored if a meta-analysis was performed.

trials. Four of the 20 reviews (Shoemaker et al. [35] Milder et al. [32] Barbay et al. [36] and Vasta et al. [30]) included seven studies of other designs (case series (2), reliability study (1), prospective cohort (1), case report (2) case-control (1)).

Patient population

Ten reviews examined both THR and TKR patients [30, 32, 36–43], with nine reviews examining only TKR patients [14, 17, 27, 31, 35, 45–48], and one only examining THR patients [32]. Cabilan et al. [33] and Milder et al. [32] included 5 trials from other surgical specialties (upper GI, colorectal, cardiac and thoracic) and data from these patient groups were not included in our analyses. Understanding demographics is essential to ensure prehabilitation evidence can meet the needs of populations served by healthcare providers.

A total of 5344 participants were included in the unique trials and studies reported in the selected twenty systematic reviews (range 82–3640 participants). Given that the 67 unique clinical trials, and seven studies of other designs were often duplicated in the included systematic reviews, tallying up participants from the reviews would have grossly overestimated the number of participants. Likewise, average age reported varied between from 48.0 years old to 83.0 years old with females reported between 12.2% and 66.0% in the analysed papers.

Prehabilitation interventions

Exercise and education were the two most commonly used intervention components with, 17 of the 20 reviews describing pre-operative exercise, whilst 13 reported on education. Other studies reported using acupuncture (2), neuro-muscular stimulation (NMS) (6), nutrition (3), and relaxation (1). Some of the reviews collated evidence from papers that used dual or tri-modality interventions with the most common combination being exercise and education.

In 70% of the reviews (14/20), compliance was not reported. None of the reviews described intervention 'monitoring' to ensure intervention delivery as planned. All 74 papers described the components of each intervention (Table 1).

Outcome measures

The systematic reviews reported the following outcomes:

- Self-reported function: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Harris Hip Score (HHS), Knee Injury and Osteoarthritis Outcome Score (KOOS)
- 2. **Quality of life:** 36-Item Short-Form Health Survey (SF-36) or EQ5D.
- Pain: WOMAC, Knee/Hip Osteoarthritis Outcome Score (KOOS/HOOS), SF-36, VAS.
- 4. Length of hospital stay
- 5. Functional outcomes: 6-metre walk test, 25/50 metre walk test, Timed sit to stand, Standing balance
- 6. **Lower limb strength**: maximum knee extension strength and/or maximum leg press.

Outcomes

Results are reported by intervention type. Ten reviews meta-analysed their data (Table 2). Significant and

