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Does Preoperative Rehabilitation for Patients Planning to Undergo Joint Replacement Surgery Improve Outcomes?

A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Keywords: Physiotherapy, Exercise, Prehabilitation, Joint Replacement, Meta-analysis

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Abstract:

Objectives: Although claims suggest preoperative physiotherapy and exercise programs (prehabilitation) will improve recovery after joint replacement, their clinical impact remains controversial. This systematic review aimed to assess the clinical impact of prehabilitation before joint replacement.

Design: We searched PubMed, Embase, and Cochrane CENTRAL up to November 2014 for randomized trials comparing prehabilitation versus no prehabilitation before joint replacement surgery. Postoperative pain and function scores were converted to WOMAC pain and function subscales (0-100, high scores indicate worse outcome). Random effects meta-analysis was performed to calculate weighted mean differences (WMD, 95%CI), subgrouped by hip and knee surgery.

Primary and Secondary Outcomes: Postoperative pain scores [Visual Analogue Scale (VAS), or pain subcomponents of Western Ontario and McMaster Universities osteoarthritis index (WOMAC) or pain-related subdomains of other instruments], and patient functionality.

Results: Of 22 studies (1,492 patients), 18 had high risk of bias. Prehabilitation slightly reduced pain scores within 4 weeks postoperatively (WMD -6.1, 95%CI -10.6 to -1.6), but differences did not remain beyond 4 weeks. Prehabilitation slightly improved WOMAC function score at 6-8 weeks and 12 weeks (WMD -4.0, 95%CI -7.5 to -0.5), and time to climbing stairs (WMD -1.4 days, 95%CI -1.9 to -0.8 days), toilet use (-0.9 days, 95%CI -1.3 to -0.5 days), and chair use (WMD -1.2 days, 95%CI -1.7 to -0.8 days). Effects were similar for knee and hip surgery. Differences were not found for SF-36 scores, length of stay and total cost.

Conclusions: Existing evidence suggests that prehabilitation may slightly improve early postoperative pain and function among patients undergoing joint replacement; however, effects

remain too small to be considered clinically-important and did not affect outcomes of greatest interest (ie, length of stay, quality of life, costs).

Article Summary

Strengths and Limitations of Study

- The methodology was rigorous, and included a comprehensive systematic search without limits by language, date or publication status, which identified 7 RCTs not included in any previous systematic reviews.
- We went beyond previous systematic reviews published by analyzing the effect of prehabilitation by converting to a standardized measurement of WOMAC pain and function scores, and used different presentation methods to enhance interpretability and to improve ability to find potential signals in effect size through meta-analysis.
- This meta-analysis addressed all available clinically relevant outcomes, while previous reviews addressed only a few selected outcomes. Application of GRADE for rating quality of evidence provides improved context for interpreting the findings in light of inherent strengths and limitations of the included studies.
- There is a lack of large randomized controlled trials that have been conducted in this area
- Compliance with prehabilitation was problematic in some studies, and was not reported in a number of studies

Key words: Physiotherapy, Exercise, Prehabilitation, Joint Replacement, Meta-analysis

INTRODUCTION

Total joint replacement surgery is considered as one of the most successful medical interventions with significant pain relief and improvement in physical function and quality of life for patients with severe osteoarthritis [1]. However, the recovery for a significant proportion of patients remains difficult, prolonged, and many never restore optimal functionality postoperatively [2-4]. Therefore, researchers, clinicians and policy makers are still looking for better ways to improve the timelines and extent of recovery for patients undergoing total joint replacement.

Physiotherapy has been delivered to patients, traditionally after total joint replacement for rehabilitation. However, preoperative physiotherapy and exercise programs (also known as 'prehabilitation') have been proposed as a potential way to expedite recovery times and improve overall extent of recovery in patients planning to undergo joint replacement. One recently published review recommended preoperative exercise to maintain or improve function and pain [5]; however, this recommendation was based on only one narrative systematic review with indeterminate effects [6]. Although it seems intuitive that prehabilitation should improve patient disposition at the time of surgery, and may prepare patients for a better recovery after surgery, significant uncertainties remain about the overall balance of benefits and risks (and costs) for prehabilitation.

A number of related systematic reviews or meta-analyses have been published in the recent decade with inconsistent methods and varied conclusions [6-13]. Two of them suggested that prehabilitation reduced pain for patients undergoing joint replacement [8, 11], and improved

physical function for patients undergoing hip replacement surgery, but not knee replacement surgery [8], while the remainder suggested prehabilitation did not clearly demonstrate beneficial effects or were unable to provide definitive conclusions [6, 7, 9, 10, 12, 13].

Furthermore, significant methodological limitations or errors have been identified among the existing systematic reviews. Some of them only qualitatively summarized the results [6, 7, 9, 11-13]; another two meta-analyses [8, 10] are outdated, or mistakenly included some trials in which postoperative outcomes were not reported.

Thus, we conducted an updated methodologically rigorous systematic review with meta-analysis to clarify whether evidence supports prehabilitation for patients planning to undergo joint replacement.

METHODS

Eligibility criteria

We systematically searched three databases up to November 14, 2014, including PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL). Eligible studies had to be randomized controlled trials comparing preoperative rehabilitation programs (ie, prescribed and supervised exercises or physiotherapy with or without co-interventions such as education, nutritional counseling, acupuncture, transcutaneous electrical nerve stimulation, etc.) versus no formal preoperative rehabilitation programs, reporting at least one clinically-relevant outcome of interest during the postoperative period. Clinical outcomes of interest included postoperative pain scores [Visual Analogue Scale (VAS), or pain subcomponents of Western Ontario and

McMaster Universities osteoarthritis index (WOMAC) or pain-related subdomains of other instruments], patient functionality (WOMAC function score, SF-36 physical functioning subdomain or other function-related instruments), time to resume activities of daily living, quality of life, patient satisfaction, infection, transfusions, stroke, death, or overall postoperative complications. Resource-related outcomes of interest included hospital length of stay, readmissions, and total hospital costs or total health system costs. Timeframes of relevance included in-hospital outcomes, as well as clinical or resource-related outcomes over the longer-term postoperatively.

Search terms included MeSH and keyword terms for exercise, prehabilitation, physiotherapy, physical therapy, activity, weight training, weight lifting, aquatic, swimming, strength training, endurance training, cycling, biking, kinesiotherapy, hydrotherapy, fitness, orthopedic surgery, and joint replacement and "random*". No limitations were placed on date of publication or language. Detailed search strategies are provided in the Appendix.

Literature screening and data extraction

Two reviewers (ML, ZZ) independently screened the articles by title and abstract using the pre-determined eligibility criteria. Any disagreements were resolved by the third reviewer (LW). The third reviewer (LW) also checked all the reference lists of existing systematic reviews or meta-analyses and other reviews for potentially additional eligible articles.

Two reviewers (ML, JM) independently assessed the risk of bias of the included trials using the methods recommended by Cochrane Collaboration [14], including random sequence generation,

allocation concealment, missing or incomplete outcome data, and blinding of patients, study personnel, and outcome assessors. Any discrepancies were resolved by the third reviewer (LW).

Standardized data extraction forms were developed to specify the study characteristics, patient characteristics and outcomes. Three reviewers (ML, ZZ, and LW) extracted the data. Data was verified by a fourth reviewer (JM).

Statistical analysis

Meta-analysis was performed using the random effects model. For discrete outcomes, relative risk and 95% confidence intervals (RR, 95%CI) were calculated. For continuous outcomes, e.g. pain score and function score, weighted mean differences (WMD, 95%CI) were calculated after conversion to the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) pain score (0-100) and WOMAC function score (0-100), in which a higher score indicates worse outcome. Sensitivity analysis was conducted by calculating standardized mean differences (SMD) and ratio of means (RoM).

If different pain scores were reported in one article (e.g. WOMAC pain, SF-36 pain score), the WOMAC pain score was preferentially used. If WOMAC pain score was not reported, the pain score reported in the study was converted to WOMAC pain scores to allow for comparison across studies, and to allow for estimation of overall effect size. If pain scores were reported at rest and during activity, the pain score during activity was preferentially used for analysis. If pain scores were reported during different types of activities, the largest change of pain score during the most active movement was used preferentially. If different function scores were

reported, the WOMAC function score was used preferentially for analysis. In the absence of WOMAC function scores, the alternate function score provided in the study was converted to a WOMAC function score. Two studies [15, 16] only reported total scores of Hospital for Special Surgery Knee Rating System (HSSK) and WOMAC respectively. Given the function score accounting for most of the total score and with similar trends of change over time as total score, we used the total score to replace the function score. To test whether this changed the effect size, sensitivity analysis was performed after removing the total scores from function measures to recalculate effect size.

To improve clinical relevance and interpretation of the results for postoperative pain and function improvement, we also converted continuous data from WOMAC pain score and WOMAC function score to a relative risk (RR) for achieving a "patient acceptable symptom state" (defined as the number of patients achieving the threshold pain score or function score at which patients consider themselves 'well' or 'satisfied') derived from previous research [17-20]. To calculate the RR, we assumed a normal distribution of WOMAC pain or function scores for the intervention and control groups, and we used a threshold of 30 on the WOMAC 0-100 scale to represent the threshold for the patient acceptable symptom state. The proportion of patients in the intervention and control groups with WOMAC pain or function ≤ 30 was then calculated, and combined across studies to derive a pooled relative risk [21, 22]. Finally, to further add to clinical applicability of the patient reported outcomes we calculated the risk difference for the number of patients achieving this threshold of ≤ 30 per 100 patients using the relative risk and median risk among the control groups in the included studies [23]. Subsequently, sensitivity analyses were performed to explore whether using different thresholds (20 and 40) changed the conclusions,

since our threshold of 30 represents a compromise of 20 to 40 suggested in previous studies of hip or knee surgery over the short term or long-term.

Heterogeneity was estimated using the Chi-squared test and I^2 statistic. Pre-defined subgroup analyses included separate analysis for hip and knee surgery patients, to test the existing hypothesis from a previous systematic review that prehabilitation improves postoperative pain and function more among patients undergoing hip replacement than patients with knee replacement [8]. Publication bias was explored using both visual inspection of funnel plots and Egger's test only when there were at least 10 studies included in the meta-analysis [14].

GRADE methodology was used to summarize certainty in estimates of effect (quality of evidence) in the critically important outcomes for decision-making [23-29], including WOMAC pain scores and function scores from early follow-up to 24 weeks after surgery.

RESULTS

Studies identified

Figure 1 outlines study inclusion and exclusion. A total of 319 titles and abstracts were screened for inclusion, of which 93 studies were collected in full-text for review. Of these, 71 were excluded for the following reasons: no prehabilitation arm (ie. education only or postoperative rehabilitation only, n=41), not randomized (n=17), duplicate studies (n=4), no postoperative outcomes data (n=7), no outcome of interest (n=1), and protocol only (n=1). In total, 22 randomized studies (1492 patients) of prehabilitation versus no prehabilitation met the inclusion

criteria. Twenty studies provided usable data for the meta-analysis, and 22 studies contributed qualitative or quantitative data.

Description of included studies

Among 22 included studies, eight studies were of patients undergoing total hip replacement [16, 30-36]; 12 studies included patients undergoing total knee replacement [15, 37-47] and two studies included either hip or knee replacement [48, 49]. Most studies were conducted in developed countries (North American and Europe), except for three in developing countries (Serbia [34], Thailand [45] and Turkey [32]). The median sample size of included studies was 54, ranging from 21 to 165 patients. Mean age ranged from 51 to 76 (Table 1).

Table 1 Characteristics of included RCTs

Study Name	No. of patients	Type of surgery	Countries	Mean age	% Female	Mean BMI%	Total OA %
Beaupre 2004	131	TKR	Canada	67	55	31.4	NR
Bitterli 2011	80	THR	Switzerland	66.9	38	27.4	NR
Brown 2012	32	TKR	USA	NR	NR	36.8	NR
D'Lima 1996	30	TKR	USA	69.8	46.6	NR	83.3
Evgeniadis 2008	48	TKR	Greece	68.3	76.3	34.1	100
Ferrara 2008	23	THR	Italy	63.4	60.8	NR	100
Gilbey 2003	76	THR	Australia	65.2	61.8	27.94	NR
Gocen 2004	60	THR	Turkey	51.3	35.5	NR	49
Gstoettner 2011	38	TKR	Australia	69.7	78.9	27.8	100
Hoogeboom 2010	21	THR	Netherland	76	66	NR	NR
Matassi 2014	122	TKR	Italy	66.5	48	28.5	NR
McKay 2012	22	TKR	Canada	61.3	59	34.3	100

Mitchell 2005	160	TKR	UK	70.3	57.9	NR	100
Oosting 2012	30	THR	Netherland	76	80	28.2	100
Rooks 2006	108	THR/TKR	USA	64.1	56	31.6	100
Topp 2009	54	TKR	USA	63.8	68	32.1	100
Tungtrongjit 2012	60	TKR	Thailand	64.5	83.3	24.8	100
Villadsen 2014	165	THR/TKR	Denmark	67	56	30.3	100
Vukomanovic 08	45	THR	Serbia	58.4	67	NR	100
Wang 2002	28	THR	Australia	67.1	64	NR	89
Weidenhielm 1993	39	TKR	Sweden	63.5	51.3	29.6	100
Williamson 2007	120	TKR	UK	69.8	52.9	32.7	100

TKR: total knee replacement; THR: Total hip replacement; USA: United States of America; UK: United Kingdom; BMI: Body mass index; OA: Osteoarthritis**;** NR: not reported

Nine studies compared physiotherapist supervised exercise plus home exercise versus no intervention or usual care [16, 35, 36, 38, 40-42, 44, 46]. Five compared physiotherapist supervised exercise versus no intervention or usual care [15, 33, 37, 39, 50]. Two studies compared home exercise only versus no intervention [30, 45]. Three studies compared physiotherapist supervised exercise plus education versus no intervention [31, 32, 34]. One each compared physiotherapist supervised exercise plus education versus education [48], kinesiologist supervised exercise versus placebo (kinesiologist supervised upper body exercise) [43], and physiotherapist supervised exercise plus home exercise versus education plus home exercise [47] respectively (Supplementary Table 1).

Risk of bias

Among 22 trials, adequate sequence generation was reported in 17 trials [15, 30-33, 36-43, 45-48], allocation concealment in 8 trials [30, 33, 37, 39, 42, 43, 47, 49]. The patients were blinded in one study[39], health care providers were blinded in three studies [30, 39, 44], and outcome assessors were blinded in 12 studies [30-33, 36, 37, 41, 44, 45, 47-49]. Seventeen studies [16, 30-34, 36-40, 42, 43, 46-49] reported loss to follow-up, ranging from 1.7% to 65.3%; among which the proportion of loss to follow up was more than 15% in 10 studies [30, 34, 36-39, 42, 43, 47, 48]. Ten out of 17 studies with incomplete data used intention to treat analysis [30, 33, 36, 37, 39, 42, 43, 47-49]. Overall, 4 out of 22 included trials were rated as low risk of bias [30, 33, 37, 39] and 18 trials as high risk of bias (Table 2)

Table 2: Risk of Bias for Included Studies

	Random sequence generation	Allocation concealment	Blinding of patients	Blinding of health care providers	Blinding of outcome assessors	Incomplete outcome data	Intention to treat analysis	Risk of bias
Beaupre 2004	Yes	Yes	No	No	Yes	Yes, LTFU>15%	Yes	Low risk
Bitterli 2011	Yes	Yes	No	Yes	Yes	Yes, LTFU>15%	Yes	Low risk
Brown 2012	Yes	Unclear	No	Unclear	Unclear	Yes, LTFU>15%	No	High risk
D'Lima 1996	Yes	Unclear	Unclear	Unclear	Unclear	No	Not Applicable	High risk
Evgeniadis 2008	Yes	Yes	Yes	Yes	Unclear	Yes, LTFU>15%	Yes	Low risk
Ferrara 2008	Yes	Unclear	No	No	Yes	Yes	No	High risk
Gilbey 2003	Unclear	Unclear	Unclear	Unclear	No	Yes	No	High risk
Gocen 2004	Yes	Unclear	No	Unclear	Yes	Yes	No	High risk
Gstoettner 2011	Yes	No	Unclear	Unclear	Unclear	Yes	No	High risk
Hoogeboom 2010	Yes	Yes	No	No	Yes	Yes	Yes	Low risk
Matassi 2014	Yes	Unclear	No	No	Yes	No	Not Applicable	High risk
McKay 2012	Yes	Yes	Unclear	Unclear	Unclear	Yes, LTFU>15%	Yes	High risk
Mitchell 2005	Yes	Yes	No	No	Unclear	Yes, LTFU>15%	Yes	High risk
Oosting 2012	Yes	Unclear	No	No	Yes	Yes, LTFU>15%	Yes	High risk
Rooks 2006	Yes	Unclear	Unclear	Unclear	Yes	Yes, LTFU>15%	Yes	High risk
Topp 2009	Unclear	Unclear	No	Yes	Yes	No	Not Applicable	High risk

Tungtrongjit 2012	Yes	Unclear	No	No	Yes	No	Not Applicable	High risk
Villadsen 2014	Unclear	Yes	No	No	Yes	Yes	Yes	High risk
Vukomanovic 08	Unclear	Unclear	Unclear	Unclear	Unclear	Yes, LTFU>15%	No	High risk
Wang 2002	Unclear	Unclear	Unclear	Unclear	No	No	Not Applicable	High risk
Weidenhielm 1993	Yes	Unclear	Unclear	Unclear	Unclear	Yes	No	High risk
Williamson 2007	Yes	Yes	No	No	Yes	Yes, LTFU>15%	Yes	High risk

LTFU: lost to follow-up

Supplementary Table 2 qualitatively summarizes the major findings of included studies. In total, 22 studies described at least one clinical or resource-related benefit for prehabilitation versus control, and 18 studies [15, 30-37, 39, 40, 42-48] described no significant improvement for prehabilitation versus control. We conducted meta-analysis for pain scores, function scores, SF-36 PCS and MCS, hospital length of stay, and total costs based on the data availability.

Postoperative pain

Fifteen trials with 18 comparisons and 1046 patients reported postoperative pain scores using different instruments, i.e. WOMAC [31, 37, 40, 42, 43, 45, 48], VAS [32, 34, 36, 44, 47], Knee injury and Osteoarthritis Outcome Score (KOOS)/Hip disability and Osteoarthritis Outcome Score (HOOS)[49], and 10-graded scale [46]. Only two trials [31, 49] reported significant improvement in pain at early follow-up (≤3 months), including VAS pain at 3 months [31], and KOOS/HOOS pain at 6 weeks postoperatively, but not significant at 3 months [49].

After converting to WOMAC pain 0-100, prehabilitation significantly reduced postoperative pain at 4 weeks or less (WMD -6.1, 95%CI -10.6 to -1.6, Figure 2, GRADE: low certainty in estimates, Table 4). Differences in WOMAC pain scores after 4 weeks were no longer statistically significant for prehabilitation versus control (WOMAC pain score at 6 to 8 weeks, WMD -1.4, 95%CI -5.5 to +2.6; at 12 weeks, WMD -2.9, 95%CI -6.2 to +0.3; at 24 weeks, -2.5, 95%CI -5.6 to +0.6; at 1 year, WMD -2.0, 95%CI -7.5 to +3.5; GRADE: low to moderate certainty in estimates, Table 4).

When expressed as a relative risk (RR), patients undergoing prehabilitation were more likely to achieve the acceptable pain state (WOMAC pain score ≤ 30) with RR 1.09. When expressed as an absolute risk difference, 3.9% more patients with prehabilitation achieved the acceptable pain state (WOMAC pain score≤ 30) than patients without prehabilitation at 4 weeks (Supplementary table 3). However, this small difference would be considered clinically nominal.

Postoperative function

Of 16 trials reporting on postoperative function, only four reported significant improvement in function [16, 31, 41, 49], including higher hip external rotation [31] or higher flexion range of motion (ROM) scores, WOMAC physical function and total score [16], and less time to reached 90° of knee flexion [41] and great improvement in activities of daily living (ADL) [49] after surgery .

Sixteen trials (1118 patients) reported postoperative function scores using different instruments, i.e. WOMAC [16, 31, 37, 40, 42, 43, 45, 47, 48], Harris hip score [32, 34], SF-36 physical component summary (PCS) [30], SF-36 physical functioning score [38], HSSK score [15], HOOS function in daily living [36], and KOOS/HOOS ADL[49]. After converting function scores to WOMAC function score (0-100), the difference was slightly improved (but numerically small on a scale of 0-100) with prehabilitation versus no prehabilitation at early follow-up (WOMAC function score at 6 to 8 weeks, WMD -3.9, 95%CI-7.6 to -0.3, RR=1.10, Figure 3, GRADE: moderate certainty in estimates, Table 4), and at 12 weeks (WMD -4.0, 95%CI -7.5 to -0.5, RR=1.02, Figure 4, GRADE: very low certainty in estimates, Table 4). No significant difference for WOMAC function score was found after 12 weeks (at 24 weeks, WMD -0.5, 95%CI -5.8 to +4.7; at 1 year, WMD -0.6, 95%CI -2.6 to +1.5, GRADE: low certainty in estimates, Table 4).

When expressed as a relative risk for achieving the acceptable threshold, the relative increases were small (RR 1.10 at 6-8 weeks; 1.02 at 12 weeks). When expressed as an absolute difference in likelihood of achieving the acceptable threshold, the differences ranged from 1.3% to 5.4% more patients achieving a WOMAC function score ≤ 30 at 6-8 weeks and 12 weeks respectively (Supplementary table 3).

Resumption of activities of daily living

Resumption of activities of daily living was rarely reported. In the two studies (99 patients) [32, 34] that reported activities of daily living, meta-analysis suggested significantly earlier resumption of activities, including climbing stairs (WMD -1.4 days, 95%CI-1.9 to -0.8 days), use of toilet (-0.9 day, 95%CI-1.3 to -0.5 days), use of chair (-1.2 days, 95%CI -1.7 to -0.8 days), but not for time to first day of walking (-0.2 day , 95%CI -0.4 to +0.0 day), (Table 3). However, based on the total time-course of recovery, the difference was small.