_	Author	Country	N = studies	Interventions [no of trials]	Meta-analysis of outcomes (or when MA not reported: Number of trails reporting significant results and number trials reporting non- significant results.)
1.	Peer et al (2017)	UK	3	Exercises [3]	STRENGTH - No significant difference – (MD-0.12 (-0.45 – 0.21) 95%CI – 2 trials – 42 participants) WOMAC and SF-36 - resistance training had small to moderate effects at 6 weeks and small to large effects at 12 weeks post- operatively [2 trials] (results not meta-analysed)
2.	Chesham et al (2016)	UK	10	Education [2], Exercise [10], Acupuncture [2], Neuromuscular stimulation [1]	MA not conducted. Significantly enhanced standing balance [1 trial] No significant differences in SF-36 [4 trials]
3.	Simmons et al (2013)	UK	11	Exercise [11], Nutrition [1], Education [2], Neuromuscular stim [1]	SF-36 - No significant difference at 12 week post-operatively (P 0.17; MD 4.18; 95% Cl: 10.6, 1.81, 2 trials 245 participants) and at 6 months post-TKA (P 0.32; MD 3.63; 95% Cl: -3.54 , 10.80; 2 trials, 160 participants) WOMAC function - No significant difference 6-8 weeks post TKA - (P = 0.55 MD 1.89 95%Cl [-4.28,8.05] - 2 trials, 43 participants), and 12 weeks - (P 0.54, MD 1.53; 95% Cl: 6.38, 3.33; 2 trials, 128 participants)
4.	Wallis et al (2011)	AUS	23	Exercise [19], Education [8], Acupuncture [4], Neuromuscular stim [1]	PAIN KNEE – reduced pain prior to TKR (SMD (95% Cl) ¹ / ₄ 0.43 [0.13, 0.73] – 4 trials 240 participants) PAIN HIP – reduced pain prior to THR (SMD (95% Cl) ¹ / ₄ 0.52 [0.04, 1.01]- two trials, 69 participants) Activity -exercise improved activity prior to hip replacement (SMD (95% Cl) 0.47 [0.11, 0.83] 3 trials 126 participants) FUNCTION exercise and education combined improved activity after hip replacement with reduced time to reach functional milestones during hospital stay (SMD (95% Cl) MD 0.50 [0.10, 0.90] – 2 trials – 99 participants)
5.	McDonald et al (2014)	AUS	18	Education [18], Nutrition [1]	 PAIN KNEE – 12 months postoperative pain was 2 points lower (95% CI –3.45 to 7.45; 1 RCT, 109 participants, an absolute risk difference of –2% (95% CI –4% to 8%). PAIN HIP – 3 months post operatively pain was 0.34 points lower (95% CI –0.94 to 0.26; 3 RCTs, 227 participants), an absolute risk difference of –3% (95% CI –9% to 3%) - not statistically significant. QOL KNEE – 12 months postoperatively (lower score represents worse quality of life) – 3 points lower with preoperative education (95% CI –6.38 to 0.38; 1 RCT, 109 participants), an absolute risk difference of –3% (95% CI –6% to 1%). WOMAC KNEE - no different (0; 95% CI –5.63 to 5.63; 1 RCT, 109 participants), an absolute risk difference of 0% (95% CI –6% to 6%). WOMAC HIP – 3 to 24 months postoperatively score was 4.84 points lower (95% CI –10.23 to 0.66; 4 RCTs, 177 participants), an absolute risk difference of 7% (95% CI –15% to 1%). ANXIETY HIP – 6 weeks post op score was 2.28 points lower (95% confidence interval (CI) –5.68 to 1.12; 3 RCTs, 264 participants, low-quality evidence), an absolute risk difference of –4% (95%CI –10% to 2%) not statistically significant.
6.	Hoogeboom et al (2012)	NED	12	Exercise [12]	 WOMAC – KNEE -Non-significant SMD for the effect of structured exercise in short term (3 months) (SMD 20.15 (95% CI, 0.41 to 0.11; 12, 0.0%, P for heterogeneity =0.478, 6 studies, 230 patients) WOMAC HIP -Non-significant SMD of 20.31 (95% CI, 1.46 to 0.85, 12, 80.2%, P for heterogeneity =0.024, 2 studies, 72 patients)
7.	Jordan et al (2014)	UK	11	Exercise [7], Education [4]	MA not conducted Statistically significant increase in the vitality component of the SF-36 for exercise combined with education [4 trials]; Statistically significant reduction in HSS [1 trial]; No statistically significant difference in SF 36 in education only group [4 trials] No statistically significant difference in WOMAC at any time [4 trials]
8.	Baker et al (2012)	US	7	Exercise [7]	Meta analyses conduced, but poorly reported. No statistically significant difference WOMAC (pain, stiffness or function) [4 trials]; No statistically significant difference LOS [3 trials], No statistically significant difference strength [2 trials], No statistically significant difference ROM [2 trials]
9.	Skoffer et al (2015)	DEN	7	Exercise [7], Neurostimulation [1]	MA not conducted THR strength – improved but not significant [2 studies] significant improvement [1 study] TKR strength – no effect on isometric knee extension or flexion [2 studies], significant improved normalised maximum isometric voluntary contraction [2 studies] TKR FUNCTION – no significant difference THR FUNCTION – mild improvement, not significant