Table 3 Summary of results for prehabilitation vs. no prehabilitation

Outcomes	No. of studies	No. of patients	heterogeneity test p value	I^2 (%)	WMD & 95%CI
Pain at 4 weeks or less	4	213	0.08	55	-6.1 (-10.6 to -1.6) *
Pain at 6 to 8 weeks	5	488	0.31	16	-1.4 (-5.5 to +2.6)
Pain at 12 weeks	10	806	0.05	46	-2.9 (-6.2 to +0.3)
Pain at 24 weeks	3	247	0.22	33	-2.5 (-5.6 to +0.6)

Pain at 1 year or more	1	109	NA	NA	-2.0 (-7.5 to +3.5)
Function at 4 weeks or less	5	257	<0.001	79	-3.6 (-7.7 to +0.5)
Function at 6 to 8 weeks	5	488	0.21	31	-3.9 (-7.6 to -0.3) *
Function at 12 weeks	12	836	<0.001	69	-4.0 (-7.5 to -0.5) *
Function at 24 weeks	5	345	<0.001	89	-0.5 (-5.8 to +4.7)
Function at 1 year or more	6	296	0.99	0	-0.6 (-2.6 to +145)
First days of climbing stairs (days)	2	99	0.44	0	-1.4 (-1.9 to -0.8) *
First days of walking (days)	2	99	0.24	29	-0.2 (-0.4 to +0.002)
First days of use of toilet (days)	2	99	0.87	0	-0.9 (-1.3 to -0.5) *
First days of use of chair (days)	2	99	0.50	0	-1.2 (-1.7 to -0.8) *
SF-36 PCS at 6 weeks	1	19	NA	NA	2.7 (-9.4 to +14.7)
SF-36 PCS at 12 weeks	3	149	0.13	50	-0.3 (-5.4 to +4.7)
SF-36 PCS at 24 weeks	1	109	NA	NA	0.0 (-3.4 to +3.4)
SF-36 PCS at 1 year	1	109	NA	NA	-3.0 (-6.4 to +0.4)
SF-36 MCS at 6 weeks	1	17	NA	NA	-3.4 (-19.9 to +13.0)
SF-36 MCS at 12 weeks	3	149	0.72	0	-0.4 (-3.7 to +2.9)
SF-36 MCS at 24 weeks	1	109	NA	NA	-1.0 (-4.9 to +2.9)
SF-36 MCS at 1 year	1	109	NA	NA	-2.0 (-5.1 to +1.1)
Length of stay (days)	7	507	0.68	0	-0.3 (-0.8 to + 0.1)
Total cost (Canadian dollars)	2	242	0.99	0	+5 (-384 to +393)

PCS: physical component summary; MCS: mental component summary; WMD: Weighted mean difference; NA: not applicable;

Pain and function scores were converted to WOMAC (Western Ontario and McMaster Universities osteoarthritis index) 0-100 subscales, and high score indicates more pain or dysfunction.

* $p<0.05$

Quality of life

Significant differences in quality of life were not found in 9 studies for SF-36 [30, 37, 39, 42, 43], Quality of Well Being instrument [15], HOOS Hip-related quality of life [36], KOOS/HOOS Quality of Life subscale [49], and Patient Specific Complaints (PSC) questionnaire [33, 36]; while three trials reported significant difference in quality of life score [31, 38, 49], including higher physical function score or physical composite score using SF-36 [31, 38] or better EuroQol 5 Dimension Health Questionnaire (EQ5D) [49]; however, the numeric differences were small [31, 38, 49] and the significance disappeared at 3 months [31, 49].

Three studies including 149 patients reported SF-36 Physical Component Summary (SF-36 PCS) and Mental Component Summary (SF-36 MCS). Meta-analysis of SF-36 PCS and MCS did not detect significant differences at any time-point (from 6 weeks to 1 year, Table 3).

Length of hospital stay and total cost

Only one [41] out of 10 studies [15, 30, 32-34, 36, 37, 41, 42, 47] found a significant reduction in hospital length of stay (mean difference = -0.8 day). Meta-analysis of these studies did not detect significant differences in hospital length of stay for prehabilitation versus control (7 studies, 507 patients, WMD -0.3 days, 95%CI -0.8 to + 0.1 days, Figure 5).

Of the few studies [37, 42, 47] that reported on costs, none of them reported significant reduction of overall costs with prehabilitation, but one [42] described significantly increased physiotherapy

costs with prehabilitation (mean difference= –£ 136.5). Even when total costs were converted to Canadian dollars and combined through meta-analysis, the results did not differ for prehabilitation versus none (2 studies, 242 patients, WMD + $ 0.5, 95%CI -$ 384 to +$ 393).

Other outcomes

Other outcomes of interest, including patient satisfaction, stroke, cardiovascular events, and readmissions were inadequately reported for meta-analysis. Adverse events and discontinuations were rarely reported within the studies; however, in at least one study, there was concern about increased cardiovascular events and stroke, and poorer SF-36 general health, energy and mental health among the withdrawn patients although the author stated no evidence that study withdrawal varied by group [42]. In some studies, there were reports of patient withdrawals due to adverse events [34, 42, 49]. Some studies reported no significant postoperative complications between groups [35-37], no serious adverse events [33, 35, 36] or no adverse events [47].

Subgroup analysis and sensitivity analysis

Effect sizes were similar between hip and knee replacement subgroups for WOMAC pain and function scores (supplementary table 3), as indicated by non-significant p-values for interaction.

Sensitivity analysis using SMD (instead of WMD), RoM, and different thresholds for defining patient acceptable symptom state (20 and 40, instead of 30), and replacing function sub-score with total score did not materially change the results (supplementary table 4 and 5).

While publication bias was not indicated for pain score; however, asymmetric funnel plots indicated the possibility of publication bias for function scores (supplementary figure 1 to figure 2, table 2).

INTERPRETATION

Main findings

Existing evidence from 22 randomized studies suggests that prehabilitation for patients planning to undergo joint replacement does not materially affect postoperative pain and function (and this is based on studies with significant limitations, providing very low certainty in estimates). While some differences reached statistical significance, the effects are too small to be considered clinically important (ie, an improvement of a few points on a scale of 0-100 is likely clinically irrelevant, and undetectable to patients). For example, prehabilitation reduced WOMAC pain score by 6 with 95%CI (-10.6 to -1.6) within 4 weeks, and with no difference remaining beyond 4 weeks, which is generally smaller than the minimal clinically important improvement (MCII) of at least 9.7 at 6 weeks even when the most optimistic extremes of the confidence intervals are considered in our analysis. Even when patient accepted pain state was defined as achieving ≤ 30 in WOMAC pain subscale 0-100, there was only an absolute increase of 3.9% of patients achieving this threshold. Similarly for function improvement, prehabilitation improved early function by 3.9 to 4.0 points on the WOMAC function subscale 0-100, which is much smaller than the threshold of minimally important difference ranged from 7.9 to 25.9 [51-56], and only 1.3% to 5.4% more patients reached a WOMAC function score ≤ 30. Although prehabilitation promoted patients to resume activities of daily living 0.9 to 1.4 days earlier than no formal prehabilitation, the difference is trivial, and importantly, very few studies reported on this time

point (ie, 2 of 22 studies) which prevents definitive conclusions. Similarly, for the outcome of length of stay, there was no difference between groups, and if statistical significance had been achieved, the difference would have been only 0.3 days, which is a minimal difference. Jurisdictions considering implementation (or continuation) of prehabilitation services should consider whether resources could be better spent elsewhere on interventions of proven clinical benefit. Until sufficient evidence accrues to definitively conclude that prehabiliation provides meaningful benefit, investment in prehabilitation does not represent the best use of limited resources in a healthcare system where other opportunities with proven benefits could be funded instead.

Relation to prior reviews

Similar to this meta-analysis, most previous meta-analyses [10, 11] and systematic reviews [7, 9, 12] suggested that the impact of prehabilitation has not been proven by the existing evidence. In contrast to our analysis, Gill 2013 et al [8] suggested that exercise-based interventions reduce pain and improve physical function for people awaiting hip replacement surgery, but not knee replacement surgery. It is notable that there were some limitations in Gill 2013 [8], wherein some included trials did not report if the patients underwent surgery after the intervention [57, 58], and/or failed to report postoperative outcomes [59, 60], and one included trial allocated patients based on the geographic availability which may have introduced selection bias and unit of measurement errors. Furthermore, a total of 9 relevant trials [30, 34, 38, 40-42, 44, 45, 50] were not included in Gill 2013.

Strengths and limitations

Strengths of this review include rigorous methodology, including the comprehensive systematic search without limits by language, date or publication status, which identified 7 RCTs [30, 34, 38, 40, 41, 45, 50] not included in any previous systematic reviews [6-13]. Furthermore, we analyzed the effect

of prehabilitation by converting to a standardized measurement of WOMAC pain and function scores, and used different presentation methods to enhance interpretability and to improve ability to find potential signals in effect size through meta-analysis [61], which is beyond what other systematic reviews published. In addition, this meta-analysis addressed all available clinically relevant outcomes, while previous reviews addressed only a few selected outcomes. Application of GRADE for rating quality of evidence provides improved context for interpreting the findings in light of inherent strengths and limitations of the included studies [62, 63].

There were a number of specific limitations in the existing clinical trials comparing prehabilitation with control. The most significant limitation is the lack of large randomized controlled trials that have been conducted in this area. Included studies were small (median 81 patient, ranging from 21 to 165), of relatively short duration of follow up (median 3 months, ranging from 4 weeks to 1 year), and many of them provided inadequate description of the frequency, intensity and duration of prehabilitation provided. Definitions for prehabilitation,and for outcomes measurements ,were heterogeneous across studies. Compliance with prehabilitation was problematic in some studies, about 75% in 3 studies [41, 42, 50], about 90% or greater in only 7 studies [16, 30, 33, 35, 36, 43, 48], and was not reported in a number of studies. In a number of studies, co-interventions were provided in the prehabilitation (e.g. education), and in some cases, these co-interventions were not provided in the control group [31, 32, 34]. Nevertheless, this would likely provide an overestimate of the potential benefit for prehabilitation; and despite this potential positive bias, still no differences were found for prehabilitation. The high risk of bias in the studies, combined with the selective reporting of important outcomes across the studies (ie, only

two studies reported time to return of activities of daily living, and total costs) precludes definitive conclusions, despite at least 22 randomized studies being conducted.

CONCLUSION

Existing evidence suggests that the effect of prehabilitation (exercise/physiotherapy programs in the months prior to surgery) on pain and function among patients undergoing joint replacement are too small to be considered clinically-important, were not robust over time, and did not affect outcomes of greatest interest (ie, length of stay, quality of life, costs). Prehabilitation did not result in clinically important (or statistically significant) differences in most measures of patient recovery, quality of life, length of stay and costs. Future research of sufficient power to measure clinically-relevant outcomes is required to identify which, if any, form of prehabilitation achieves better outcomes than in these trials. Jurisdictions considering implementation of prehabilitation services should consider whether resources could be better spent elsewhere on interventions of proven clinical benefit.

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Competing Interest Statement:

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare; funding was provided in part by "AMOSO Innovation Fund" (Project #INN 11-008, to Dr. J. Martin and Dr. D. Cheng). The funders had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work [or describe if any]

Transparency Declaration

I Dr. Janet Martin affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Table Legends

Table 1: Characteristics of included RCTs

Table 2: Risk of Bias for Included Studies

Table 3: Summary of results for prehabilitation vs. no prehabilitation

Table 4: GRADE Evidence Profile: prehabilitation vs no formal prehabilitation for total joint replacement

Supplementary table 1: Intervention characteristics of included RCTs

Supplementary Table 2: Description of RCTs of Prehabilitation versus No Prehabilitation for TKR/THR

Supplementary Table 3: Subgroup Analysis of TKR and THR

Supplementary Table 4 Sensitivity Analysis to test robustness of results after removing total score

Supplementary Table 5: Sensitivity analysis using different thresholds of patient acceptable symptom state (PASS)

Figure Legend

Figure 1: PRISMA flow diagram of study selection

Figure 2. Pain score at 4 weeks or less (converted to WOMAC pain subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery

Figure 3. Function score at 6 to 8 weeks (converted to WOMAC function subscale 0-100) for prehab vs no prehab in joint replacement surgery

Figure 4. Function score at 12 weeks (converted to WOMAC function subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery

Figure 5. Hospital length of stay (days) for prehabilitation vs no prehabilitation in joint replacement surgery

Supplementary figure 1. Funnel plot to explore publication bias for pain scores

Supplementary figure 2. Funnel plot to explore publication bias for function scores

Table 4 GRADE Evidence Profile: prehabilitation vs no formal prehabilitation for total joint replacement

Quality assessment							Summary of Findings		
Participants (studies) Follow up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall quality of evidence**	**Relative effect or WMD** (95% CI)	**Anticipated absolute effects**	
								Median risk with non-prehabilitation	**Risk difference with prehabilitation** (95% CI)
Pain score at 4 weeks or less, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									
213 (4 studies) ≤4 weeks	Serious risk of bias[1] Unclear concealment: 4 studies; Outcome assessors not blinded: 1; Missing data >15%: 1	Serious inconsistency; p-value on test for heterogeneity 0.08, I^2= 55%	No serious indirectness	No serious imprecision	Uncertain (only 4 studies)	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -6.1** (-10.6, -1.6)	**43.8%** patients achieved acceptable pain state of ≤30 on WOMAC pain (0-100) scale	**3.9% more** patients achieving acceptable pain state of ≤30 on WOMAC pain (0-100) scale
Pain score at 6 to 8 weeks, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									

488 (5 studies) 6 to 8 weeks	Serious risk of bias[1] Unclear concealment: 3 studies; outcome assessors not blinded: 2; Missing data >15%: 3	No serious inconsistency; p-value on test for heterogeneity 0.31, I^2= 16%	No serious indirectness	No serious imprecision [2]	Uncertain (only 5 studies)	⊕⊕⊕⊖ **MODERATE** due to risk of bias	**WMD -1.4** (-5.5, +2.6)	**62.2%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)	**0% more** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)
Pain score at 12 weeks, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									
806 (10 studies) 12 weeks	Serious risk of bias[1] Unclear concealment: 5 studies; outcome assessors not blinded: 4; Missing data >15%: 4	Serious inconsistency; p-value on test for heterogeneity 0.05, I^2= 46%	No serious indirectness	No serious imprecision	Undetected; Egger's test p=0.35	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -2.9** (-6.2, +2.8)	**60.9%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)	**1.2% more** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)

Pain score at 24 weeks, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									
247 (3 studies) 24 weeks	Serious risk of bias[1] Unclear concealment: 2 studies; outcome assessors not blinded: 0; Missing data >15%: 2	No serious inconsistency; p-value on test for heterogeneity 0.22, I^2= 33%	No serious indirectness	No serious imprecision	Uncertain (only 3 studies)	⊕⊕⊕⊖ **Moderate** due to risk of bias	**WMD -2.5** (-5.6, +0.6)	**98%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)	**0%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)
Function score at 4 weeks or less, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
257 (5 studies) <=4 weeks	Serious risk of bias[1] Unclear concealment: 5 studies; outcome assessors not blinded: 2; Missing data	Serious inconsistency; p-value on test for heterogeneity <0.001, I^2= 79%	No serious indirectness	No serious imprecision [2]	Uncertain (only 5 studies)	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -3.6** (-7.7, +0.5)	**26.8%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**6.2% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)

	>15%: 1								
Function score at 6 to 8 weeks, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
488 (5 studies) 6 to 8 weeks	Serious risk of bias[1] Unclear concealment: 3 studies; outcome assessors not blinded: 2; Missing data >15%: 3	No serious inconsistency; p-value on test for heterogeneity =0.21, I^2= 30%	No serious indirectness	No serious imprecision	Uncertain (only 5 studies)	⊕⊕⊕⊖ **Moderate** due to risk of bias	**WMD -3.9** (-7.6, -0.3)	**54.3%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**5.4% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)
Function score at 12 weeks, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
836 (12 studies) 12 weeks	Serious risk of bias[1] Unclear concealment: 6 studies; outcome assessors not blinded: 4;	Serious inconsistency; p-value on test for heterogeneity <0.001, I^2= 69%	No serious indirectness	No serious imprecision	Serious; Asymmetry on funnel plot; Egger's test p=0.04	⊕⊖⊖⊖ **VERY LOW** due to risk of bias, inconsistency and publication bias	**WMD -4.0** (-7.5, -0.5)	**62.6%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**1.3% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)

	Missing data >15%: 6								
Function score at 24 weeks, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
345 (7 studies) 24 weeks	Serious risk of bias[1] Unclear concealment: 4 studies; outcome assessors not blinded: 2; Missing data >15%: 2	Serious inconsistency; p-value on test for heterogeneity <0.001, I^2= 89%	No serious indirectness	No serious imprecision [2]	Uncertain (only 7 studies)	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -0.5** (-5.8, +4.7)	**97.4%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**0% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)

1. None of studies in the meta-analyses blinded patients and only 2 study blinded the care providers.
2. We did not rate down due to imprecision although 95% confidence interval includes no effect because either extreme of the 95%CI is too small to be clinically important difference.

Appendix Search Strategies

PubMed

1	((((((((((((((((((((((exercise[tiab] OR prehabilitation[tiab] OR prehab[tiab] OR "physical therapy"[tiab] OR physiotherapy[tiab] OR "therapeutic exercise"[tiab] OR "therapeutic activity"[tiab] OR activity[tiab] OR "preoperative rehabilitation"[tiab] OR "weight training"[tiab] OR "weight lifting"[tiab] OR aquatic[tiab] or swimming[tiab] Or "strength training"[tiab] OR "endurance training"[tiab] OR cycling[tiab] OR biking[tiab] OR "weight reduction"[tiab] OR "weight loss"[tiab] OR kinesiotherapy[tiab] OR hydrotherapy[tiab] OR fitness[tiab] OR "exercise therapy"[tiab])
2	(((Arthroplast*[tiab] OR replace*[tiab] OR "orthopedic surgery"[tiab])))) AND ((hip*[tiab] OR knee*[tiab]))
3	1 AND 2
4	(((((pre-operative[tiab] OR preoperative[tiab] OR pre-op[tiab] OR preop[tiab] OR preoperative care[MeSH Terms])
5	3 AND 4
6	random*
7	5 AND 6

Emabase

1	exercise.ti,ab.
2	Prehabilitation.ti,ab.
3	Physical therapy.ti,ab.

4	Physiotherapy.ti,ab.
5	Therapeutic exercise.ti,ab.
6	Therapeutic activity.ti,ab.
7	Activity.ti,ab.
8	Preoperative rehabilitation.ti,ab.
9	Weight training.ti,ab.
10	Weight lifting.ti,ab.
11	Aquatic.ti,ab.
12	Swimming.ti,ab.
13	Strength training.ti,ab.
14	Endurance training.ti,ab.
15	Cycling.ti,ab.
16	Biking.ti,ab.
17	Weight reduction.ti,ab.
18	Weight loss.ti,ab.
19	Kinesiotherapy.ti,ab.
20	Hydrotherapy.ti,ab.
21	Fitness.ti,ab.
22	Exercise therapy.ti,ab.
23	or/1-22
24	arthroplast*.ti,ab.
25	replacement.ti,ab.
26	resurfac*.ti,ab.