(continued)

Table 2. Continued

	Author	Country	N = studies	Interventions [no of trials]	Meta-analysis of outcomes (or when MA not reported: Number of trails reporting significant results and number trials reporting non- significant results.)
10.	Chen et al (2018)	CHIN	16	Exercise [14], Education [1], Neurostimulation [1]	WOMAC – KNEE Non-significant - (I2 = 0, MD −1.1, 95% CI −3.92 to 1.72, P > 0.05- 7 trials, 408 participants) No statistical difference in WOMAC stiffness (I2 = 59%, MD −0.26, 95% CI −0.65 to 0.13, P > 0.05 – 5 trials, 357 participants) LOS - shorter length of hospital stay when compared with the control group (I2 = 45%, MD −0.8, 95% CI −1.11 to −0.48, P < 0.05, 5 trials, 791 participants) KNEE ROM - significant difference between the groups (I2 = 22, MD 3.62, 95% CI 0.05–7.19, P $<$ 0.05, 3 studies – number of participants unknown) KNEE STRENGTH - no sig diff - (I2 = 69%, MD 0.2, 95% CI −0.25 to 0.64, P > 0.05, 3 trials, 213 participants) SIT TO STAND – significant difference (I2 = 60%, MD 1.68, 95% CI 1.25–2.1, P $<$ 0.05, 2 trials, 114 participants) 6 MIN WALK – No significant difference 6-min walk test (I2 = 32%, MD −19.55, 95% CI −42.37 to 3.28, P > 0.05, 3 trials, number of participants unknown)
11.	Aydin et al (2015)	DEN	12	Education [12]	 MA not conducted Significant reduction in anxiety [6 studies], No significant reduction in anxiety [2 studies] HSS – patients expectations lowered to match surgeons [2 studies], LOS – no significant difference [7 trials] significant difference [2 trials], Function – no significant difference [2 trials]
12.	Louw et al	US	13	Education [13]	MA not conducted
13.	(2013) Barbay (2009)	US	3	Exercise [3]	Pain – no significant difference – [7 studies] MA not conducted Strength – no significant difference [1 trial], LOS – no significant difference, LOS – no significant difference, WOMAC – no significant difference (THR or TKR) at 6 or 26 weeks, SF-36 – no cignificant difference (THR or TKR) at 6 or 26 weeks, SF-36 – no
14.	Shoemaker et al (2013)	US	17	Exercise [17], Education [1], Neurostimulation [1]	significant difference THR or TKR MA not conducted QOL SF-36 – no significant difference, WOMAC function – significant within-group differences [3 trials], LOS – no significant difference [4 trials] significant difference [1 trial]
15.	Kwok et al (2015)	UK	11	Exercise [11]	MA not conducted LOS – no significant difference [4 trials] significant difference [1 trial], Pain VAS – No significant difference, Pain WOMAC – no significant difference [5 studies], function WOMAC no significant difference [5 studies], QOL SF-36 No significant difference [5 studies]
16.	Wang et al (2015)	CAN	22	Exercise [22], Education [5]	 MA conducted but results not clearly divided between THR and TKR patients. QOL SF-36 – no significant difference at 6 weeks or 1 year, WOMAC function significant improvement [4 trials] no significant improvement in pain at 6 weeks not 3 months [2 trials], VAS pain significant improvement in pain at 6 weeks not 3 months [2 trials], LOS – no significant difference [9 trials] significant difference [1 trial], stair
17.	Caliban et al (2016)	AUS	12 (+5 studies – other surgery)	Exercises [17], Education [2], Relaxation [1]	 climbing – significant improvement [2 trial] THR FUNCTION (timed up and go)– No significant improvement in functional mobility at 3 months or 6 months no p value reported [1 trial] THR FUNCTION WOMAC -No significant difference at 3 months (SMD – 0.38, 95% CI [– 1.22, 0.46] 2 trials, 62 participants) TKR FUNCTION WOMAC – No significant difference at 3 months [SMD – 0.06, 95% CI [– 0.39, 0.26] 2 trials, 143 participants)
18.	Midler et al (2018)	AUS	3 (+3 other surgery)	Exercise [6], Nutrition [2]	MA not conducted THR 6 minute walk test - improved
19.	(2018) Vasta et al (2020)	ITALY	15	Exercise [7], Education [1]	MA not conducted; TKR LOS – significant difference [1 trial]; TKR FUNCTION WOMAC – trend towards improvement; THR LOS – no significant difference; THR FUNCTION – no improvement
20.	Dennis et al (2020)	UK	5	Exercise [8] Education [2]	Exercise – TKR pain at 12 months KOOS – little suggestion of difference between groups (SMD 0.08, 95%CI – 0.29 to 0.45; participants = 110; I2 = 0%), exercise and education (TKR) no clear difference between intervention and standard care on long-term pain as assessed by the WOMAC pain scale (MD 2.00, 95%CI – 3.45 to 7.45), education alone – TKR - no clear difference between intervention and standard care in terms of longterm pain as assessed on the KOOS (MD –2.55, 95%CI –6.35 to 1.24)

This is a long-table with multiple domains showing the data that has been extracted from each of the 20 systematic reviews. Where systematic reviews analysed underlying Randomised Control Trials (RCTs), the number of RCTs has been included too. Further the domain of prehabilitation each paper has analysed, whether that be education, exercise, acupuncture or neuromuscular stimulation has been included in the table. LEGEND: ROM Range of motion, MA meta-analysis, THR Total Hip Replacement, TKR Total Knee Replacement, ortho orthopaedics, WOMAC The Western Ontario and McMaster Universities Arthritis Index, HSS Hospital for Special Surgery Survey, Grey rows indicate non meta-analysed results, LOS Length of Stay.

non-significant results for each outcome are described when meta-analysis was not used. Economic outcomes were not reported, however hospital length of stay was often given as a marker of service utilisation. Where abbreviations are used MD = Meandifferences, SMD = Standardised mean difference, WMD = Weighted Mean Difference.

Exercise

The most commonly reported outcome was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), reported in 15/20 systematic reviews which analyse 15 unique RCTs.

WOMAC function TKR. Fifteen reviews reported WOMAC outcomes for TKR patients. Meta-analyses in 5/15 reviews (Table 2) revealed no significant differences between intervention and control group at any time point before or after TKR. No significant differences were observed in the short term - six to eight weeks post TKA – (p=0.55 MD 1.89 95%CI[-4.28, 8.05] - 2 trials - Simmons et al. [45]- exercise and NMS), or at 12 weeks - (P50.54, MD51.53; 95% CI: 26.38, 3.33; 2 trials - Simmons et al. [45] exercise and NMS); (SMD -0.15 (95% CI, 0.41 to 0.11; I2, 0.0%, P for heterogeneity =0.478, 6 studies, 230 patients - Hoogeboom et al. [39]- exercise alone); (SMD - 0.06, 95% CI [- 0.39, 0.26] 2 trials, 143 participants - Cabilan et al. [33] - exercise alone). Meta-analysis could not be extracted from Baker et al. [46] but they identified no significant difference after pooling data. One review revealed no significant difference WOMAC stiffness sub-section (I2 = 59%, MD -0.26, 95% CI -0.65 to 0.13, p > 0.05 - 5 trials, 357 participants) [14].

Three reviews show non-significant but slightly improved scores after prehabilitation involving exercise alone (a mix of home exercise and Physiotherapy supervised), at six and eight weeks [30, 43], with larger differences favouring the intervention group at 12 weeks [17]. One review reported significant within-group differences in three of their eight included studies [35].