27	orthopedic surgery.ti,ab.
28	hip*.ti,ab.
29	knee*.ti,ab.
30	or/24-27
31	28 or 29
32	30 and 31
33	23 and 32
34	random*.mp.
35	33 and 34
36	exp animals/
37	exp human/
38	(dog or dogs or canine or canines or pig or pigs or porcine or rat or rats or cat or feline or felines or lamb or lambs or mouse or mice or rabbit or rabbits).ti,ab.
39	36 not 37
40	38 or 39
41	35 not 39
42	pre-operative.mp.
43	preoperative.mp.
44	preoperative care/
45	Preop*.mp.
46	Pre-op*.mp.
47	or/42-46
48	41 and 47

Cochrane CENTRAL

1	"exercise":ti,ab,kw (Word variations have been searched)
2	"prehabilitation":ti,ab,kw (Word variations have been searched)
3	"physical therapy":ti,ab,kw (Word variations have been searched)
4	"physiotherapy":ti,ab,kw (Word variations have been searched)
5	"therapeutic exercise":ti,ab,kw (Word variations have been searched)
6	"therapeutic activity":ti,ab,kw (Word variations have been searched)
7	"activity":ti,ab,kw (Word variations have been searched)
8	"Preoperative rehabilitation":ti,ab,kw (Word variations have been searched)
9	"weight training":ti,ab,kw (Word variations have been searched)
10	"weight lifting":ti,ab,kw (Word variations have been searched)
11	"aquatic":ti,ab,kw (Word variations have been searched)
12	"swimming":ti,ab,kw (Word variations have been searched)
13	"strength training":ti,ab,kw (Word variations have been searched)
14	"Endurance training":ti,ab,kw (Word variations have been searched)
15	"cycling":ti,ab,kw (Word variations have been searched)
16	"biking":ti,ab,kw (Word variations have been searched)
17	"weight reduction":ti,ab,kw (Word variations have been searched)
18	"weight loss":ti,ab,kw (Word variations have been searched)
19	"kinesiotherapy":ti,ab,kw (Word variations have been searched)
20	"hydrotherapy":ti,ab,kw (Word variations have been searched)

21	"fitness":ti,ab,kw (Word variations have been searched)
22	"Exercise therapy":ti,ab,kw (Word variations have been searched)
23	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 of #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
24	"arthroplasty":ti,ab,kw (Word variations have been searched)
25	"replacement":ti,ab,kw (Word variations have been searched)
26	"resurface":ti,ab,kw (Word variations have been searched)
27	"orthopedic surgery":ti,ab,kw (Word variations have been searched)
28	#24 or #25 or #26 or #27
29	"hip":ti,ab,kw (Word variations have been searched)
30	"knee":ti,ab,kw (Word variations have been searched)
31	#29 or #30
32	"preoperative":ti,ab,kw (Word variations have been searched)
33	"pre-operative":ti,ab,kw (Word variations have been searched)
34	"preop":ti,ab,kw (Word variations have been searched)
35	"pre-op":ti,ab,kw (Word variations have been searched)
36	#32 or #33 or #34 or #35
37	#28 and #31
38	#23 and #37
39	#36 and #38

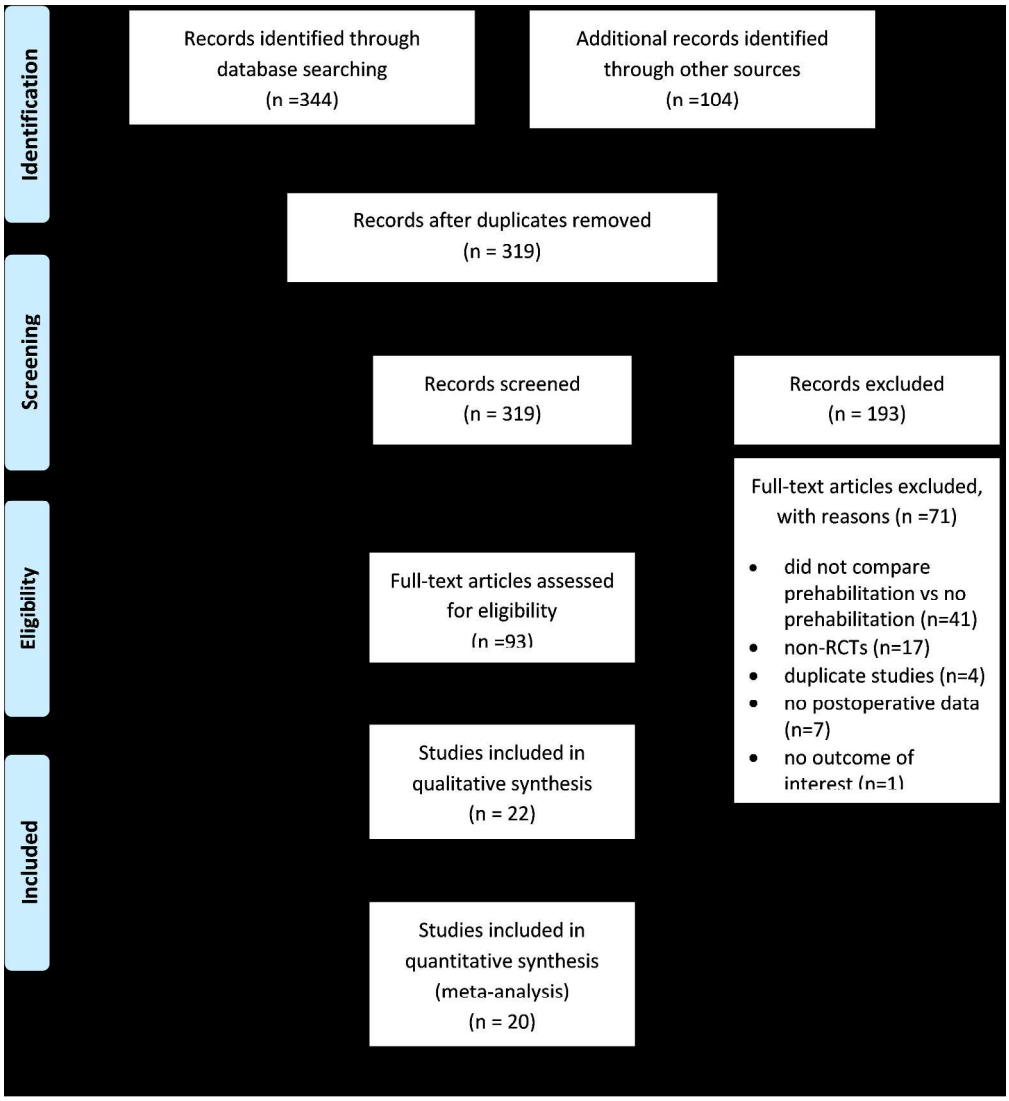


Figure 1 PRISMA flow diagram
1117x1217mm (96 x 96 DPI)

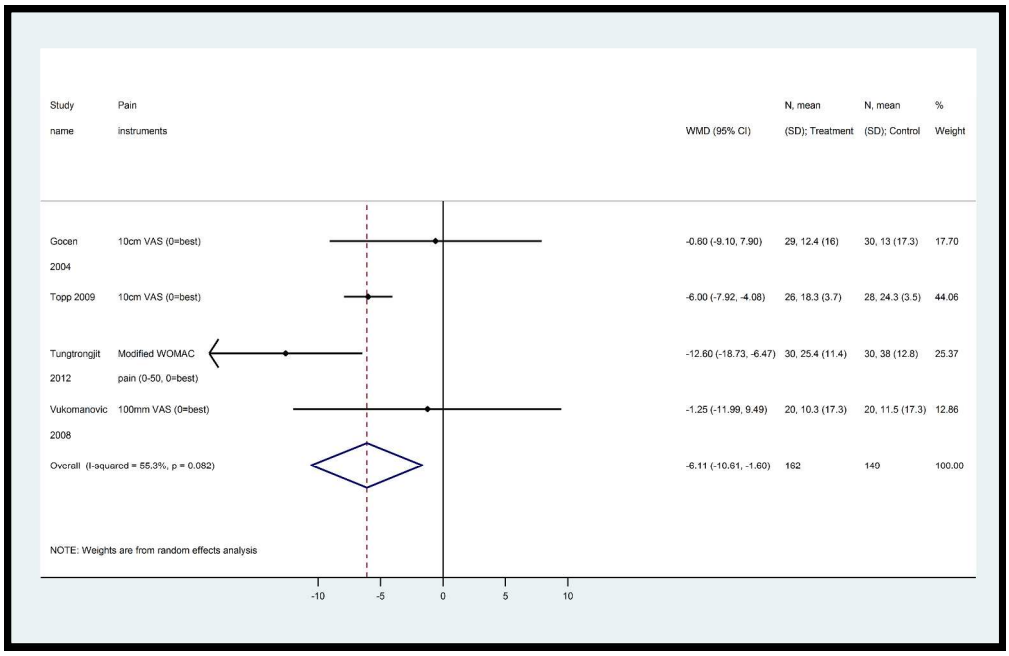


Figure 2. Pain score at 4 weeks or less (converted to WOMAC pain subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery
1718x1109mm (96 x 96 DPI)

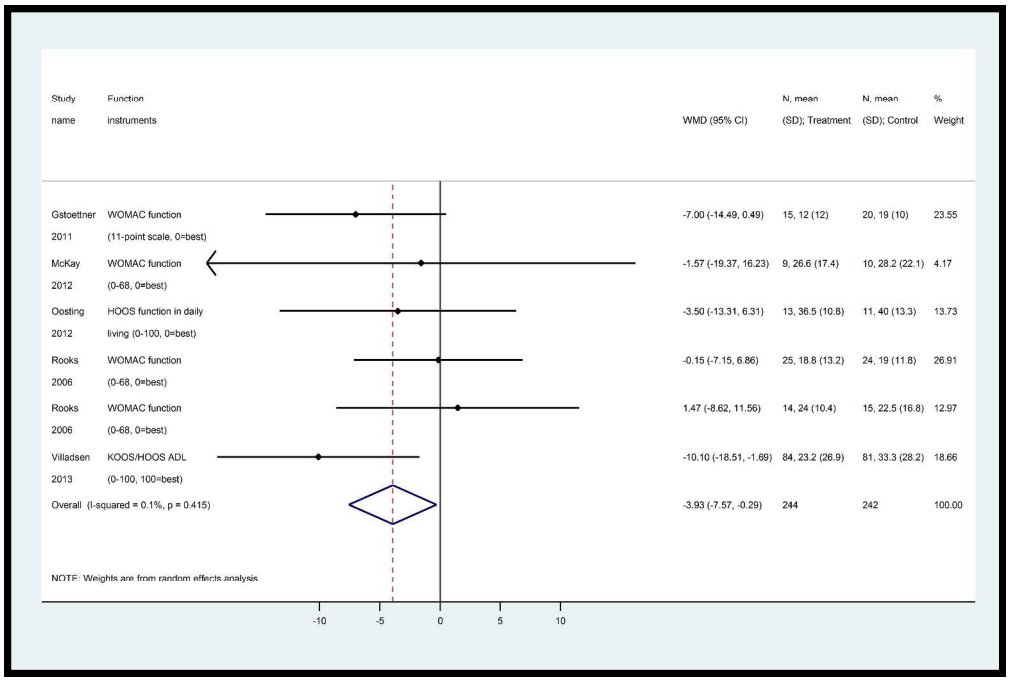


Figure 3. Function score at 6 to 8 weeks (converted to WOMAC function subscale 0-100) for prehab vs no prehab in joint replacement surgery
1726x1159mm (96 x 96 DPI)

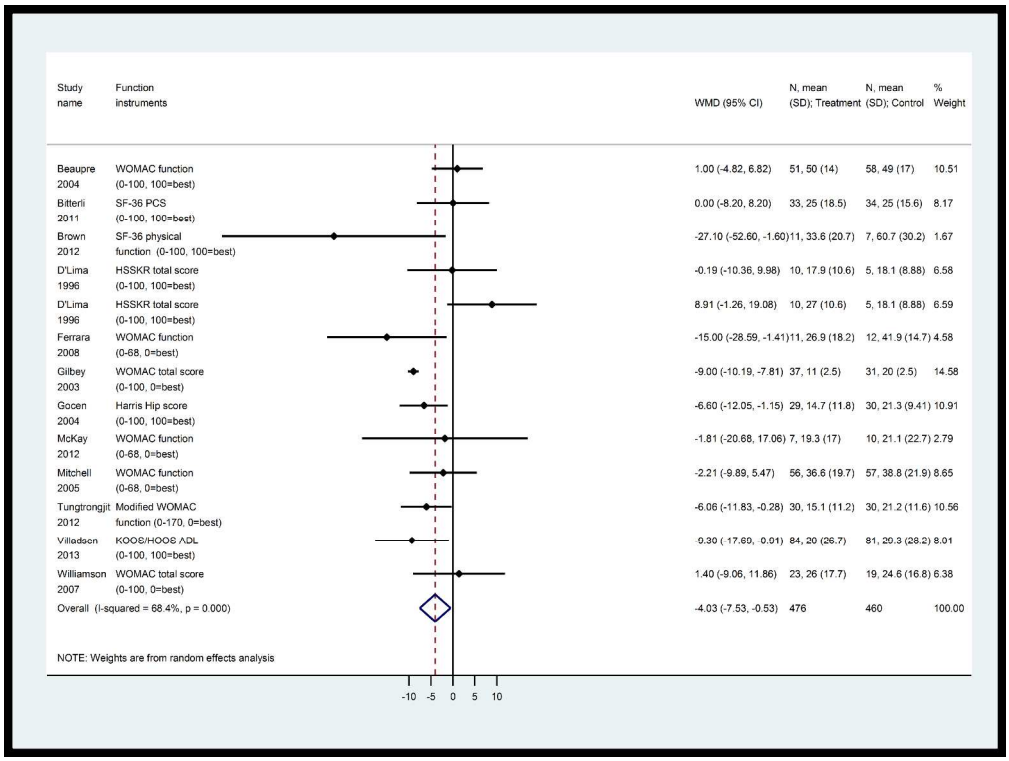


Figure 4. Function score at 12 weeks (converted to WOMAC function subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery

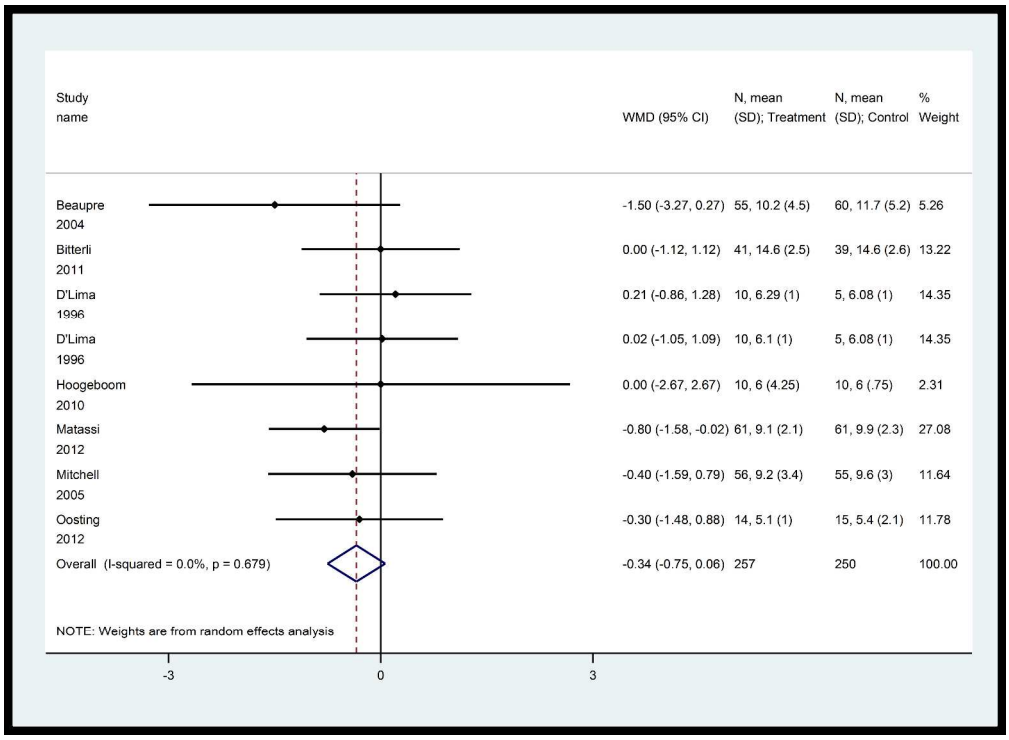
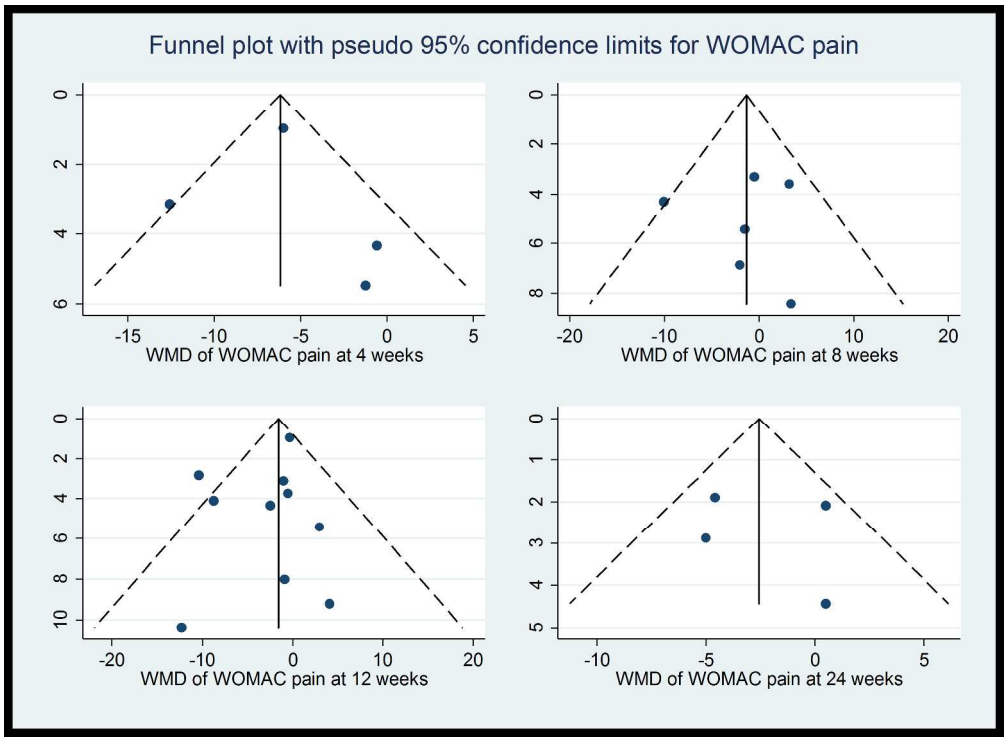
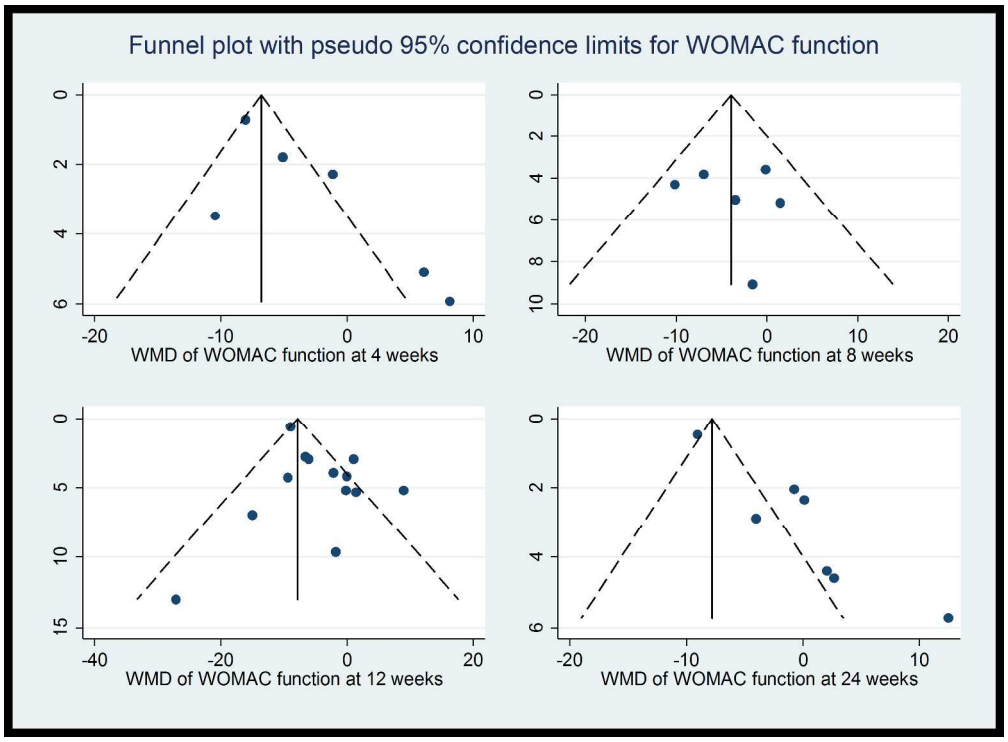


Figure 5. Hospital length of stay (days) for prehabilitation vs no prehabilitation in joint replacement surgery
1749x1273mm (96 x 96 DPI)



Supplementary figure 1. Funnel plot to explore publication bias for pain scores
890x650mm (96 x 96 DPI)



Supplementary figure 2. Funnel plot to explore publication bias for function scores
890x650mm (96 x 96 DPI)

Supplementary table 1 Intervention characteristics of included RCTs

Study Name		Intervention	Compliance	Control	Postop intervention
Beaupre 2004	physiotherapist supervised exercise	land based: strengthening, aerobic; supervised by physiotherapist; 3 times/week * 4 weeks + education	all but 1 participant completed the 12 sessions	usual care: regular activities and other treatment at discretion of physician	standard postoperative mobilization routine
Bitterli 2011	home exercise	land based: strengthening and stretching, home exercises from 2 to 6 weeks, twice daily; 2 verbal and written instruction	exercises completed on 91% of the days	no intervention	usual care (outpatient rehabilitation or rehabilitation clinic)
Brown 2012	physiotherapist supervised exercise + home exercise	land based: strengthening and stretching, supervised by physiotherapist once a week + home exercise 2 times/week * 8 weeks	not reported	usual care	not reported
D'Lima 1996	physiotherapist supervised exercise	Intervention A: land based: strengthening, stretching. Intervention B: land based and pool based: strengthening, stretching, aerobic; once a week * 8weeks	not reported	no intervention	routine care

Evgeniadis 2008	physiotherapist or orthopedist supervised exercise	land based: strengthening (mostly upper limb and trunk), 3 times/week * 3	not reported	no intervention	standard rehabilitation
Ferrara 2008	physiotherapist supervised exercise + education	land based: strengthening, aerobic; supervised by physiotherapist; 5 times/week * 4 weeks + education	not reported	no intervention	postop rehabilitation programme
Gilbey 2003	physiotherapist supervised exercise+ home exercise	land based and pool based: strengthening, stretching, aerobic, supervised by physiotherapist + home exercise: 2 times/week *8weeks	97% of sessions complete	routine in-hospital physical therapy	clinic-based
Gocen 2004	physiotherapist supervised exercise + education	land based: strengthening, stretching, supervised by physiotherapist for 8 weeks; +education	not reported	no intervention	postoperative and education programme
Gstoettner 2011	physiotherapist supervised exercise + home exercise	land based: strengthening, stretching, balance; supervised by physiotherapist; once a week * 6 weeks +daily home training with written instructions	not reported	no intervention	not reported