WOMAC function THR. Seven reviews reported WOMAC scores for THR patients, with four providing meta-analyses. Hoogeboom et al. [39] and Cabilan et al. [33] report non-significant differences at 3 months post-operative (SMD 20.31 (95% CI, 1.46 to 0.85, I2, 80.2%, P for heterogeneity = 0.024, 2 studies, 72 patients) [39], (SMD – 0.38, 95% CI [- 1.22, 0.46] 2 trials, 62 participants.) [33] Wang et al. [48] report significant improvement in 4 trials at six to eight and 12 weeks but no significant improvement in 12 trials. Wallis et al. [37] reports improved physical function (measured with WOMAC, but also timed chair rise, 6-metre walk test, and timed up and go test) prior to hip replacement (SMD (95% CI) 0.47 [0.11, 0.83] 3 trials 126 participants), but no difference in WOMAC at eight weeks after THR. Wallis et al. also found that when exercise was combined with education, statistically significant differences were observed, with reduced time to functional milestones during hospital stay and up to 3 weeks post-operatively (SMD (95% CI) 0.50 [0.10, 0.90] 2 trials, 99 participants).

Three non-meta-analysed reviews [30], identified no significant differences between the intervention and control groups. Two of these reported a nonsignificant weak effect of prehabilitation on function as scored by WOMAC between three weeks and six months post-operatively [30].

Pain THR and TKR. Three reviews provided metaanalyses for pain and found conflicting results. Wallis et al. found reduced pain prior to TKR using exercise and acupuncture separately (SMD (95% CI)¹/₄ 0.43 [0.13, 0.73] – 4 trials 240 participants) and prior to THR (SMD (95% CI)¹/₄ 0.52 [0.04, 1.01]two trials, 69 participants) with exercise alone [37]. Chen et al. showed that exercise does not reduce pain at any point before or after TKR (MD –0.23, 95% CI –0.64 to 0.18, p > 0.05 - seven RCTs) [14]. Dennis et al. [31] found no clear difference between groups for exercise, exercise and education, or education for chronic pain in TKR patients.

SF-36 TKR and THR. The second most common outcome was SF-36, reported in 11 reviews (describing nine unique RCTs) which examined exercise. Ten reviews reported no significant difference in SF-36. Meta-analysis, conducted in two reviews, show no effect for TKR patients at 12 weeks post-operatively (P 0.17; MD 4.18; 95% CI: -10.6, 1.81, 2 trials 245 participants) [45] and at six months (P 0.32; MD 3.63; 95% CI: -3.54, 10.80; 2 trials, 160 participants) [45], or at six weeks and one year post operatively for both THR and TKR patients (meta-analysis data unavailable) [48].

One review identified a statistically significant increase in the vitality component of the SF-36 for exercise combined with education, but no statistically significant difference in SF 36 for education only post-operatively [28]. Two reviews which give non-significant results, demonstrate scores were consistently slightly improved in the prehabilitation group at 6 weeks post-operatively [17, 30].

Balance – TKR and THR. Three reviews [17, 45, 46] referenced the same RCT by Gstöettner et al. with 18 participants [12] During the first 12 post-operative weeks' patients receiving proprioceptive training

had improved standing balance. A repeated measures ANOVAs test tested the change between the three time points (baseline, after training, after TKA) achieving a P value of 0.045, demonstrating a change from baseline to after TKA.

Length of stay TKR and THR. Length of Stay (LOS) was reported in eight reviews [14, 30, 35, 36, 41, 46–49]. Chen et al. [14] pooled data to show a reduced LOS for TKR patients receiving exercise alone pre-operatively (2 RCT's), pre-operative exercise and education (2 RCT's) and pre-operative exercise and acupuncture (1 RCT) (I2=45%, MD –0.8, 95% CI –1.11 to –0.48, $p \leq 0.05 - 5$ trials, 791 participants) [14]. Wang et al. [48] report no significant difference in nine trials for THR and TKR patients receiving pre-operative exercise alone (eight trials) and pre-operative exercise and education (one trial) (pooled data unavailable).

Non-meta-analysed reviews (Vasta et al. [30], Kwok et al. [47], Shoemaker et al. [35] and Chesham et al. [44] report significant improvements (decreased) in LOS by analysing three RCTs by Matassi et al. [49], Huang et al. [50] and Crowe and Henderson [51]. These trials show that LOS is significantly shorter in prehabilitated TKR patients; by 0.8 day (pre-operative exercise alone) [49]; 1 day (pre-operative exercise, education) [50]; and 4 days (pre-operative exercise, education and dietician counselling) [51].

McDonald [38] meta-analysed two RCT's combining pre-operative education with exercise for TKR patients reporting a reduced LOS by 1.86 days.

Strength - **TKR** and **THR**. Strength was reported in six reviews [14, 17, 36, 40, 46, 47], describing eight unique RCTs. Outcome was measured with knee extension strength (eight RCTs) or a leg press (two RCTs). Chen et al. [14] report no significant difference for strength after TKR ($I^2 = 69\%$, MD 0.2, 95% CI -0.25 to 0.64, p > 0.05 – two trials). Peer et al. [17] also report no significant difference (WMD -0.12 CI-0.45, 0.21 – two trials). The three reviews which did not meta-analyse this outcome concluded that resistance training offered no additional gains in isometric quadriceps and hamstring strength at 6 and 12 weeks post-operatively for TKR patients [36, 40, 47].There was some weak benefit for THR patients [46].

Education

Three reviews [38, 41, 42] focussed solely on education and conclude that pre-operative education may not produce post-operative patient benefit for THR and TKR patients, except when combined with exercise, which yielded a LOS reduction for TKR patients of 1.86 days (two trials, 183 participants, MD -1.86; 95% CI -3.40 to -0.32 [38].

Wallis et al. [37] examined the impact of combining exercise and education on pain. Two RCTs combining exercise and education (N=68) did not show any difference for pain before THR. One RCT showed improved pain at 12 weeks post operative (THR) with combined exercise and education, however the education was provided post-operatively (Ferrara et al. cited in Wallis).

Neuro-muscular stimulation

A RCT by Walls et al. [52] was analysed in five reviews [35], and one review [40] included the paper by Petterson et al. [53] Walls et al. [52] (with a population of nine TKR patients) found that while strength did not improve, stand-to-sit and stair climbing tests did at 12 weeks post operatively. Petterson et al. [53] found significant improvement in voluntary muscle activation up to 52 weeks post operative with NMS delivered at prehabilitation. Walls et al. provided NMS over 37 sessions and Petterson et al. [53] gave 17 sessions combined with home-based exercise.

Acupuncture

Two reviews reported on Accupuncture [37, 44], used pre-operatively. None of the studies demonstrated any significant effect on function, however one study found that the acupuncture group had significantly reduced pain at three months post-operative [54].

Nutrition

Six reviews reported the efficacy of nutrition and all referenced the same paper by Crowe and Henderson [51] which was the only RCT to provide nutritional support and dietician counselling to TKR patients. Whilst pre-operative anxiety, number of days to independently get out of bed and LOS were significantly reduced as reported in the reviews, this intervention was delivered in combination with exercise and hence the role of dietary advice in isolation cannot be assessed. Additionally, in this study the control group had significantly poorer function prior to receiving the intervention [38].

Relaxation

Four reviews included relaxation, which described two RCTs. Daltroy et al. [55] examined the effect of relaxation on THR and TKR patients and found it to be non-significant in influencing post-operative pain and anxiety. Patients received training in Benson's Relaxation Response and an 18-minute bedside audiotape the day before surgery. They were instructed on how to use relaxation to lessen anxiety and asked to practice before surgery. Berge et al. [56] taught relaxation for THR patients as part of an exercise program to improve the quality of rest, sleep and activity. This achieved a modest reduction in pain, and improved sleep, but no improvement in function.