Hoogeboom 2010	physiotherapist supervised exercise	land based: strengthening, aerobic, functional; + education	91% of the sessions completed	usual care + education	postop usual care protocol
Matassi 2014	physiotherapist supervised exercise + home exercise	land based: increasing lower extremity muscle strengthening supervised by physiotherapist; once a week* 1 week+ home exercise 5 times/week * 6weeks+ written instructions	79.4% completed	regular activities	same physiotherapy routines
McKay 2012	kinesiologist supervised exercise	land based: aerobic, strengthening, supervised by kinesiologist; 3 times/week * 6 weeks	98% of the sessions completed	placebo (upper body exercises)	standard postop care
Mitchell 2005	physiotherapist supervised exercise + home exercise	land based: pain relief, increase knee flexion and extension, gait re-education ,supervised by physiotherapist; 3 times/week * 8 weeks + home exercise 4 times/week * 8 weeks	73.6% sessions completed	preoperative consultation	usual hospital physiotherapy (post-discharge only)
Oosting 2012	physiotherapist supervised exercise +home exercise	land based: "functional tasks exercise", supervised by physiotherapist; 2 times/week + home exercise 4 times/week * 3 to 6 weeks	99% of the sessions completed	usual care (30min supervised class)	not reported

Rooks 2006	physiotherapist supervised exercise +education	land based and pool based: strengthening, stretching, aerobic, supervised by physiotherapist; 3 times/week * 6 weeks; +education on home modifications	89% of sessions completed	education via leaflet and telephone + 30-60min supervised class	not reported
Topp 2009	physiotherapist supervised exercise + home exercise	land based: resistance training, flexibility, step training, supervised by physiotherapist, once a week + home exercise 2 times /week	13 sessions completed (range 4 to 23)	no intervention	postop rehabilitation
Tungtrongjit 2012	home exercise	land based: home quadriceps strengthening exercise for 3 weeks	Not reported	no intervention	postop rehabilitation
Villadsen 2014	physiotherapist supervised exercise	land based: standard preoperative educational package + NEMEX programme; supervised by physiotherapist; 2 times/week * 8 weeks	74% attended the pre-specified goal of 12 or more exercise	standard preoperative educational package	postop rehabilitation
Vukomanovic 2008	physiotherapist supervised exercise +education	land based: physical therapy +education	not reported	no intervention	postop rehabilitation
Wang 2002	physiotherapist supervised exercise + home exercise	land based and pool based: strengthening, stretching, aerobic, supervised by physiotherapist+ home exercise; 2 times/week	97% of sessions complete	routine perioperative care	postop rehabilitation

		* 8 weeks			
Weidenhielm 1993	physiotherapist supervised exercise + home exercise	land based: strengthening, stretching, aerobic, supervised by physiotherapist, 3 times/week * 5 weeks; + home exercise daily	not reported	no intervention	not reported
Williamson 2007	physiotherapist supervised exercise + home exercise	land based: strengthening, stretching, balance, supervised by physiotherapist; 1 times/week * 6 weeks + home exercise	not reported	education and leaflet +1 hour supervised class + home exercise	not reported

NEMEX: neuromuscular exercise programme

Supplementary Table 2 Description of RCTs of Prehabilitation versus No Prehabilitation for TKR/THR

Study Name	No. of patients	Type of surgery	Comparison	Rehabilitation	Results				
					Pain	Function improvement	Quality of Life	Resource use	others
Beaupre 2004	131	TKR	PT supervised exercise + postop education vs. usual care	Standard postop mobilization routine	WOMAC pain: NS SF-36 bodily pain: NS from 3mo. to 1 year postoperatively	Knee ROM: NS; Quadriceps strength: NS; Hamstring Strength: NS WOMAC stiffness and function: NS; SF-36 physical functioning: NS from 3mo. to 1 year postoperatively	SF-36: NS in each domains, PCS, and MCS from 3mo. to 1 yr postoperatively	Acute care LOS, transfer LOS, readmission LOS, and total LOS: NS (total LOS: -1.5 d) Institutional costs, homecare costs, readmission costs, total costs: NS (total cost: + $33);	Postoperative complications:e.g. pulmonary emboli (n=2), deep vein thrombosis (n=9), infection (n=5), postoperative Angina: NS
Bitterli 2011	80	THR	Preoperative sensorimotor training at home (daily exercises at home) vs. no	Postop. Standard therapy protocol in hospital	SF-36 pain: : NS after surgery (4mo.,1year)	SF-36 physical function: NS after surgery (4mo,1 year) WOMAC: NS after surgery (4mo, 1year)	SF-36: NS in each domains after surgery (4mo.,1year)	LOS: NS (14.6 vs. 14.6 d)	-

			therapy	Usual care therapeutic modalities after discharge					
Brown 2012	32	TKR	Preop. exercise intervention vs. no prehabilitation	-	SF-36 pain : NS at 3mo. after surgery	SF-physical function score: ↑(MD+27.1)	SF-36:↑ in physical function score (MD+27.1) NS in other domains	-	-
D'Lima 1996	30	TKR	Preop physical therapy vs. cardiovascular conditioning program with exercise vs. no intervention	-	Hospital for Special Surgery Knee Rating pain(0-30):NS from 3wk 1yr	Hospital for Special Surgery Knee Rating function (0-52):NS from 3wk to 1yr	Quality of Well Being scores (0-1): Percentage improvement - NS Arthritis impact measurement scale scores (0-10): Percentage improvement NS	LOS: NS	-
Evgeniadis 2008	48	TKR	Preop.exercise vs. no intervention	-	-	ILAS score: NS after surgery(2, 6, 10, 14wks) Active ROM:NS after surgery	SF-36: NS at 1 day pervious to surgery (preop)	-	-

						(2, 10, 14wks)			
Ferrara 2008	23	THR	Educational and PT supervised physiotherapy program vs. no intervention	Postop. 4weeks standard exercise protocol	VAS: ↓ at 1, 3 mo. (MD -1.8, -0.97) WOMAC pain: NS at 3 mo.	ROM external rotation: ↑at 15days, 1 and 3 mo. after surgery (MD +7.69, +0.14) Harris Hip Score: NS at 1 and 3mo Barthel Index: NS at 1 and 3mo WOMAC stiffness and function: NS at 3mo	SF-36 PCS: ↑at 1 mo, but NS at 3 mo (MD +7.1 at 1 mo) SF-36 MCS: NS	-	-
Gilbey 2003	76	THR	8wks customized exercise program vs. no exercise	Postop. Exercise program (until 12wks after surgery) VS routine in-hospital PT	WOMAC pain: NS	Mean ROM at 3, 12, 24wks:↑ (MD+6,+11,+12) Hip strength mean Z score after surgery (12, 24wks): ↑ (MD+0.35, +0.6) WOMAC total score after surgery (3,12,24wks):↑(MD+8, +9, +9) WOMAC stiffness: NS, 3,12,24wks		-	-

						WOMAC function:↑ 3, 12, 24wks				
Gocen 2004	60	THR	Physiotherapy and educational program vs. no exercise or education	Routine postop. Exercise and educational program	VAS at rest at discharge: NS (MD-0.12) VAS at activity at discharge: NS (MD-0.06)	Hip adduction at discharge: NS (MD-0.1) Harris Hip Score: NS at 3mo, 2 years after surgery (MD+0.9,+4)	-	LOS: NS	-
Gstoettner 2011	38	TKR	PT supervised exercise vs. no exercise	-	WOMAC pain: NS; 6wk postoperatively	KSS: NS; KSS function: NS; WOMAC stiffness: NS; WOMAC function: NS; Gait speed (60m):NS; Gait speed (stairs up):NS; Gait speed (stairs down): NS; Knee stability (OSI): NS; Knee stability (MLSI) : NS; 6wk postoperatively Knee stability (APSI) : ↓ (MD -0.6) 6wkpostoperatively	-	-	-

Hoogebo om 2010	21	THR	Therapeutic exercise program vs. usual care	Postop. usual care protocol till discharge	HOOS pain: NS VAS: NS At baseline and preop,	Functional recovery: NS HOOS (in all domains): NS LASA physical activity questionnaire (all domains): NS At baseline and preop	Patient-specific complaints (PSK): NS At baseline and preop	LOS: NS 6 vs. 6 days	2 postoperative complications in exercise group: femur fracture and intestinal obstruction. no serious AE
Matassi 2014	122	TKR	Preoperative home exercise program vs. regular activities	Same postop. physiotherapy routine	-	Mean time to reach 90° of knee ROM: ↓ (MD -1.1 day) Active knee flexion: NS at 6wks. 6mo, 1yr Passive knee flexion: NS at 6wks. 6mo, 1yr Knee score or patient function score (Knee Society Clinical Rating System): NS at 6wks, 6 mos. 1 yrs.	-	LOS: ↓ (MD -0.8 day)	-
McKay 2012	22	TKR	Lower-body strength training program vs. nonspecific upper-body	Standard postop. care	WOMAC pain: NS, MD+0.7, +0.9 at 6 and 12wks.	SF-36 PSC: NS Quadriceps strength: NS 50-foot walk: NS Stair test: NS Arthritis self–efficacy	SF-36 (PCS, MCS): NS after surgery	-	-

			strength training program (placebo)			(including pain, physical function, and other symptoms): NS			
Mitchell 2005	160	TKR	PT supervised pre- & postop home exercise (home PT) vs. no pre-op exercise + usual hospital PT postop	Postop home exercise or hospital PT	WOMAC pain: NS SF-36 bodily pain: NS at 12wk	WOMAC physical function: NS; WOMAC stiffness: NS; SF-36 physical function: NS at 12wk	SF-36: NS in each domains SF-6D: NS Patient satisfaction with PT: NS (86% in both groups) at 12wk	LOS: NS (MD -0.4d) Cost of PT: NS(MD + £1.4) Total cost: NS(MD + £4.7)	45 withdrawn patients had significantly poor score on the SF-36 general health, energy, and more reported heart problems and stroke/TIA.
Oosting 2012	30	THA	PT supervised exercise vs. usual care	-	HOOS pain: NS VAS: NS 6wk changes from baseline.	TUG: NS; CRT: ↓ (MD -9.2s); 6MWT: NS; PSC: NS; HOOS other symptoms, function in daily living, function in sport and recreation: NS; LAPAQ: NS;	HOOS hip-related quality of life: NS Patient Specific Complaints (PSC) questionnaire score: NS	LOS: NS (MD -0.3d) Nursing home after discharge: NS	No severe adverse events Complications: e.g. Wound, delirium, loss of sensation, decubitus ulcers, and

						6wk post-discharge changes from baseline			bowel obstruction) NS
Rooks 2006	108	THA+ TKA	PT supervised exercise+education vs. education	-	For THR: WOMAC pain: NS SF-36 pain: NS 8wk and 26wk postoperatively For TKR: WOMAC pain: NS 8wk and 26wk postoperatively SF-36 pain: NS 8wk postoperatively SF-36 pain: ↑(MD+11.5) 26wk changes from baseline	For both THR and TKR: WOMAC function: NS; SF-36 physical function: NS SF-36 role limitation physical: NS; 1-repetition maximum: NS ; Timed up and go: NS ; 8wk and 26wk postoperatively Functional reach: NS ; 8wk and 26wkpostoperatively	-	-	-
Topp 2009	54	TKA	PT supervised exercise vs. usual care	Postoperative rehabilitation	Pain in Sit-to-stand, 6MWT, Ascent and descent stairs: NS? at 1, 3mo.	Sit-to-stand: NS? 6MWT: NS? Ascent and descent stairs: NS? Maximum extension strength of	-	-	-

					postoperatively No between-group comparison	the surgical knee, nonsurgical knee: ? Maximum extension strength of the surgical knee:? at 1, 3mo. postoperatively No between-group comparison				
Tungtrongjit 2012	60	TKA	Quadriceps exercise vs. usual care	-	Modified WOMAC pain score: ↓ (MD -6.3) VAS: ↓ (MD -0.9) at 1 mo postoperatively Modified WOMAC pain score: ↓ (MD -5.2) VAS: ↓ (MD -1) at 3 mo postoperatively Modified WOMAC	Total Modified WOMAC score: ↓ (MD -26.7) Modified WOMAC stiffness score: ↓ (MD -2.5) Modified WOMAC function score: ↓ (MD -17.7) Quadriceps strength: ↑(MD+1.5) at 1 mo postoperatively Total Modified WOMAC score: ↓ (MD -17.7) Modified WOMAC stiffness score: ↓ (MD -2) Modified WOMAC function	-	-	-

	pain score: ↓ (MD -2.3) VAS: NS at 6 mo postoperatively	score: ↓ (MD -10.3) Quadriceps strength: ↑(MD+2.2) at 3 mo postoperatively Total Modified WOMAC score: NS Modified WOMAC stiffness score: NS Modified WOMAC function score: NS Quadriceps strength: NS at 6 mo postoperatively Knee Flexion: NS Knee Extension: NS Total knee ROM: NS at 1, 3, 6 mo postoperatively

Villadsen 2014	165	THA+ TKA	PT supervised exercise + education vs. education	Postoperative rehabilitation	For THR+TKR: KOOS/HOOS Pain: ↓ (MD -5.4) For THR: KOOS/HOOS Pain: NS changes at 6wk and 3mo postop from base line For TKR: KOOS/HOOS Pain: ↓ (MD -8)	For both THR+TKR or For TKR: KOOS/HOOS ADL: ↑ at 6wkpostop, but NS at 3mo postop For THR: KOOS/HOOS ADL: NS at 6wk and 3mo postop For THR+TKR or THR or TKR: KOOS/HOOS symptoms: NS KOOS/HOOS sport and recreation: NS At 6wk or 3 mo postop changes from baseline. Single-joint hip extension and hip abduction: ↑ (~15% and 35% improvement)	For both THR+TKR or For TKR: EQ5D VAS: ↓ (MD -7.6) at 6wk postop, but NS at 3mo postop For THR: EQ5D VAS: NS At 6wk and 3mo postop For TKR: EQ5D VAS: ↓ (MD -8.8) changes at 6wk postop from baseline, but NS changes at 3mo postop from baseline For THR+TKR or THR or TKR: EQ5D index: NS	-	One patient with hip OA discontinued the exercise due to an increase in pain. 2 patients from the control group developed deep periprosthetic infection.

						Chair stand: NS 20-m walk: NS Knee bends: NS Contra: NS at 3mo	KOOS/HOOS QOL: NS At 6wk or 3 mo postop changes from baseline.		
Vukoma novic 08	45	THA	PT supervised exercise +education vs. no interventions	Postoperative rehabilitation	Pain at rest (VAS): NS Pain on movement (VAS): NS at discharge postop	First day of activities – use of toilet↓ (MD -0.9d), use of chair↓ (MD -1.05d), and walking up and down stairs: ↓ (MD -1.67d) Changing position in bed: ↑(MD +0.95) Changing position on the edge: ↑(MD +0.9) From sitting to standing: ↑(MD +1.05) Standing: ↑(MD +1.1) Changing position to lying: ↑(MD +1.15) Walking: ↑(MD +1.15)	-	LOS: NS (- MD +0.4d) Class with the therapist: ↓ (MD-1.65)	Five patients were excluded postoperatively because of complications during and post operation.

	Use of toilet: ↑(MD +1.9) Use of Chair: ↑(MD +1.9) Walking up and down stairs: ↑(MD +1.8) Endurance while walking: ↑(MD +1) at the 3rd day postoperatively Changing position in bed: ↑(MD +0.4) Changing position on the edge: ↑(MD +0.45) From sitting to standing: ↑(MD +0.45) Standing: ↑(MD +0.45) Changing position to lying: ↑(MD +0.45) Walking: ↑(MD +0.5) Use of toilet: ↑(MD +1) Use of Chair: ↑(MD +1.25) Walking up and down stairs:

						↑(MD +1.85) Endurance while walking: ↑(MD +1) at the discharge Flexion of the hip flexed knee: NS Flexion of the hip extended knee: NS Abduction:: NS Harris hip score: NS JOA hip score: NS At discharge postoperatively Oxford Hip Score: NS At 15 mo postoperatively			
Wang 2002	28	THA	PT supervised pre- & post-operative exercise vs. PT supervised pre- & post-operative	Postoperative exercise or usual care	-	Cadence (steps/min): ↑(MD +18) Stride length: ↑(MD +0.06m) Gait velocity: ↑(MD +0.28) At 3 wk postoperatively	-	-	Complications: NS no wound infections, joint

			usual care			Cadence (steps/min): ↑(MD +9) Stride length: NS Gait velocity: ↑(MD +0.2) At 12 wk postoperatively Cadence (steps/min): ↑(MD +10) Stride length: NS Gait velocity: ↑(MD +0.21) At 24 wk postoperatively 6MWT: NS At 12 wk postoperatively 6MWT: ↑(MD +64m) At 24 wk postoperatively			dislocations, complications requiring return to the operating room, or major medical complications
Weidenhielm 1993	39	TKP	PT supervised exercise vs. no exercise	-	VRS (no, mild, moderate, and severe pain): NS	Passive ROM: NS No. patients grading the knee as stable or unstable: NS	-	-	-

					Pain at walk: NS At 3mo.	Isokinetic quadriceps strength (at 30 and 90 degree): NS Walking speed (self-selected and maximal): NS at 3 mo postoperatively			
Williams on 2007	120	TKR	PT supervised exercise vs. education leaflet	-	VAS: NS (MD -0.09 at 3mo postop)	OKS: NS (MD +1.61) 50-m walk: NS (MD +2.51s) WOMAC: NS (MD+1.33) at 3mo postop	HAD score anxiety: NS (MD +1.84) HAD score depression: NS (MD -0.25)	HLOS: NS (MD -1.27d) Cost of PT: £9 per patient	No adverse responses

6MWT: 6-minute walk test; ADL: activities of daily living; APSI: anteroposterior stability index; EQ5D: EuroQol 5 Dimension Health Questionnaire; HAD: Hospital Anxiety and Depression score; HOOS: Hip disability and Osteoarthritis Outcome Score; ILAS: Iowa Level of Assistance Scale; KOOS: Knee injury and Osteoarthritis Outcome Score; KSS: Knee Society Score; LASA: Longitudinal Aging Study Amsterdam; LOS: length of stay; MCS: mental component summary; MD: mean difference; MLSI : medio-lateral stability index; NS: not significant; OA: Osteoarthritis; OKS: Oxford Knee Score questionnaire; OSI: overall stability index; PCS: physical component summary; postop: postoperative; preop: preoperative; PT: physical therapist; ROM: range of motion; THR: total hip replacement; TKP: total knee replacement; TUG: Timed Up & Go; VAS: visual analogue scale; VRS: verbal rating scale; WOMAC: Western Ontario and McMaster Universities Arthritis Inde

Supplementary Table 3: Subgroup Analysis of TKR and THR

Outcomes	Sub-group	No. of studies	No. of patients	Hetero-geneity test p value	I^2 (%)	WMD (95%CI)	interaction p value
Pain at 4 weeks or less	TKR	2	114	0.04	75	-8.6 (-15.0 to -2.3)	0.26
	THR	2	99	0.93	0	-0.9 (-7.5 to +5.8)	
Pain at 6 to 8 weeks	TKR	4	164	0.04	64	-2.7 (-11.7 to +6.3)	0.88
	THR	3	159	0.92	0	-1.3 (-6.5 to +4.0)	
Pain at 12 weeks	TKR	9	534	0.02	55	-3.2 (-7.1 to +0.7)	0.24
	THR	2	107	0.86	0	-3.0 (-9.8 to +3.9)	
Pain at 24 weeks	TKR	3	198	0.54	0	-4.1 (-7.1 to -1.0)	0.47
	THR	1	59	NA	NA	+0.5 (-3.6 to +4.6)	
Function at 4 weeks or less	TKR	3	90	0.004	82	+0.7 (-12.1 to +13.5)	0.47
	THR	3	167	0.009	79	-0.5 (-9.1 to -1.4)	
Function at 6 to 8 weeks	TKR	4	164	0.004	64	-6.3 (-13.9 to +1.3)	0.34
	THR	3	157	0.119	45	-1.7 (-6.9 to +3.5)	

Function at 12	TKR	9	470	0.04	51	-2.4 (-7.0 to +2.2)	0.14
weeks	THR	5	301	0.16	39	-7.2 (-10.7 to -3.8)	
Function at 24	TKR	5	228	0.12	45	-4.1 (-7.1 to -1.2)	0.22
weeks	THR	2	117	<0.001	93	+0.5 (-3.6 to +4.6)	
Function at 1 year	TKR	3	139	0.87	0	-0.5 (-4.2 to +3.3)	0.85
or more	THR	2	117	0.21	35	+0.2 (-3.8 to +4.2)	

TKR: total knee replacement; THR: total hip replacement; NA: not applicable

Supplementary Table 4 Sensitivity Analysis to test robustness of results after removing total score

Outcomes	SMD (95%CI)	RoM (95%CI)	WMD (95%CI) after removing total score
Pain at 4 weeks or less	-0.70 (-1.46 to +0.06)	0.74 (0.68 to 0.81)	NR
Pain at 6 to 8 weeks	-0.17 (-0.38 to +0.05)	0.88 (0.73 to 1.06)	NR
Pain at 12 weeks	-0.20 (-0.40 to 0.00)	0.87 (0.76 to 1.01)	NR
Pain at 24 weeks	-0.26 (-0.56 to +0.04)	0.78 (0.60 to 1.02)	NR
Pain at 1 year or more	-0.14 (-0.51 to +0.24)	0.90 (0.68 to 1.20)	NR
Function at 4 weeks or less	-0.58 (-1.45 to +0.29)	0.90 (0.79 to 1.04)	-5.0 (-9.4 to - 0.6)
Function at 6 to 8 weeks	-0.27 (-0.49 to -0.05)	0.86 (0.76 to 1.00)	NR
Function at 12 weeks	-0.48 (-0.91 to -0.05)	0.82 (0.67 to 1.00)	-4.5 (-7.9 to -1.1)
Function at 24 weeks	-0.49 (-1.47 to +0.49)	0.87 (0.56 to 1.33)	+0.1 (-4.1 to +4.3)
Function at 1 year or more	-0.01 (-0.24 to +0.22)	1.01 (0.88 to 1.15)	-0.4 (-2.6 to +1.8)

SMD: Standardized mean difference; RoM: Ratio of mean; WMD: Weighted mean difference; NR: not relevant since total score was not included

Supplementary Table 5 Sensitivity analysis using different thresholds of patient acceptable symptom state (PASS)

Outcomes	PASS <=30			PASS <=40			PASS <=20		
	RR	median baseline risk	RD	RR	median baseline risk	RD	RR	median baseline risk	RD
Pain at 4 weeks or less	1.09	43.8%	3.9%	1.04	94.1%	3.8%	1.76	8.0%	6.1%
Pain at 6 to 8 weeks	1.00	62.2%	0%	1.00	78.3%	0%	1.02	45.0%	0.9%
Pain at 12 weeks	1.02	60.9%	1.2%	1.01	79.2%	0.8%	1.10	40.2%	4.0%
Pain at 24 weeks	1.00	98.0%	0%	1.00	99.9%	0%	1.04	84.7%	3.4%
Function at 4 weeks or less	1.23	26.8%	6.2%	1.10	71.7%	7.2%	1.67	4.9%	3.3%
Function at 6 to 8 weeks	1.10	54.3%	5.4%	1.02	69.1%	1.4%	1.20	38.8%	7.8%
Function at 12 weeks	1.02	62.6%	1.3%	1.02	79.8%	1.6%	1.34	39.2%	13.3%
Function at 24 weeks	1.00	97.4%	0%	1.00	99.9%	0%	1.01	84.7%	0.8%
Function at 1 year or more	0.97	88.1%	-2.6%	0.97	98.1%	-2.9%	1.30	66.4%	19.9%

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	16-21
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	13-15
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	10

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	13-15
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	11-12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13-15
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Suppl Table 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	16-21 Table 3 Table 4 Suppl Table 3 Suppl Table 4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13-15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	21-22
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22-23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23-25
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	25
FUNDING			

PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	26

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Does Preoperative Rehabilitation for Patients Planning to Undergo Joint Replacement Surgery Improve Outcomes? A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Does Preoperative Rehabilitation for Patients Planning to Undergo Joint Replacement Surgery Improve Outcomes?