Quality of the evidence and AMSTAR 2 scores. Follow up in prehabilitation studies is generally inadequate [38], and we have validated this conclusion, finding that only a handful of studies within our 20 reviews followed up data collection for a year or more, with most limiting data collection to three to six months post-operative. Four reviews were high quality [33, 38, 39, 48], eight were moderate [30, 36, 37, 40, 41, 44, 46, 47], three were low [17, 28, 31] and four were of critically low quality [32, 35, 42, 45] (Table 1). The most impactful omission was inadequate evaluation of bias, particularly on participant selection and blinding. Only one review was registered prior to completion.

Discussion

The main finding from this study is that a combination of interventions shortened LOS (for TKR patients). When the majority of studies meta-analysed evaluated exercise alone, no significant effect on LOS was observed Wang et al. [48]. Similarly, meta-analyses of education when provided alone – does not improve LOS [37]. Yet, when meta-analyses included combinations of exercise and education, or exercise and acupuncture, better results were seen. Similarly, non-meta-analysed reports of individual studies combining multiple pre-operative interventions (Huang [50] and Crowe and Henderson [51] also show improvements in LOS.

Only one (small) trial has combined three interventions (exercise, education and dietary counselling) [51], and more high-quality trials which consistently implement multi-modal prehabilitation are needed to identify whether dual or tri-modal prehabilitation should be provided for THR and TKR patients. Combining pre-operative interventions to safely promote earlier discharge and shorten LOS, could be vital at a time when the COVID-19 pandemic still places a magnifying glass on the core challenges on healthcare.

A second major finding is that exercise improved pre-operative activity levels (for THR patients) but not post-operative outcomes (including self-reported function) [Wallis et al.]. Yet, this is contradicted by Chen et al. [14], with no improvement in pain postoperatively, after receiving an exercise programme before surgery. Exercise prior to THR or TKR surgery did not affect strength at all. By adding education to exercise, THR patients have improved pre-operative WOMAC and SF-36 scores.

Given the large number of papers we reviewed, it is surprising that dose and delivery method were poorly reported. Poor intervention reporting is not uncommon in surgery [57], and in other specialties [58] but reporting checklists can be used to improve this [59]. Moving forwards, researchers should report the dose and delivery of prehabilitation interventions more fully to aid adoption of effective interventions into practice, and to ensure that studies can be effectively synthesised in systematic reviews.

Another recently published review of systematic reviews by Almeida et al. [9] who included ten systematic reviews on prehabilitation, is also available to clinicians. However, unlike our review, which is the first to offer a comprehensive review of dual and trimodality prehabilitation interventions, Almeida et al. [9] only review the provision of exercise. In current times patients waiting for surgery tend to be less fit, with less exposure to weight bearing exercise and progression of symptoms. Therefore, although there is insufficient evidence to support each element of a multi-modal package, service providers advocate a multi-modal approach as it allows each intervention component to synergistically prepare patients for surgery [60]. Some components seek to improve pain (acupuncture, relaxation), whilst others aim to increase muscle strength to facilitate a quicker return to function (exercise, NMS) or to improve knowledge/reduce anxiety to improve length of stay (education).

Socio-economic factors such as social status/deprivation, education and income may also affect outcome, yet none of the 20 reviews included them. It is perhaps surprising that frailty was only mentioned in one of the 20 systematic reviews we included – Milder et al. [32] This is a significant finding because arthroplasty is most commonly performed in patients who are older than 65 and identifying and adapting surgical care pathways in the light of patients' frailty has recently been emphasised by the new Centre for Perioperative Care guidelines [61]. Finally, this paper only investigated the intervention stage of prehabilitation, the other three stages (screening, assessment, and monitoring) are not discussed here.

Due to the heterogeneity of intervention types, there are seemingly endless variables of who delivers it, duration, intensity and format. Therefore, future prehabilitation exercise trials should include a range of components, stretching, strengthening, range of motion and endurance exercises, (delivered in a home exercise plan, in a group, and face-to-face). Combining education with exercise has been shown to be beneficial when education was delivered faceto-face and supported with written materials [28, 38]. Specific modifications shown to give benefit, include adjusting educational material to suit learning styles [62], and tailoring elements to suit individual needs, providing unique resources for each patient.

Further work is required to evaluate the individual value of prehabilitation components – especially nutritional and psychological support which has been under researched in THR and TKR populations. While our question 'does prehabilitation improve outcomes in specific populations of THR and TKR patients?' has been answered here, with 'no, not always' – we argue that this conclusion should be interpreted with caution. Until a full-scale trial is conducted, which is purposefully designed to overcome design problems, we cannot know what the true impact of prehabilitation on orthopaedic populations might be.

This review has limitations. We used single data extraction which has been deemed inferior to double extraction (two reviewers independently extracting all the data). Yet, single data extraction allowed for pragmatism and for us to meet time contraints [63]. Also, our data extraction sheet included quantitative data (such as number of education interventions), which is less likely to result in error than extracting more complex qualitative data [63].

Conclusion

Pre-operative therapeutic interventions can affect recovery after hip and knee arthroplasty, but the evidence is weak. We identified six intervention types: exercise, education, acupuncture, nutrition, relaxation and neuromuscular stimulation. Preoperative education may not provide post-operative benefit for THR and TKR patients except to reduce LOS [37, 38]. Exercise shortens LOS (between 0.8 and 4 days) and post-operative balance for TKR patients and pre-surgery functional status (timed chair rise, six-metre walk test, and timed up and go test) for THR patients.

Further work is required to evaluate the value of pre-operative nutritional and psychological support, acupuncture and neuro-muscular stimulation, and the effect of combining some or all of the six intervention types analysed in this paper as results were inconclusive or marginal. Acupuncture and relaxation therapies may improve pain whereas NMS and nutrition may improve function at 12-months though results are more difficult to interpret based on reviews due to multi-modality interventions.

This paper identifies commonly used outcome measures and recommends the development of a core outcome set to support future meta-analysis in this exciting and developing field.

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Appendix 1. Search strategy

Topic: Joint replacement	Topic: Systematic reviews	Topic: prehab	
COMBINE USING OR	COMBINE USING OR	COMBINE USING OR	COMBINE USING OR
(Hip\$ or knee\$) adj5 (arthroplast\$ or prosthe\$ or replac\$).mp	Controlled.ab	Prehab\$.mp	Excercis\$
Exp Joint Prosthesis/	Extraction.ab	Pre-hab\$.mp	Rehab\$
Exp arthroplasty/	Meta-analysis.pt	preoperative	Re-hab\$
Arthroplast\$.mp.	Randomized controlled trials.sh	Pre-operativ\$	Physical therapy modalities/
	Review.pt	Pre operativ\$	Physical therap\$
	Selection.ab	Pre-surg\$	Physiotherap\$
	Studies.ab	Pre surg\$	nutrition
	Study.ab	conditioning	exp Dietary Supplements/ exp Food, Fortified/Nutrition Therapy/ exp diet therapy/
		Pre-conditioning	oral or food or multinutrient\$ or multi- nutrient\$ or multivitamin\$ or iron or protein or folate or vitamin\$) adj3 supplement\$).ti,ab
		Optimis\$	Cognitive Therapy/ or Psychotherapy/ or exp Mind-body therapies/ or behavior therapy/ or mindfulness/
		Optimiz\$	CBT or (cognitive or talking or mental health or behavio?ral) adj3 (intervention\$ or therap\$))).ti,ab.
		Preoperative Care/	Education\$

The search strategy used to identify papers in database searches has been highlighted in a table. This shows various methods including use of special operators to identify papers.