A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Keywords: Physiotherapy, Exercise, Prehabilitation, Joint Replacement, Meta-analysis

Word Count: 4,215

Abstract:

Objectives: The clinical impact of preoperative physiotherapy on recovery after joint replacement remains controversial. This systematic review aimed to assess the clinical impact of prehabilitation before joint replacement.

Design: We searched PubMed, Embase, and Cochrane CENTRAL up to November 2015 for randomized controlled trials comparing prehabilitation versus no prehabilitation before joint replacement surgery. Postoperative pain and function scores were converted to Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function subscales (0-100, high scores indicate worse outcome). Random effects meta-analysis was performed to calculate weighted mean differences (WMD, 95%CI), subgrouped by hip and knee surgery.

Primary and Secondary Outcomes: Postoperative pain and function scores, time to resume activities of daily living, quality of life, length of hospital stay, total cost, patient satisfaction, postoperative complications, any adverse events and discontinuations..

Results: Of 22 studies (1,492 patients), 18 had high risk of bias. Prehabilitation slightly reduced pain scores within 4 weeks postoperatively (WMD -6.1 points, 95%CI -10.6 to -1.6 points, on a scale of 0-100), but differences did not remain beyond 4 weeks. Prehabilitation slightly improved WOMAC function score at 6-8 weeks and 12 weeks (WMD -4.0, 95%CI -7.5 to -0.5), and time to climbing stairs (WMD -1.4 days, 95%CI -1.9 to -0.8 days), toilet use (-0.9 days, 95%CI -1.3 to -0.5 days), and chair use (WMD -1.2 days, 95%CI -1.7 to -0.8 days). Effects were similar for knee and hip surgery. Differences were not found for SF-36 scores, length of stay and total cost. Other outcomes of interest were inadequately reported.

Conclusions: Existing evidence suggests that prehabilitation may slightly improve early postoperative pain and function among patients undergoing joint replacement; however, effects

remain too small and short-term to be considered clinically-important, and did not affect key outcomes of interest (ie, length of stay, quality of life, costs).

Article Summary

Strengths and Limitations of Study

- The methodology was rigorous, and included a comprehensive systematic search without limits by language, date or publication status, which identified 7 randomized controlled trials (RCTs) not included in any previous systematic reviews.
- We went beyond previous systematic reviews published by analyzing the effect of prehabilitation by converting to a standardized measurement of WOMAC pain and function scores, and used different presentation methods to enhance interpretability and to improve ability to find potential signals in effect size through meta-analysis.
- This meta-analysis addressed all available clinically relevant outcomes, while previous reviews addressed only a few selected outcomes. Application of GRADE for rating quality of evidence provides improved context for interpreting the findings in light of inherent strengths and limitations of the included studies.
- Compliance with prehabilitation was problematic in some studies, and was not reported in a number of studies

Key words: Physiotherapy, Exercise, Prehabilitation, Joint Replacement, Meta-analysis

INTRODUCTION

Total joint replacement surgery is considered as one of the most successful medical interventions with significant pain relief and improvement in physical function and quality of life for patients with severe osteoarthritis [1]. However, the recovery for a significant proportion of patients remains difficult, prolonged, and many never restore optimal functionality postoperatively [2-4]. Therefore, researchers, clinicians and policy makers are still looking for better ways to improve the timelines and extent of recovery for patients undergoing total joint replacement.

Physiotherapy has been delivered to patients, traditionally after total joint replacement for rehabilitation. However, preoperative physiotherapy and exercise programs (also known as 'prehabilitation') have been proposed as a potential way to expedite recovery times and improve overall extent of recovery in patients planning to undergo joint replacement. One recently published review recommended preoperative exercise to maintain or improve function and pain [5]; however, this recommendation was based on only one narrative systematic review with indeterminate effects [6]. Although it seems intuitive that prehabilitation should improve patient disposition at the time of surgery, and may prepare patients for a better recovery after surgery, significant uncertainties remain about the overall balance of benefits and risks (and costs) for prehabilitation.

A number of related systematic reviews or meta-analyses have been published in the recent decade with inconsistent methods and varied conclusions [6-13]. Two of them suggested that prehabilitation reduced pain for patients undergoing joint replacement [8, 11], and improved

physical function for patients undergoing hip replacement surgery, but not knee replacement surgery [8], while the remainder suggested prehabilitation did not clearly demonstrate beneficial effects or were unable to provide definitive conclusions [6, 7, 9, 10, 12, 13]. Furthermore, significant methodological limitations or errors have been identified among the existing systematic reviews. Some of them only qualitatively summarized the results [6, 7, 9, 11-13] ; another two meta-analyses [8, 10] are outdated, or mistakenly included some trials in which postoperative outcomes were not reported. Thus, we conducted an updated methodologically rigorous systematic review with meta-analysis to clarify whether evidence supports prehabilitation for patients planning to undergo joint replacement.

METHODS

Eligibility criteria

We systematically searched three databases up to November 10, 2015, including PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL). Eligible studies had to be randomized controlled trials comparing preoperative rehabilitation programs (ie, prescribed and supervised exercises or physiotherapy with or without co-interventions such as education, nutritional counseling, acupuncture, transcutaneous electrical nerve stimulation, etc.) versus no formal preoperative rehabilitation programs, reporting at least one clinically-relevant outcome of interest during the postoperative period. Clinical outcomes of interest included postoperative pain scores [Visual Analogue Scale (VAS), or pain subcomponents of Western Ontario and McMaster Universities osteoarthritis index (WOMAC) or pain-related subdomains of other instruments], patient functionality (WOMAC function score, SF-36 physical functioning subdomain or other function-related instruments), time to resume activities of daily living,

quality of life, patient satisfaction, infection, transfusions, stroke, death, or overall postoperative complications. Resource-related outcomes of interest included hospital length of stay, readmissions, and total hospital costs or total health system costs. Timeframes of relevance included in-hospital outcomes, as well as clinical or resource-related outcomes over the longer-term postoperatively.

Search terms included MeSH and keyword terms for exercise, prehabilitation, physiotherapy, physical therapy, activity, weight training, weight lifting, aquatic, swimming, strength training, endurance training, cycling, biking, kinesiotherapy, hydrotherapy, fitness, orthopedic surgery, and joint replacement and "random*". No limitations were placed on date of publication or language. Detailed search strategies are provided in the Appendix.

Literature screening and data extraction

Two reviewers (ML, ZZ) independently screened the articles by title and abstract using the pre-determined eligibility criteria. Any disagreements were resolved by the third reviewer (LW). The third reviewer (LW) also checked all the reference lists of existing systematic reviews or meta-analyses and other reviews for potentially additional eligible articles.

Two reviewers (ML, JM) independently assessed the risk of bias of the included trials using the methods recommended by Cochrane Collaboration [14], including random sequence generation, allocation concealment, missing or incomplete outcome data, and blinding of patients, study personnel, and outcome assessors. Any discrepancies were resolved by the third reviewer (LW).

Standardized data extraction forms were developed to specify the study characteristics, patient characteristics and outcomes. Three reviewers (ML, ZZ, and LW) extracted the data. Data was verified by a fourth reviewer (JM).

Statistical analysis

Meta-analysis was performed using the random effects model. For discrete outcomes, relative risk and 95% confidence intervals (RR, 95%CI) were calculated. For continuous outcomes, e.g. pain score and function score, weighted mean differences (WMD, 95%CI) were calculated after conversion to the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) pain score (0-100) and WOMAC function score (0-100), in which a higher score indicates worse outcome. Sensitivity analysis was conducted by calculating standardized mean differences (SMD) and ratio of means (RoM).

If different pain scores were reported in one article (e.g. WOMAC pain, SF-36 pain score), the WOMAC pain score was preferentially used. If WOMAC pain score was not reported, the pain score reported in the study was converted to WOMAC pain scores to allow for comparison across studies, and to allow for estimation of overall effect size [15]. If pain scores were reported at rest and during activity, the pain score during activity was preferentially used for analysis. If pain scores were reported during different types of activities, the largest change of pain score during the most active movement was used preferentially. If different function scores were reported, the WOMAC function score was used preferentially for analysis. In the absence of WOMAC function scores, the alternate function score provided in the study was converted to a WOMAC function score [15]. Two studies [16, 17] only reported total scores of Hospital for Special

Surgery Knee Rating System (HSSK) and WOMAC respectively. Given the function score accounting for most of the total score and with similar trends of change over time as total score, we used the total score to replace the function score. To test whether this changed the effect size, sensitivity analysis was performed after removing the total scores from function measures to recalculate effect size.

To improve clinical relevance and interpretation of the results for postoperative pain and function improvement, we also converted continuous data from WOMAC pain score and WOMAC function score to a relative risk (RR) for achieving a "patient acceptable symptom state" (defined as the number of patients achieving the threshold pain score or function score at which patients consider themselves 'well' or 'satisfied') derived from previous research [18-21]. To calculate the RR, we assumed a normal distribution of WOMAC pain or function scores for the intervention and control groups, and we used a threshold of 30 on the WOMAC 0-100 scale to represent the threshold for the patient acceptable symptom state. The proportion of patients in the intervention and control groups with WOMAC pain or function ≤ 30 was then calculated, and combined across studies to derive a pooled relative risk [15, 22]. Finally, to further add to clinical applicability of the patient reported outcomes we calculated the risk difference for the number of patients achieving this threshold of ≤ 30 per 100 patients using the relative risk and median risk among the control groups in the included studies [23]. Subsequently, sensitivity analyses were performed to explore whether using different thresholds (20 and 40) changed the conclusions, since our threshold of 30 represents a compromise of 20 to 40 suggested in previous studies of hip or knee surgery over the short term or long-term.

Heterogeneity was estimated using the Chi-squared test and I^2 statistic. Pre-defined subgroup analyses included separate analysis for hip and knee surgery patients, to test the existing hypothesis from a previous systematic review that prehabilitation improves postoperative pain and function more among patients undergoing hip replacement than patients with knee replacement [8]. Publication bias was explored using both visual inspection of funnel plots and Egger's test only when there were at least 10 studies included in the meta-analysis [14].

GRADE methodology was used to summarize certainty in estimates of effect (quality of evidence) in the critically important outcomes for decision-making [23-29], including WOMAC pain scores and function scores from early follow-up to 24 weeks after surgery.

RESULTS

Studies identified

Figure 1 outlines study inclusion and exclusion. A total of 399 titles and abstracts were screened for inclusion, of which 110 studies were collected in full-text for review. Of these, 88 were excluded for the following reasons: no prehabilitation arm (ie. education only or postoperative rehabilitation only, n=46), not randomized (n=21), duplicate studies (n=4), no postoperative outcomes data (n=9), no outcome of interest (n=2), conference abstracts (n=3) and protocol only (n=3). In total, 22 randomized controlled trials (1492 patients) of prehabilitation versus no prehabilitation met the inclusion criteria. Twenty studies provided usable data for the meta-analysis, and 22 studies contributed qualitative or quantitative data.

Description of included studies

Among 22 included studies, eight studies were of patients undergoing total hip replacement [16, 30-36]; 12 studies included patients undergoing total knee replacement [15, 37-47] and two studies included either hip or knee replacement [48, 49]. Most studies were conducted in developed countries (North American and Europe), except for three in developing countries (Serbia [34], Thailand [45] and Turkey [32]). The median sample size of included studies was 54, ranging from 21 to 165 patients. Mean age ranged from 51 to 76 (Table 1).

Table 1 Characteristics of included RCTs

Study Name	No. of patients	Type of surgery	Countries	Mean age	% Female	Mean BMI%	Total OA %
Beaupre 2004	131	TKR	Canada	67	55	31.4	NR
Bitterli 2011	80	THR	Switzerland	66.9	38	27.4	NR
Brown 2012	32	TKR	USA	NR	NR	36.8	NR
D'Lima 1996	30	TKR	USA	69.8	46.6	NR	83.3
Evgeniadis 2008	48	TKR	Greece	68.3	76.3	34.1	100
Ferrara 2008	23	THR	Italy	63.4	60.8	NR	100
Gilbey 2003	76	THR	Australia	65.2	61.8	27.94	NR
Gocen 2004	60	THR	Turkey	51.3	35.5	NR	49
Gstoettner 2011	38	TKR	Australia	69.7	78.9	27.8	100
Hoogeboom 2010	21	THR	Netherland	76	66	NR	NR
Matassi 2014	122	TKR	Italy	66.5	48	28.5	NR
McKay 2012	22	TKR	Canada	61.3	59	34.3	100
Mitchell 2005	160	TKR	UK	70.3	57.9	NR	100
Oosting 2012	30	THR	Netherland	76	80	28.2	100
Rooks 2006	108	THR/TKR	USA	64.1	56	31.6	100
Topp 2009	54	TKR	USA	63.8	68	32.1	100
Tungtrongjit 2012	60	TKR	Thailand	64.5	83.3	24.8	100

Villadsen 2014	165	THR/TKR	Denmark	67	56	30.3	100
Vukomanovic 08	45	THR	Serbia	58.4	67	NR	100
Wang 2002	28	THR	Australia	67.1	64	NR	89
Weidenhielm 1993	39	TKR	Sweden	63.5	51.3	29.6	100
Williamson 2007	120	TKR	UK	69.8	52.9	32.7	100

TKR: total knee replacement; THR: Total hip replacement; USA: United States of America; UK: United Kingdom; BMI: Body mass index; OA: Osteoarthritis**;** NR: not reported

Nine studies compared physiotherapist supervised exercise plus home exercise versus no intervention or usual care [16, 35, 36, 38, 40-42, 44, 46]. Five compared physiotherapist supervised exercise versus no intervention or usual care [15, 33, 37, 39, 50]. Two studies compared home exercise only versus no intervention [30, 45]. Three studies compared physiotherapist supervised exercise plus education versus no intervention [31, 32, 34]. One each compared physiotherapist supervised exercise plus education versus education [48], kinesiologist supervised exercise versus placebo (kinesiologist supervised upper body exercise) [43], and physiotherapist supervised exercise plus home exercise versus education plus home exercise [47] respectively (Supplementary Table 1).

Risk of bias

Among 22 trials, adequate sequence generation was reported in 17 trials [15, 30-33, 36-43, 45-48], allocation concealment in 8 trials [30, 33, 37, 39, 42, 43, 47, 49]. The patients were blinded in one study[39], health care providers were blinded in three studies [30, 39, 44], and outcome assessors were blinded in 12 studies [30-33, 36, 37, 41, 44, 45, 47-49]. Seventeen studies [16, 30-34, 36-40, 42, 43, 46-49] reported loss to follow-up, ranging from 1.7% to 65.3%; among which the proportion of loss to follow up was more than 15% in 10 studies [30, 34, 36-39, 42, 43, 47, 48]. Ten out of 17 studies with incomplete data used intention to treat analysis [30, 33, 36, 37, 39, 42, 43, 47-49]. Overall, 4 out of 22 included trials were rated as low risk of bias [30, 33, 37, 39] and 18 trials as high risk of bias (Table 2)

Table 2: Risk of Bias for Included Studies

	Random sequence generation	Allocation concealment	Blinding of patients	Blinding of health care providers	Blinding of outcome assessors	Incomplete outcome data	Intention to treat analysis	Risk of bias
Beaupre 2004	Yes	Yes	No	No	Yes	Yes, LTFU>15%	Yes	Low risk
Bitterli 2011	Yes	Yes	No	Yes	Yes	Yes, LTFU>15%	Yes	Low risk
Brown 2012	Yes	Unclear	No	Unclear	Unclear	Yes, LTFU>15%	No	High risk
D'Lima 1996	Yes	Unclear	Unclear	Unclear	Unclear	No	Not Applicable	High risk
Evgeniadis 2008	Yes	Yes	Yes	Yes	Unclear	Yes, LTFU>15%	Yes	Low risk
Ferrara 2008	Yes	Unclear	No	No	Yes	Yes	No	High risk
Gilbey 2003	Unclear	Unclear	Unclear	Unclear	No	Yes	No	High risk
Gocen 2004	Yes	Unclear	No	Unclear	Yes	Yes	No	High risk
Gstoettner 2011	Yes	No	Unclear	Unclear	Unclear	Yes	No	High risk
Hoogeboom 2010	Yes	Yes	No	No	Yes	Yes	Yes	Low risk
Matassi 2014	Yes	Unclear	No	No	Yes	No	Not Applicable	High risk
McKay 2012	Yes	Yes	Unclear	Unclear	Unclear	Yes, LTFU>15%	Yes	High risk
Mitchell 2005	Yes	Yes	No	No	Unclear	Yes, LTFU>15%	Yes	High risk
Oosting 2012	Yes	Unclear	No	No	Yes	Yes, LTFU>15%	Yes	High risk
Rooks 2006	Yes	Unclear	Unclear	Unclear	Yes	Yes, LTFU>15%	Yes	High risk
Topp 2009	Unclear	Unclear	No	Yes	Yes	No	Not Applicable	High risk

Tungtrongjit 2012	Yes	Unclear	No	No	Yes	No	Not Applicable	High risk
Villadsen 2014	Unclear	Yes	No	No	Yes	Yes	Yes	High risk
Vukomanovic 08	Unclear	Unclear	Unclear	Unclear	Unclear	Yes, LTFU>15%	No	High risk
Wang 2002	Unclear	Unclear	Unclear	Unclear	No	No	Not Applicable	High risk
Weidenhielm 1993	Yes	Unclear	Unclear	Unclear	Unclear	Yes	No	High risk
Williamson 2007	Yes	Yes	No	No	Yes	Yes, LTFU>15%	Yes	High risk

LTFU: lost to follow-up

Supplementary Table 2 qualitatively summarizes the major findings of included studies. In total, 22 studies described at least one clinical or resource-related benefit for prehabilitation versus control, and 18 studies [15, 30-37, 39, 40, 42-48] described no significant improvement for prehabilitation versus control. We conducted meta-analysis for pain scores, function scores, SF-36 PCS and MCS, hospital length of stay, and total costs based on the data availability.

Postoperative pain

Fifteen trials with 18 comparisons and 1046 patients reported postoperative pain scores using different instruments, i.e. WOMAC [31, 37, 40, 42, 43, 45, 48], VAS [32, 34, 36, 44, 47], Knee injury and Osteoarthritis Outcome Score (KOOS)/Hip disability and Osteoarthritis Outcome Score (HOOS)[49], and 10-graded scale [46]. Only two trials [31, 49] reported significant improvement in pain at early follow-up (≤3 months), including VAS pain at 3 months [31], and KOOS/HOOS pain at 6 weeks postoperatively, but not significant at 3 months [49].

After converting to WOMAC pain 0-100, prehabilitation significantly reduced postoperative pain at 4 weeks or less; however, the reduction of pain was clinically nominal (4 trials, 213 patients, WMD -6.1, 95%CI -10.6 to -1.6, Figure 2, GRADE: low certainty in estimates, Table 3 & Table 4). Differences in WOMAC pain scores after 4 weeks were no longer statistically significant for prehabilitation versus control (WOMAC pain score at 6 to 8 weeks, 5 trials, 488 patients, WMD -1.4, 95%CI -5.5 to +2.6; at 12 weeks, 10 trials, 806 patients, WMD -2.9, 95%CI -6.2 to +0.3; at 24 weeks, 3 trials, 247 patients, -2.5, 95%CI -5.6 to +0.6; at 1 year,1 trial, 109 patients, WMD -2.0, 95%CI -7.5 to +3.5; GRADE: low to moderate certainty in estimates, Table 3 & Table 4).

When expressed as a relative risk (RR), patients undergoing prehabilitation were more likely to achieve the acceptable pain state (WOMAC pain score ≤ 30) with RR 1.09. When expressed as an absolute risk difference, 3.9% more patients with prehabilitation achieved the acceptable pain state (WOMAC pain score≤ 30) than patients without prehabilitation at 4 weeks (Supplementary table 3). However, this small difference would be considered clinically nominal.[18-21]

Table 3 Summary of results for prehabilitation vs. no prehabilitation

Outcomes	No. of studies	No. of patients	heterogeneity test p value	I^2 (%)	WMD & 95%CI
Pain at 4 weeks or less	4	213	0.08	55	-6.1 (-10.6 to -1.6) *
Pain at 6 to 8 weeks	5	488	0.31	16	-1.4 (-5.5 to +2.6)
Pain at 12 weeks	10	806	0.05	46	-2.9 (-6.2 to +0.3)
Pain at 24 weeks	3	247	0.22	33	-2.5 (-5.6 to +0.6)
Pain at 1 year or more	1	109	NA	NA	-2.0 (-7.5 to +3.5)
Function at 4 weeks or less	5	257	<0.001	79	-3.6 (-7.7 to +0.5)
Function at 6 to 8 weeks	5	488	0.21	31	-3.9 (-7.6 to -0.3) *
Function at 12 weeks	12	836	<0.001	69	-4.0 (-7.5 to -0.5) *
Function at 24 weeks	5	345	<0.001	89	-0.5 (-5.8 to +4.7)
Function at 1 year or more	6	296	0.99	0	-0.6 (-2.6 to +145)
First days of climbing stairs (days)	2	99	0.44	0	-1.4 (-1.9 to -0.8) *
First days of walking (days)	2	99	0.24	29	-0.2 (-0.4 to +0.002)

First days of use of toilet (days)	2	99	0.87	0	-0.9 (-1.3 to -0.5) *
First days of use of chair (days)	2	99	0.50	0	-1.2 (-1.7 to -0.8) *
SF-36 PCS at 6 weeks	1	19	NA	NA	2.7 (-9.4 to +14.7)
SF-36 PCS at 12 weeks	3	149	0.13	50	-0.3 (-5.4 to +4.7)
SF-36 PCS at 24 weeks	1	109	NA	NA	0.0 (-3.4 to +3.4)
SF-36 PCS at 1 year	1	109	NA	NA	-3.0 (-6.4 to +0.4)
SF-36 MCS at 6 weeks	1	17	NA	NA	-3.4 (-19.9 to +13.0)
SF-36 MCS at 12 weeks	3	149	0.72	0	-0.4 (-3.7 to +2.9)
SF-36 MCS at 24 weeks	1	109	NA	NA	-1.0 (-4.9 to +2.9)
SF-36 MCS at 1 year	1	109	NA	NA	-2.0 (-5.1 to +1.1)
Length of stay (days)	7	507	0.68	0	-0.3 (-0.8 to + 0.1)
Total cost (Canadian dollars)	2	242	0.99	0	+5 (-384 to +393)

PCS: physical component summary; MCS: mental component summary; WMD: Weighted mean difference; NA: not applicable;

Pain and function scores were converted to WOMAC (Western Ontario and McMaster Universities osteoarthritis index) 0-100 subscales, and high score indicates more pain or dysfunction.

* $p<0.05$

Table 4 GRADE Evidence Profile: prehabilitation vs no formal prehabilitation for total joint replacement

Quality assessment							Summary of Findings		
Participants (studies) Follow up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall quality of evidence**	**Relative effect or WMD** (95% CI)	**Anticipated absolute effects**	
								Median risk with non-prehabilitation	**Risk difference with prehabilitation** (95% CI)
Pain score at 4 weeks or less, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									
213 (4 studies) ≤4 weeks	Serious risk of bias[1] Unclear concealment: 4 studies; Outcome assessors not blinded: 1; Missing data >15%: 1	Serious inconsistency; p-value on test for heterogeneity 0.08, I^2= 55%	No serious indirectness	No serious imprecision	Uncertain (only 4 studies)	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -6.1** (-10.6, -1.6)	**43.8%** patients achieved acceptable pain state of ≤30 on WOMAC pain (0-100) scale	**3.9% more** patients achieving acceptable pain state of ≤30 on WOMAC pain (0-100) scale
Pain score at 6 to 8 weeks, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									

488 (5 studies) 6 to 8 weeks	Serious risk of bias[1] Unclear concealment: 3 studies; outcome assessors not blinded: 2; Missing data >15%: 3	No serious inconsistency; p-value on test for heterogeneity 0.31, I^2= 16%	No serious indirectness	No serious imprecision [2]	Uncertain (only 5 studies)	⊕⊕⊕⊖ **MODERATE** due to risk of bias	**WMD -1.4** (-5.5, +2.6)	**62.2%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)	**0% more** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)
Pain score at 12 weeks, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									
806 (10 studies) 12 weeks	Serious risk of bias[1] Unclear concealment: 5 studies; outcome assessors not blinded: 4; Missing data >15%: 4	Serious inconsistency; p-value on test for heterogeneity 0.05, I^2= 46%	No serious indirectness	No serious imprecision	Undetected; Egger's test p=0.35	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -2.9** (-6.2, +2.8)	**60.9%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)	**1.2% more** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)

Pain score at 24 weeks, measured with: WOMAC pain subscale 0-100; Lower values indicate less pain									
247 (3 studies) 24 weeks	Serious risk of bias[1] Unclear concealment: 2 studies; outcome assessors not blinded: 0; Missing data >15%: 2	No serious inconsistency; p-value on test for heterogeneity 0.22, I^2= 33%	No serious indirectness	No serious imprecision	Uncertain (only 3 studies)	⊕⊕⊕⊖ **Moderate** due to risk of bias	**WMD -2.5** (-5.6, +0.6)	**98%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)	**0%** patients achieved acceptable pain state of ≤30 on WOMAC pain scale (0-100)
Function score at 4 weeks or less, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
257 (5 studies) <=4 weeks	Serious risk of bias[1] Unclear concealment: 5 studies; outcome assessors not blinded: 2; Missing data	Serious inconsistency; p-value on test for heterogeneity <0.001, I^2= 79%	No serious indirectness	No serious imprecision [2]	Uncertain (only 5 studies)	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -3.6** (-7.7, +0.5)	**26.8%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**6.2% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)

	>15%: 1								
Function score at 6 to 8 weeks, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
488 (5 studies) 6 to 8 weeks	Serious risk of bias[1] Unclear concealment: 3 studies; outcome assessors not blinded: 2; Missing data >15%: 3	No serious inconsistency; p-value on test for heterogeneity =0.21, I^2= 30%	No serious indirectness	No serious imprecision	Uncertain (only 5 studies)	⊕⊕⊕⊖ **Moderate** due to risk of bias	**WMD -3.9** (-7.6, -0.3)	**54.3%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**5.4% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)
Function score at 12 weeks, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
836 (12 studies) 12 weeks	Serious risk of bias[1] Unclear concealment: 6 studies; outcome assessors not blinded: 4;	Serious inconsistency; p-value on test for heterogeneity <0.001, I^2= 69%	No serious indirectness	No serious imprecision	Serious; Asymmetry on funnel plot; Egger's test p=0.04	⊕⊖⊖⊖ **VERY LOW** due to risk of bias, inconsistency and publication bias	**WMD -4.0** (-7.5, -0.5)	**62.6%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**1.3% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)

	Missing data >15%: 6								
Function score at 24 weeks, measured with: WOMAC function subscale 0-100; Lower values indicate better function									
345 (7 studies) 24 weeks	Serious risk of bias[1] Unclear concealment: 4 studies; outcome assessors not blinded: 2; Missing data >15%: 2	Serious inconsistency; p-value on test for heterogeneity <0.001, I^2= 89%	No serious indirectness	No serious imprecision [2]	Uncertain (only 7 studies)	⊕⊕⊖⊖ **LOW** due to risk of bias and inconsistency	**WMD -0.5** (-5.8, +4.7)	**97.4%** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)	**0% more** patients achieved acceptable function state ≤30 on WOMAC function scale (0-100)

1. None of studies in the meta-analyses blinded patients and only 2 study blinded the care providers.
2. We did not rate down due to imprecision although 95% confidence interval includes no effect because either extreme of the 95%CI is too small to be clinically important difference

Postoperative function

Of 16 trials reporting on postoperative function, only four reported significant improvement in function [16, 31, 41, 49], including higher hip external rotation [31] or higher flexion range of motion (ROM) scores, WOMAC physical function and total score [16], and less time to reached 90° of knee flexion [41] and great improvement in activities of daily living (ADL) [49] after surgery .

Sixteen trials (1118 patients) reported postoperative function scores using different instruments, i.e. WOMAC [16, 31, 37, 40, 42, 43, 45, 47, 48], Harris hip score [32, 34], SF-36 physical component summary (PCS) [30], SF-36 physical functioning score [38], HSSK score [15], HOOS function in daily living [36], and KOOS/HOOS ADL[49]. After converting function scores to WOMAC function score (0-100), the difference was slightly improved (but numerically small on a scale of 0-100) with prehabilitation versus no prehabilitation at early follow-up (WOMAC function score at 6 to 8 weeks,5 trials, 488 patients, WMD -3.9, 95%CI-7.6 to -0.3, RR=1.10, Figure 3, GRADE: moderate certainty in estimates, Table 3 & Table 4), and at 12 weeks (12 trials, 836 patients, WMD -4.0, 95%CI -7.5 to -0.5, RR=1.02, Figure 4, GRADE: very low certainty in estimates, Table 3 & Table 4). No significant difference for WOMAC function score was found after 12 weeks (at 24 weeks, 5 trials, 345 patients, WMD -0.5, 95%CI -5.8 to +4.7; at 1 year, 6 trials, 296 patients, WMD -0.6, 95%CI -2.6 to +1.5, GRADE: low certainty in estimates, Table 3 & Table 4).

When expressed as a relative risk for achieving the acceptable threshold, the relative increases were small (RR 1.10 at 6-8 weeks; 1.02 at 12 weeks). When expressed as an absolute difference

in likelihood of achieving the acceptable threshold, the differences ranged from 1.3% to 5.4% more patients achieving a WOMAC function score ≤ 30 at 6-8 weeks and 12 weeks respectively (Supplementary table 3).

Resumption of activities of daily living

Resumption of activities of daily living was rarely reported. In the two studies (99 patients) [32, 34] that reported activities of daily living, meta-analysis suggested significantly earlier resumption of activities, including climbing stairs (2 trials, 99 patients, WMD -1.4 days, 95%CI-1.9 to -0.8 days), use of toilet (2 trials, 99 patients, -0.9 day, 95%CI-1.3 to -0.5 days), use of chair (2 trials, 99 patients, -1.2 days, 95%CI -1.7 to -0.8 days), but not for time to first day of walking (2 trials, 99 patients, -0.2 day , 95%CI -0.4 to +0.0 day), (Table 3). However, based on the total time-course of recovery, the difference was small.

Quality of life

Significant differences in quality of life were not found in 9 studies for SF-36 [30, 37, 39, 42, 43], Quality of Well Being instrument [15], HOOS Hip-related quality of life [36], KOOS/HOOS Quality of Life subscale [49], and Patient Specific Complaints (PSC) questionnaire [33, 36]; while three trials reported significant difference in quality of life score [31, 38, 49], including higher physical function score or physical composite score using SF-36 [31, 38] or better EuroQol 5 Dimension Health Questionnaire (EQ5D) [49]; however, the numeric differences were small [31, 38, 49] and the significance disappeared at 3 months [31, 49].

Three studies including 149 patients reported SF-36 Physical Component Summary (SF-36 PCS) and Mental Component Summary (SF-36 MCS). Meta-analysis of SF-36 PCS and MCS did not detect significant differences at any time-point (from 6 weeks to 1 year, Table 3).

Length of hospital stay and total cost

Only one [41] out of 10 studies [15, 30, 32-34, 36, 37, 41, 42, 47] found a significant reduction in hospital length of stay (mean difference = -0.8 day). Meta-analysis of these studies did not detect significant differences in hospital length of stay for prehabilitation versus control (7 studies, 507 patients, WMD -0.3 days, 95%CI -0.8 to + 0.1 days, Figure 5).

Of the few studies [37, 42, 47] that reported on costs, none of them reported significant reduction of overall costs with prehabilitation, but one [42] described significantly increased physiotherapy costs with prehabilitation (mean difference= –£ 136.5). Even when total costs were converted to Canadian dollars and combined through meta-analysis, the results did not differ for prehabilitation versus none (2 studies, 242 patients, WMD + $ 0.5, 95%CI -$ 384 to +$ 393).

Other outcomes

Other outcomes of interest, including patient satisfaction, stroke, cardiovascular events, and readmissions were inadequately reported for meta-analysis. Adverse events and discontinuations were rarely reported within the studies; however, in at least one study, there was concern about increased cardiovascular events and stroke, and poorer SF-36 general health, energy and mental health among the withdrawn patients although the author stated no evidence that study withdrawal varied by group [42]. In some studies, there were reports of patient withdrawals due to

adverse events [34, 42, 49]. Some studies reported no significant postoperative complications between groups [35-37], no serious adverse events [33, 35, 36] or no adverse events [47].

Subgroup analysis and sensitivity analysis

Effect sizes were similar between hip and knee replacement subgroups for WOMAC pain and function scores (supplementary table 3), as indicated by non-significant p-values for interaction.

Sensitivity analysis using SMD (instead of WMD), RoM, and different thresholds for defining patient acceptable symptom state (20 and 40, instead of 30), and replacing function sub-score with total score did not significantly change the results (supplementary table 4 and 5).

While publication bias was not indicated for pain score; asymmetric funnel plots indicated the possibility of publication bias for function scores (supplementary figure 1 to figure 2, table 2).

INTERPRETATION

Main findings

Existing evidence from 22 randomized controlled trials suggests that prehabilitation for patients planning to undergo joint replacement does not affect postoperative pain and function to a degree that would be considered clinically relevant; however, this is based on studies with significant limitations, providing very low certainty in estimates. While some differences reached statistical significance, the effects are too small to be considered clinically important (ie, an improvement of a few points on a scale of 0-100 is likely clinically irrelevant, and undetectable to patients). Our analysis shows that prehabilitation reduced WOMAC pain score

by 6 with 95%CI (-10.6 to -1.6) within 4 weeks, and with no difference remaining beyond 4 weeks, which is generally smaller than the minimal clinically important improvement (MCII) of at least 9.7 at 6 weeks [51,52] even when the most optimistic extremes of the confidence intervals are considered in our analysis. Even when the 'patient accepted pain state' was defined as achieving ≤ 30 in WOMAC pain subscale 0-100[18-20], there was only an absolute increase of 3.9% of patients achieving this threshold. Similarly for function improvement, prehabilitation improved early function by 3.9 to 4.0 points on the WOMAC function subscale 0-100, which is much smaller than the threshold of minimally important difference ranged from 7.9 to 25.9 [51-56], and only 1.3% to 5.4% more patients reached a WOMAC function score ≤ 30. Although prehabilitation promoted patients to resume activities of daily living 0.9 to 1.4 days earlier than no formal prehabilitation, the difference is trivial, and importantly, very few studies reported on this time point (ie, 2 of 22 studies) which prevents definitive conclusions. Similarly, for the outcome of length of stay, there was no difference between groups, and if statistical significance had been achieved, the difference would have been only 0.3 days, which is a minimal difference. Jurisdictions considering implementation (or continuation) of prehabilitation services should consider whether resources could be better spent elsewhere on interventions of proven clinical benefit. Until sufficient evidence accrues to definitively conclude that prehabiliation provides meaningful benefit, investment in prehabilitation does not represent the best use of limited resources in a healthcare system where other opportunities with proven benefits could be funded instead.

Relation to prior reviews

Similar to this meta-analysis, most previous meta-analyses [10, 11] and systematic reviews [7, 9, 12] suggested that the impact of prehabilitation has not been proven by the existing evidence. In

contrast to our analysis, Gill 2013 et al [8] suggested that exercise-based interventions reduce pain and improve physical function for people awaiting hip replacement surgery, but not knee replacement surgery. It is notable that there were some limitations in Gill 2013 [8], wherein some included trials did not report if the patients underwent surgery after the intervention [57, 58], and/or failed to report postoperative outcomes [59, 60], and one included trial allocated patients based on the geographic availability which may have introduced selection bias and unit of measurement errors. Furthermore, a total of 9 relevant trials [30, 34, 38, 40-42, 44, 45, 50] were not included in Gill 2013.

Strengths and limitations

Strengths of this review include rigorous methodology, including the comprehensive systematic search without limits by language, date or publication status, which identified 7 RCTs [30, 34, 38, 40, 41, 45, 50] not included in any previous systematic reviews [6-13]. Furthermore, we analyzed the effect of prehabilitation by converting to a standardized measurement of WOMAC pain and function scores, and used different presentation methods to enhance interpretability and to improve ability to find potential signals in effect size through meta-analysis [61], which is beyond what other systematic reviews published. In addition, this meta-analysis addressed all available clinically relevant outcomes, while previous reviews addressed only a few selected outcomes. Application of GRADE for rating quality of evidence provides improved context for interpreting the findings in light of inherent strengths and limitations of the included studies [62, 63].

There were a number of specific limitations in the existing clinical trials comparing prehabilitation with control. The most significant limitation is the lack of large randomized controlled trials that have been conducted in this area. Included studies were small (median 81 patient, ranging from 21 to 165), of relatively short duration of follow up (median 3 months,

ranging from 4 weeks to 1 year), and many of them provided inadequate description of the frequency, intensity and duration of prehabilitation provided. Definitions for prehabilitation,and for outcomes measurements, were heterogeneous across studies. Patient compliance with prehabilitation was reported as 75% in 3 studies [41, 42, 50], and 90% or greater in 7 studies [16, 30, 33, 35, 36, 43, 48], and was not reported in the remainder of the studies. Most studies provided an inadequate description of the components of the prehabilitation programs provided, and few described the fidelity of program implementation.[64] Future studies in this area should follow current guidelines for intervention description (TIDieR checklist) to enable transparent evaluation and replication of programs[65]. In a number of studies, co-interventions were provided in the prehabilitation (e.g. education), and in some cases, these co-interventions were not provided in the control group [31, 32, 34]. Nevertheless, this would likely provide an overestimate of the potential benefit for prehabilitation; and despite this potential positive bias, still no differences were found for prehabilitation. Considered together, the heterogeneity of the included studies in types of prehabilitation programs, control group interventions, compliance and fidelity within the programs, and systematic differences in the study population likely impacted the ability to detect differences, if any exist. Although we performed subgroup analysis for hip versus knee replacement surgery, this failed to explain the heterogeneity across studies. Due to the limited numbers of studies, meta-analysis was not performed for the effect of different types of prehabilitation (e.g. exercise only vs exercise plus education). Publication bias was not detected; however, the methodologic quality of included studies is very low, which was the major reason that we downgraded the overall quality of evidence. The high risk of bias, combined with the selective reporting of important outcomes across the studies (for example,

only two studies reported time to return of activities of daily living, and total costs) precludes definitive conclusions, despite at least 22 randomized controlled trials being conducted.

CONCLUSION

Existing evidence suggests that, in patients undergoing joint replacement, the effect of prehabilitation (exercise/physiotherapy programs in the months prior to surgery) on pain and function are too small to be considered clinically-important and were not robust over time. Prehabilitation did not result in clinically important (or statistically significant) differences in most measures of patient recovery, quality of life, length of stay and costs. Future research of sufficient power to measure clinically-relevant outcomes is required to identify which, if any, form of prehabilitation achieves better outcomes than in these trials. Jurisdictions considering implementation of prehabilitation services should consider whether resources could be better spent elsewhere on interventions of proven clinical benefit.

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Competing Interest Statement:

None declared.

Transparency Declaration

I Dr. Janet Martin affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Authors' contribution: Li Wang contributed to the study conception and design, literature screening, acquisition of data, analysis and interpretation of data, drafting of the manuscript and revision based on the comments of coauthors. Myeongjong Lee and Zhe Zhang participated in the literature screening, data acquisition and critical revision of the manuscript. Jessica Moodie did the literature searching, article retrieval, and data acquisition. Davy Cheng contributed to study conception and design, and critical revision of the manuscript. Janet Martin guided the methodology, contributed to the study conception and design, data checking and interpretation, drafting and critical revision of the manuscript. All authors approved the version submitted for publication and agreed to act as guarantors of the work.

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Table Legends

Table 1: Characteristics of included RCTs

Table 2: Risk of Bias for Included Studies

Table 3: Summary of results for prehabilitation vs. no prehabilitation

Table 4: GRADE Evidence Profile: prehabilitation vs no formal prehabilitation for total joint replacement

Supplementary table 1: Intervention characteristics of included RCTs

Supplementary Table 2: Description of RCTs of Prehabilitation versus No Prehabilitation for TKR/THR

Supplementary Table 3: Subgroup Analysis of TKR and THR

Supplementary Table 4 Sensitivity Analysis to test robustness of results after removing total score

Supplementary Table 5: Sensitivity analysis using different thresholds of patient acceptable symptom state (PASS)

Figure Legend

Figure 1: PRISMA flow diagram of study selection

Figure 2. Pain score at 4 weeks or less (converted to WOMAC pain subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery

Figure 3. Function score at 6 to 8 weeks (converted to WOMAC function subscale 0-100) for prehab vs no prehab in joint replacement surgery

Figure 4. Function score at 12 weeks (converted to WOMAC function subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery

Figure 5. Hospital length of stay (days) for prehabilitation vs no prehabilitation in joint replacement surgery

Supplementary figure 1. Funnel plot to explore publication bias for pain scores

Supplementary figure 2. Funnel plot to explore publication bias for function scores

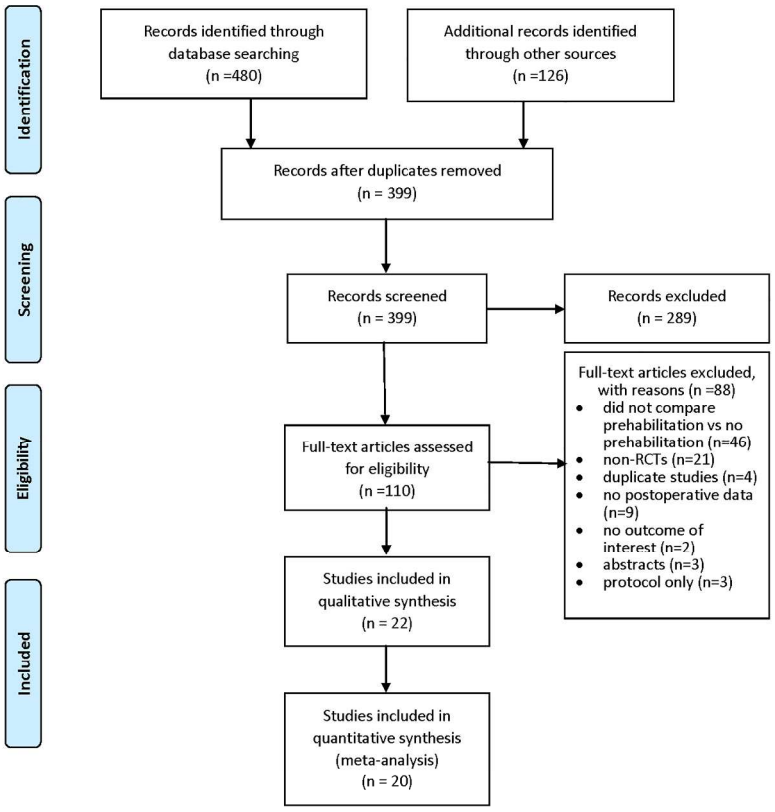

Figure 1 PRISMA flow diagram of study selection

Figure 1 PRISMA flow diagram of study selection
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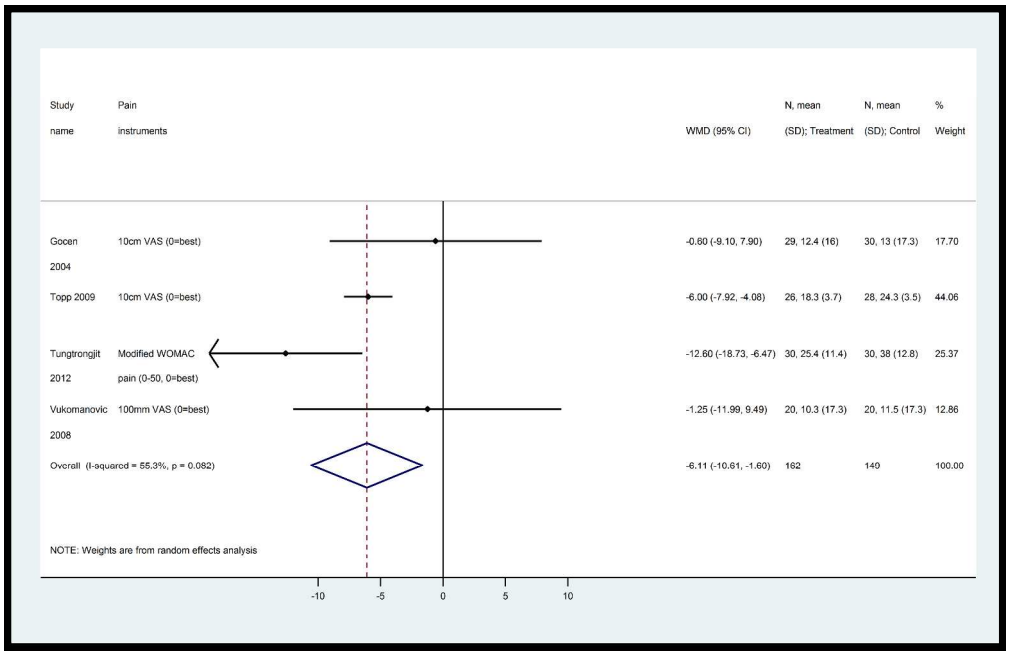

Figure 2. Pain score at 4 weeks or less (converted to WOMAC pain subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery
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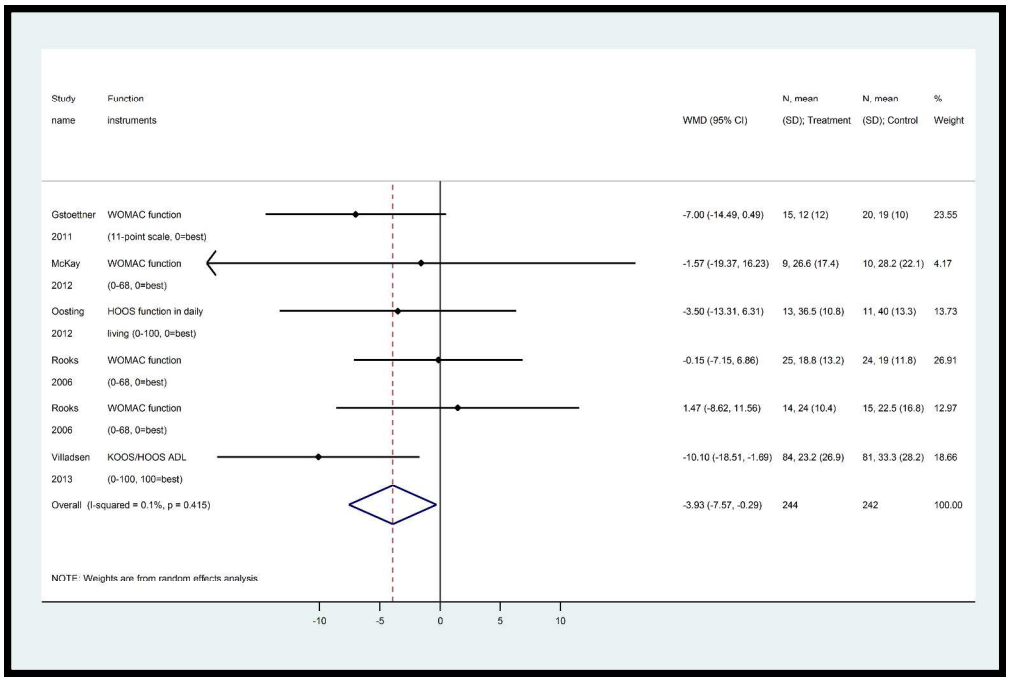

Figure 3. Function score at 6 to 8 weeks (converted to WOMAC function subscale 0-100) for prehab vs no prehab in joint replacement surgery
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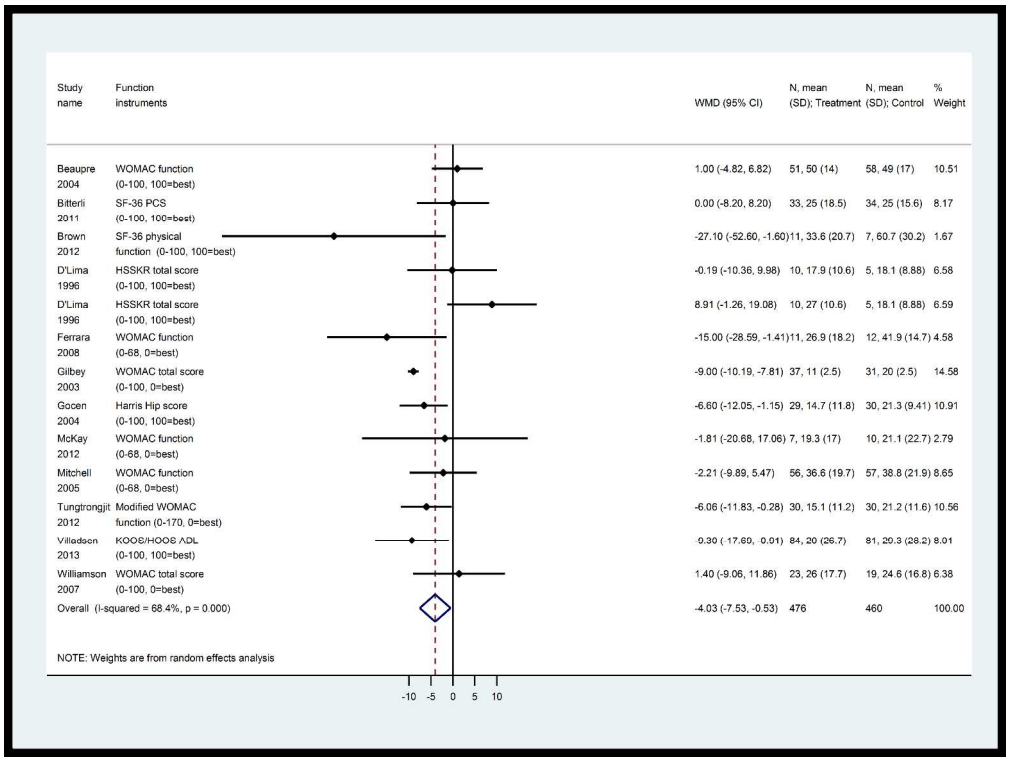

Figure 4. Function score at 12 weeks (converted to WOMAC function subscale 0-100) for prehabilitation vs no prehabilitation in joint replacement surgery

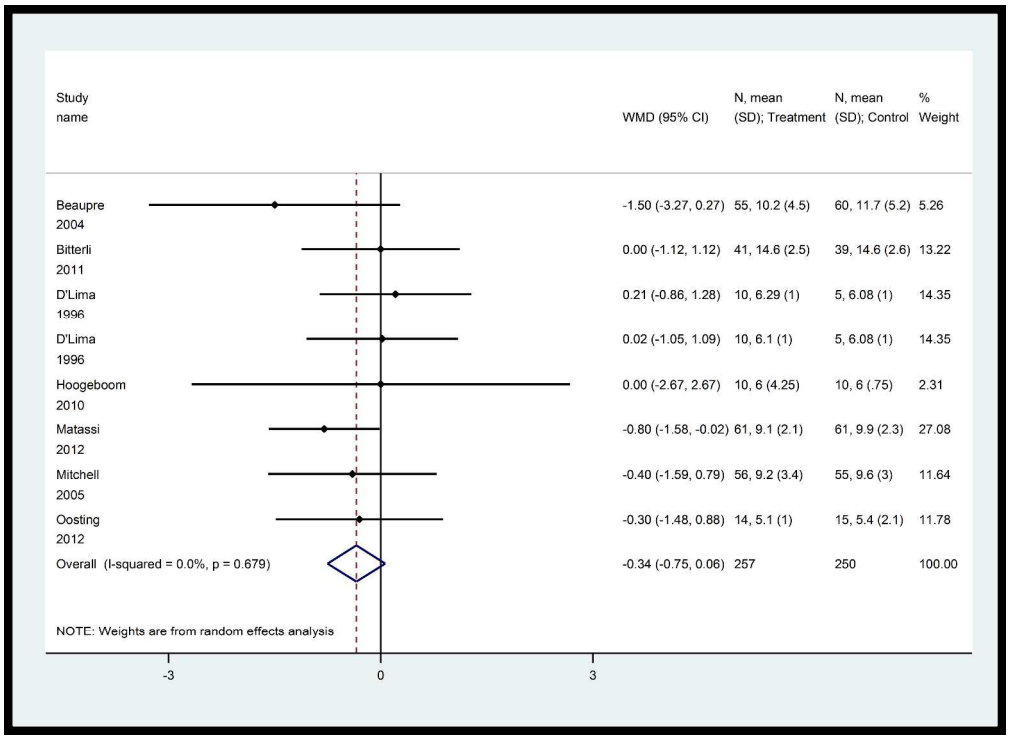

Figure 5. Hospital length of stay (days) for prehabilitation vs no prehabilitation in joint replacement surgery
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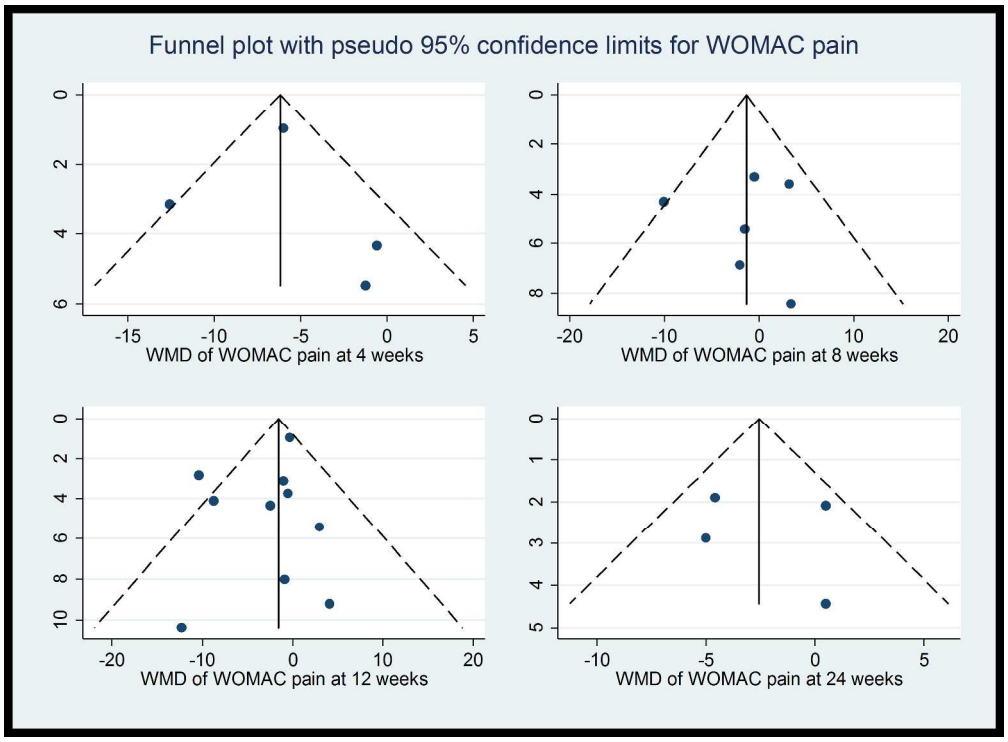

Supplementary Figure 1: Funnel plot to explore publication bias for pain scores
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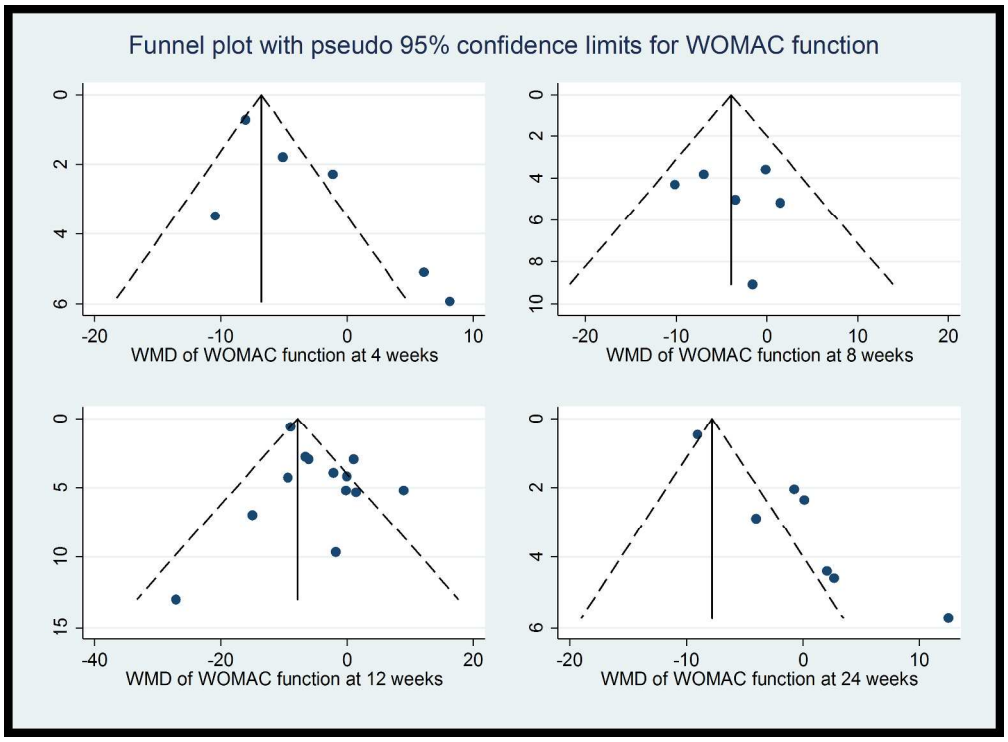

Supplementary Figure 2: Funnel plot to explore publication bias for function scores
890x650mm (96 x 96 DPI)

Supplementary table 1 Intervention characteristics of included RCTs

Study Name		Intervention	Compliance	Control	Postop intervention
Beaupre 2004	physiotherapist supervised exercise	land based: strengthening, aerobic; supervised by physiotherapist; 3 times/week * 4 weeks + education	all but 1 participant completed the 12 sessions	usual care: regular activities and other treatment at discretion of physician	standard postoperative mobilization routine
Bitterli 2011	home exercise	land based: strengthening and stretching, home exercises from 2 to 6 weeks, twice daily; 2 verbal and written instruction	exercises completed on 91% of the days	no intervention	usual care (outpatient rehabilitation or rehabilitation clinic)
Brown 2012	physiotherapist supervised exercise + home exercise	land based: strengthening and stretching, supervised by physiotherapist once a week + home exercise 2 times/week * 8 weeks	not reported	usual care	not reported
D'Lima 1996	physiotherapist supervised exercise	Intervention A: land based: strengthening, stretching. Intervention B: land based and pool based: strengthening, stretching, aerobic; once a week * 8weeks	not reported	no intervention	routine care

Evgeniadis 2008	physiotherapist or orthopedist supervised exercise	land based: strengthening (mostly upper limb and trunk), 3 times/week * 3	not reported	no intervention	standard rehabilitation
Ferrara 2008	physiotherapist supervised exercise + education	land based: strengthening, aerobic; supervised by physiotherapist; 5 times/week * 4 weeks + education	not reported	no intervention	postop rehabilitation programme
Gilbey 2003	physiotherapist supervised exercise+ home exercise	land based and pool based: strengthening, stretching, aerobic, supervised by physiotherapist + home exercise: 2 times/week *8weeks	97% of sessions complete	routine in-hospital physical therapy	clinic-based
Gocen 2004	physiotherapist supervised exercise + education	land based: strengthening, stretching, supervised by physiotherapist for 8 weeks; +education	not reported	no intervention	postoperative and education programme
Gstoettner 2011	physiotherapist supervised exercise + home exercise	land based: strengthening, stretching, balance; supervised by physiotherapist; once a week * 6 weeks +daily home training with written instructions	not reported	no intervention	not reported

Hoogeboom 2010	physiotherapist supervised exercise	land based: strengthening, aerobic, functional; + education	91% of the sessions completed	usual care + education	postop usual care protocol
Matassi 2014	physiotherapist supervised exercise + home exercise	land based: increasing lower extremity muscle strengthening supervised by physiotherapist; once a week* 1 week+ home exercise 5 times/week * 6weeks+ written instructions	79.4% completed	regular activities	same physiotherapy routines
McKay 2012	kinesiologist supervised exercise	land based: aerobic, strengthening, supervised by kinesiologist; 3 times/week * 6 weeks	98% of the sessions completed	placebo (upper body exercises)	standard postop care
Mitchell 2005	physiotherapist supervised exercise + home exercise	land based: pain relief, increase knee flexion and extension, gait re-education ,supervised by physiotherapist; 3 times/week * 8 weeks + home exercise 4 times/week * 8 weeks	73.6% sessions completed	preoperative consultation	usual hospital physiotherapy (post-discharge only)
Oosting 2012	physiotherapist supervised exercise +home exercise	land based: "functional tasks exercise", supervised by physiotherapist; 2 times/week + home exercise 4 times/week * 3 to 6 weeks	99% of the sessions completed	usual care (30min supervised class)	not reported

Rooks 2006	physiotherapist supervised exercise +education	land based and pool based: strengthening, stretching, aerobic, supervised by physiotherapist; 3 times/week * 6 weeks; +education on home modifications	89% of sessions completed	education via leaflet and telephone + 30-60min supervised class	not reported
Topp 2009	physiotherapist supervised exercise + home exercise	land based: resistance training, flexibility, step training, supervised by physiotherapist, once a week + home exercise 2 times /week	13 sessions completed (range 4 to 23)	no intervention	postop rehabilitation
Tungtrongjit 2012	home exercise	land based: home quadriceps strengthening exercise for 3 weeks	Not reported	no intervention	postop rehabilitation
Villadsen 2014	physiotherapist supervised exercise	land based: standard preoperative educational package + NEMEX programme; supervised by physiotherapist; 2 times/week * 8 weeks	74% attended the pre-specified goal of 12 or more exercise	standard preoperative educational package	postop rehabilitation
Vukomanovic 2008	physiotherapist supervised exercise +education	land based: physical therapy +education	not reported	no intervention	postop rehabilitation
Wang 2002	physiotherapist supervised exercise + home exercise	land based and pool based: strengthening, stretching, aerobic, supervised by physiotherapist+ home exercise; 2 times/week	97% of sessions complete	routine perioperative care	postop rehabilitation

		* 8 weeks			
Weidenhielm 1993	physiotherapist supervised exercise + home exercise	land based: strengthening, stretching, aerobic, supervised by physiotherapist, 3 times/week * 5 weeks; + home exercise daily	not reported	no intervention	not reported
Williamson 2007	physiotherapist supervised exercise + home exercise	land based: strengthening, stretching, balance, supervised by physiotherapist; 1 times/week * 6 weeks + home exercise	not reported	education and leaflet +1 hour supervised class + home exercise	not reported

NEMEX: neuromuscular exercise programme

Supplementary Table 2 Description of RCTs of Prehabilitation versus No Prehabilitation for TKR/THR

Study Name	No. of patients	Type of surgery	Comparison	Rehabilitation	Results				
					Pain	Function improvement	Quality of Life	Resource use	others
Beaupre 2004	131	TKR	PT supervised exercise + postop education vs. usual care	Standard postop mobilization routine	WOMAC pain: NS SF-36 bodily pain: NS from 3mo. to 1 year postoperatively	Knee ROM: NS; Quadriceps strength: NS; Hamstring Strength: NS WOMAC stiffness and function: NS; SF-36 physical functioning: NS from 3mo. to 1 year postoperatively	SF-36: NS in each domains, PCS, and MCS from 3mo. to 1 yr postoperatively	Acute care LOS, transfer LOS, readmission LOS, and total LOS: NS (total LOS: -1.5 d) Institutional costs, homecare costs, readmission costs, total costs: NS (total cost: + $33);	Postoperative complications:e.g. pulmonary emboli (n=2), deep vein thrombosis (n=9), infection (n=5), postoperative Angina: NS
Bitterli 2011	80	THR	Preoperative sensorimotor training at home (daily exercises at home) vs. no	Postop. Standard therapy protocol in hospital	SF-36 pain: : NS after surgery (4mo.,1year)	SF-36 physical function: NS after surgery (4mo,1 year) WOMAC: NS after surgery (4mo, 1year)	SF-36: NS in each domains after surgery (4mo.,1year)	LOS: NS (14.6 vs. 14.6 d)	-

			therapy	Usual care therapeutic modalities after discharge					
Brown 2012	32	TKR	Preop. exercise intervention vs. no prehabilitation	-	SF-36 pain : NS at 3mo. after surgery	SF-physical function score: ↑(MD+27.1)	SF-36:↑ in physical function score (MD+27.1) NS in other domains	-	-
D'Lima 1996	30	TKR	Preop physical therapy vs. cardiovascular conditioning program with exercise vs. no intervention	-	Hospital for Special Surgery Knee Rating pain(0-30):NS from 3wk 1yr	Hospital for Special Surgery Knee Rating function (0-52):NS from 3wk to 1yr	Quality of Well Being scores (0-1): Percentage improvement - NS Arthritis impact measurement scale scores (0-10): Percentage improvement NS	LOS: NS	-
Evgeniadis 2008	48	TKR	Preop.exercise vs. no intervention	-	-	ILAS score: NS after surgery(2, 6, 10, 14wks) Active ROM:NS after surgery	SF-36: NS at 1 day pervious to surgery (preop)	-	-

						(2, 10, 14wks)			
Ferrara 2008	23	THR	Educational and PT supervised physiotherapy program vs. no intervention	Postop. 4weeks standard exercise protocol	VAS: ↓ at 1, 3 mo. (MD -1.8, -0.97) WOMAC pain: NS at 3 mo.	ROM external rotation: ↑at 15days, 1 and 3 mo. after surgery (MD +7.69, +0.14) Harris Hip Score: NS at 1 and 3mo Barthel Index: NS at 1 and 3mo WOMAC stiffness and function: NS at 3mo	SF-36 PCS: ↑at 1 mo, but NS at 3 mo (MD +7.1 at 1 mo) SF-36 MCS: NS	-	-
Gilbey 2003	76	THR	8wks customized exercise program vs. no exercise	Postop. Exercise program (until 12wks after surgery) VS routine in-hospital PT	WOMAC pain: NS	Mean ROM at 3, 12, 24wks:↑ (MD+6,+11,+12) Hip strength mean Z score after surgery (12, 24wks): ↑ (MD+0.35, +0.6) WOMAC total score after surgery (3,12,24wks):↑(MD+8, +9, +9) WOMAC stiffness: NS, 3,12,24wks		-	-

						WOMAC function:↑ 3, 12, 24wks				
Gocen 2004	60	THR	Physiotherapy and educational program vs. no exercise or education	Routine postop. Exercise and educational program	VAS at rest at discharge: NS (MD-0.12) VAS at activity at discharge: NS (MD-0.06)	Hip adduction at discharge: NS (MD-0.1) Harris Hip Score: NS at 3mo, 2 years after surgery (MD+0.9,+4)	-	LOS: NS	-
Gstoettner 2011	38	TKR	PT supervised exercise vs. no exercise	-	WOMAC pain: NS; 6wk postoperatively	KSS: NS; KSS function: NS; WOMAC stiffness: NS; WOMAC function: NS; Gait speed (60m):NS; Gait speed (stairs up):NS; Gait speed (stairs down): NS; Knee stability (OSI): NS; Knee stability (MLSI) : NS; 6wk postoperatively Knee stability (APSI) : ↓ (MD -0.6) 6wkpostoperatively	-	-	-

Hoogebo om 2010	21	THR	Therapeutic exercise program vs. usual care	Postop. usual care protocol till discharge	HOOS pain: NS VAS: NS At baseline and preop,	Functional recovery: NS HOOS (in all domains): NS LASA physical activity questionnaire (all domains): NS At baseline and preop	Patient-specific complaints (PSK): NS At baseline and preop	LOS: NS 6 vs. 6 days	2 postoperative complications in exercise group: femur fracture and intestinal obstruction. no serious AE
Matassi 2014	122	TKR	Preoperative home exercise program vs. regular activities	Same postop. physiotherapy routine	-	Mean time to reach 90° of knee ROM: ↓ (MD -1.1 day) Active knee flexion: NS at 6wks. 6mo, 1yr Passive knee flexion: NS at 6wks. 6mo, 1yr Knee score or patient function score (Knee Society Clinical Rating System): NS at 6wks, 6 mos. 1 yrs.	-	LOS: ↓ (MD -0.8 day)	-
McKay 2012	22	TKR	Lower-body strength training program vs. nonspecific upper-body	Standard postop. care	WOMAC pain: NS, MD+0.7, +0.9 at 6 and 12wks.	SF-36 PSC: NS Quadriceps strength: NS 50-foot walk: NS Stair test: NS Arthritis self–efficacy	SF-36 (PCS, MCS): NS after surgery	-	-

			strength training program (placebo)			(including pain, physical function, and other symptoms): NS			
Mitchell 2005	160	TKR	PT supervised pre- & postop home exercise (home PT) vs. no pre-op exercise + usual hospital PT postop	Postop home exercise or hospital PT	WOMAC pain: NS SF-36 bodily pain: NS at 12wk	WOMAC physical function: NS; WOMAC stiffness: NS; SF-36 physical function: NS at 12wk	SF-36: NS in each domains SF-6D: NS Patient satisfaction with PT: NS (86% in both groups) at 12wk	LOS: NS (MD -0.4d) Cost of PT: NS(MD + £1.4) Total cost: NS(MD + £4.7)	45 withdrawn patients had significantly poor score on the SF-36 general health, energy, and more reported heart problems and stroke/TIA.
Oosting 2012	30	THA	PT supervised exercise vs. usual care	-	HOOS pain: NS VAS: NS 6wk changes from baseline.	TUG: NS; CRT: ↓ (MD -9.2s); 6MWT: NS; PSC: NS; HOOS other symptoms, function in daily living, function in sport and recreation: NS; LAPAQ: NS;	HOOS hip-related quality of life: NS Patient Specific Complaints (PSC) questionnaire score: NS	LOS: NS (MD -0.3d) Nursing home after discharge: NS	No severe adverse events Complications: e.g. Wound, delirium, loss of sensation, decubitus ulcers, and

					6wk post-discharge changes from baseline				bowel obstruction) NS
Rooks 2006	108	THA+ TKA	PT supervised exercise+education vs. education	-	For THR: WOMAC pain: NS SF-36 pain: NS 8wk and 26wk postoperatively For TKR: WOMAC pain: NS 8wk and 26wk postoperatively SF-36 pain: NS 8wk postoperatively SF-36 pain: ↑(MD+11.5) 26wk changes from baseline	For both THR and TKR: WOMAC function: NS; SF-36 physical function: NS SF-36 role limitation physical: NS; 1-repetition maximum: NS ; Timed up and go: NS ; 8wk and 26wk postoperatively Functional reach: NS ; 8wk and 26wkpostoperatively	-	-	-
Topp 2009	54	TKA	PT supervised exercise vs. usual care	Postoperative rehabilitation	Pain in Sit-to-stand, 6MWT, Ascent and descent stairs: NS? at 1, 3mo.	Sit-to-stand: NS? 6MWT: NS? Ascent and descent stairs: NS? Maximum extension strength of	-	-	-

					postoperatively No between-group comparison	the surgical knee, nonsurgical knee: ? Maximum extension strength of the surgical knee:? at 1, 3mo. postoperatively No between-group comparison				
Tungtrongjit 2012	60	TKA	Quadriceps exercise vs. usual care	-	Modified WOMAC pain score: ↓ (MD -6.3) VAS: ↓ (MD -0.9) at 1 mo postoperatively Modified WOMAC pain score: ↓ (MD -5.2) VAS: ↓ (MD -1) at 3 mo postoperatively Modified WOMAC	Total Modified WOMAC score: ↓ (MD -26.7) Modified WOMAC stiffness score: ↓ (MD -2.5) Modified WOMAC function score: ↓ (MD -17.7) Quadriceps strength: ↑(MD+1.5) at 1 mo postoperatively Total Modified WOMAC score: ↓ (MD -17.7) Modified WOMAC stiffness score: ↓ (MD -2) Modified WOMAC function	-	-	-

	pain score: ↓ (MD -2.3) VAS: NS at 6 mo postoperatively	score: ↓ (MD -10.3) Quadriceps strength: ↑(MD+2.2) at 3 mo postoperatively Total Modified WOMAC score: NS Modified WOMAC stiffness score: NS Modified WOMAC function score: NS Quadriceps strength: NS at 6 mo postoperatively Knee Flexion: NS Knee Extension: NS Total knee ROM: NS at 1, 3, 6 mo postoperatively

Villadsen 2014	165	THA+ TKA	PT supervised exercise + education vs. education	Postoperative rehabilitation	For THR+TKR: KOOS/HOOS Pain: ↓ (MD -5.4) For THR: KOOS/HOOS Pain: NS changes at 6wk and 3mo postop from base line For TKR: KOOS/HOOS Pain: ↓ (MD -8)	For both THR+TKR or For TKR: KOOS/HOOS ADL: ↑ at 6wkpostop, but NS at 3mo postop For THR: KOOS/HOOS ADL: NS at 6wk and 3mo postop For THR+TKR or THR or TKR: KOOS/HOOS symptoms: NS KOOS/HOOS sport and recreation: NS At 6wk or 3 mo postop changes from baseline. Single-joint hip extension and hip abduction: ↑ (~15% and 35% improvement)	For both THR+TKR or For TKR: EQ5D VAS: ↓ (MD -7.6) at 6wk postop, but NS at 3mo postop For THR: EQ5D VAS: NS At 6wk and 3mo postop For TKR: EQ5D VAS: ↓ (MD -8.8) changes at 6wk postop from baseline, but NS changes at 3mo postop from baseline For THR+TKR or THR or TKR: EQ5D index: NS	-	One patient with hip OA discontinued the exercise due to an increase in pain. 2 patients from the control group developed deep periprosthetic infection.

						Chair stand: NS 20-m walk: NS Knee bends: NS Contra: NS at 3mo	KOOS/HOOS QOL: NS At 6wk or 3 mo postop changes from baseline.		
Vukomanovic 08	45	THA	PT supervised exercise +education vs. no interventions	Postoperative rehabilitation	Pain at rest (VAS): NS Pain on movement (VAS): NS at discharge postop	First day of activities – use of toilet↓ (MD -0.9d), use of chair↓ (MD -1.05d), and walking up and down stairs: ↓ (MD -1.67d) Changing position in bed: ↑(MD +0.95) Changing position on the edge: ↑(MD +0.9) From sitting to standing: ↑(MD +1.05) Standing: ↑(MD +1.1) Changing position to lying: ↑(MD +1.15) Walking: ↑(MD +1.15)	-	LOS: NS (- MD +0.4d) Class with the therapist: ↓ (MD-1.65)	Five patients were excluded postoperatively because of complications during and post operation.

	Use of toilet: ↑(MD +1.9) Use of Chair: ↑(MD +1.9) Walking up and down stairs: ↑(MD +1.8) Endurance while walking: ↑(MD +1) at the 3rd day postoperatively Changing position in bed: ↑(MD +0.4) Changing position on the edge: ↑(MD +0.45) From sitting to standing: ↑(MD +0.45) Standing: ↑(MD +0.45) Changing position to lying: ↑(MD +0.45) Walking: ↑(MD +0.5) Use of toilet: ↑(MD +1) Use of Chair: ↑(MD +1.25) Walking up and down stairs:

						↑(MD +1.85) Endurance while walking: ↑(MD +1) at the discharge Flexion of the hip flexed knee: NS Flexion of the hip extended knee: NS Abduction:: NS Harris hip score: NS JOA hip score: NS At discharge postoperatively Oxford Hip Score: NS At 15 mo postoperatively			
Wang 2002	28	THA	PT supervised pre- & post-operative exercise vs. PT supervised pre- & post-operative	Postoperative exercise or usual care	-	Cadence (steps/min): ↑(MD +18) Stride length: ↑(MD +0.06m) Gait velocity: ↑(MD +0.28) At 3 wk postoperatively	-	-	Complications: NS no wound infections, joint

			usual care			Cadence (steps/min): ↑(MD +9) Stride length: NS Gait velocity: ↑(MD +0.2) At 12 wk postoperatively Cadence (steps/min): ↑(MD +10) Stride length: NS Gait velocity: ↑(MD +0.21) At 24 wk postoperatively 6MWT: NS At 12 wk postoperatively 6MWT: ↑(MD +64m) At 24 wk postoperatively			dislocations, complications requiring return to the operating room, or major medical complications
Weidenhielm 1993	39	TKP	PT supervised exercise vs. no exercise	-	VRS (no, mild, moderate, and severe pain): NS	Passive ROM: NS No. patients grading the knee as stable or unstable: NS	-	-	-

					Pain at walk: NS At 3mo.	Isokinetic quadriceps strength (at 30 and 90 degree): NS Walking speed (self-selected and maximal): NS at 3 mo postoperatively			
Williams on 2007	120	TKR	PT supervised exercise vs. education leaflet	-	VAS: NS (MD -0.09 at 3mo postop)	OKS: NS (MD +1.61) 50-m walk: NS (MD +2.51s) WOMAC: NS (MD+1.33) at 3mo postop	HAD score anxiety: NS (MD +1.84) HAD score depression: NS (MD -0.25)	HLOS: NS (MD -1.27d) Cost of PT: £9 per patient	No adverse responses

6MWT: 6-minute walk test; ADL: activities of daily living; APSI: anteroposterior stability index; EQ5D: EuroQol 5 Dimension Health Questionnaire; HAD: Hospital Anxiety and Depression score; HOOS: Hip disability and Osteoarthritis Outcome Score; ILAS: Iowa Level of Assistance Scale; KOOS: Knee injury and Osteoarthritis Outcome Score; KSS: Knee Society Score; LASA: Longitudinal Aging Study Amsterdam; LOS: length of stay; MCS: mental component summary; MD: mean difference; MLSI : medio-lateral stability index; NS: not significant; OA: Osteoarthritis; OKS: Oxford Knee Score questionnaire; OSI: overall stability index; PCS: physical component summary; postop: postoperative; preop: preoperative; PT: physical therapist; ROM: range of motion; THR: total hip replacement; TKP: total knee replacement; TUG: Timed Up & Go; VAS: visual analogue scale; VRS: verbal rating scale; WOMAC: Western Ontario and McMaster Universities Arthritis Inde

Supplementary Table 3: Subgroup Analysis of TKR and THR

Outcomes	Sub-group	No. of studies	No. of patients	Hetero-geneity test p value	I^2 (%)	WMD (95%CI)	interaction p value
Pain at 4 weeks or less	TKR	2	114	0.04	75	-8.6 (-15.0 to -2.3)	0.26
	THR	2	99	0.93	0	-0.9 (-7.5 to +5.8)	
Pain at 6 to 8 weeks	TKR	4	164	0.04	64	-2.7 (-11.7 to +6.3)	0.88
	THR	3	159	0.92	0	-1.3 (-6.5 to +4.0)	
Pain at 12 weeks	TKR	9	534	0.02	55	-3.2 (-7.1 to +0.7)	0.24
	THR	2	107	0.86	0	-3.0 (-9.8 to +3.9)	
Pain at 24 weeks	TKR	3	198	0.54	0	-4.1 (-7.1 to -1.0)	0.47
	THR	1	59	NA	NA	+0.5 (-3.6 to +4.6)	
Function at 4 weeks or less	TKR	3	90	0.004	82	+0.7 (-12.1 to +13.5)	0.47
	THR	3	167	0.009	79	-0.5 (-9.1 to -1.4)	
Function at 6 to 8 weeks	TKR	4	164	0.004	64	-6.3 (-13.9 to +1.3)	0.34
	THR	3	157	0.119	45	-1.7 (-6.9 to +3.5)	

Function at 12	TKR	9	470	0.04	51	-2.4 (-7.0 to +2.2)	0.14
weeks	THR	5	301	0.16	39	-7.2 (-10.7 to -3.8)	
Function at 24	TKR	5	228	0.12	45	-4.1 (-7.1 to -1.2)	0.22
weeks	THR	2	117	<0.001	93	+0.5 (-3.6 to +4.6)	
Function at 1 year	TKR	3	139	0.87	0	-0.5 (-4.2 to +3.3)	0.85
or more	THR	2	117	0.21	35	+0.2 (-3.8 to +4.2)	

TKR: total knee replacement; THR: total hip replacement; NA: not applicable

Supplementary Table 4 Sensitivity Analysis to test robustness of results after removing total score

Outcomes	SMD (95%CI)	RoM (95%CI)	WMD (95%CI) after removing total score
Pain at 4 weeks or less	-0.70 (-1.46 to +0.06)	0.74 (0.68 to 0.81)	NR
Pain at 6 to 8 weeks	-0.17 (-0.38 to +0.05)	0.88 (0.73 to 1.06)	NR
Pain at 12 weeks	-0.20 (-0.40 to 0.00)	0.87 (0.76 to 1.01)	NR
Pain at 24 weeks	-0.26 (-0.56 to +0.04)	0.78 (0.60 to 1.02)	NR
Pain at 1 year or more	-0.14 (-0.51 to +0.24)	0.90 (0.68 to 1.20)	NR
Function at 4 weeks or less	-0.58 (-1.45 to +0.29)	0.90 (0.79 to 1.04)	-5.0 (-9.4 to - 0.6)
Function at 6 to 8 weeks	-0.27 (-0.49 to -0.05)	0.86 (0.76 to 1.00)	NR
Function at 12 weeks	-0.48 (-0.91 to -0.05)	0.82 (0.67 to 1.00)	-4.5 (-7.9 to -1.1)
Function at 24 weeks	-0.49 (-1.47 to +0.49)	0.87 (0.56 to 1.33)	+0.1 (-4.1 to +4.3)
Function at 1 year or more	-0.01 (-0.24 to +0.22)	1.01 (0.88 to 1.15)	-0.4 (-2.6 to +1.8)

SMD: Standardized mean difference; RoM: Ratio of mean; WMD: Weighted mean difference; NR: not relevant since total score was not included

Supplementary Table 5 Sensitivity analysis using different thresholds of patient acceptable symptom state (PASS)

Outcomes	PASS <=30			PASS <=40			PASS <=20		
	RR	median baseline risk	RD	RR	median baseline risk	RD	RR	median baseline risk	RD
Pain at 4 weeks or less	1.09	43.8%	3.9%	1.04	94.1%	3.8%	1.76	8.0%	6.1%
Pain at 6 to 8 weeks	1.00	62.2%	0%	1.00	78.3%	0%	1.02	45.0%	0.9%
Pain at 12 weeks	1.02	60.9%	1.2%	1.01	79.2%	0.8%	1.10	40.2%	4.0%
Pain at 24 weeks	1.00	98.0%	0%	1.00	99.9%	0%	1.04	84.7%	3.4%
Function at 4 weeks or less	1.23	26.8%	6.2%	1.10	71.7%	7.2%	1.67	4.9%	3.3%
Function at 6 to 8 weeks	1.10	54.3%	5.4%	1.02	69.1%	1.4%	1.20	38.8%	7.8%
Function at 12 weeks	1.02	62.6%	1.3%	1.02	79.8%	1.6%	1.34	39.2%	13.3%
Function at 24 weeks	1.00	97.4%	0%	1.00	99.9%	0%	1.01	84.7%	0.8%
Function at 1 year or more	0.97	88.1%	-2.6%	0.97	98.1%	-2.9%	1.30	66.4%	19.9%

Appendix Search Strategies

Search Updated: November 10th, 2015

PubMed

1	((((((((((((((((((((((exercise[tiab] OR prehabilitation[tiab] OR prehab[tiab] OR "physical therapy"[tiab] OR physiotherapy[tiab] OR "therapeutic exercise"[tiab] OR "therapeutic activity"[tiab] OR activity[tiab] OR "preoperative rehabilitation"[tiab] OR "weight training"[tiab] OR "weight lifting"[tiab] OR aquatic[tiab] or swimming[tiab] Or "strength training"[tiab] OR "endurance training"[tiab] OR cycling[tiab] OR biking[tiab] OR "weight reduction"[tiab] OR "weight loss"[tiab] OR kinesiotherapy[tiab] OR hydrotherapy[tiab] OR fitness[tiab] OR "exercise therapy"[tiab])
2	(((Arthroplast*[tiab] OR replace*[tiab] OR "orthopedic surgery"[tiab]))) AND ((hip*[tiab] OR knee*[tiab]))
3	1 AND 2
4	(((((pre-operative[tiab] OR preoperative[tiab] OR pre-op[tiab] OR preop[tiab] OR preoperative care[MeSH Terms])
5	3 AND 4
6	random*
7	5 AND 6

Emabase

1	exercise.ti,ab.
2	Prehabilitation.ti,ab.
3	Physical therapy.ti,ab.
4	Physiotherapy.ti,ab.
5	Therapeutic exercise.ti,ab.
6	Therapeutic activity.ti,ab.
7	Activity.ti,ab.
8	Preoperative rehabilitation.ti,ab.
9	Weight training.ti,ab.
10	Weight lifting.ti,ab.
11	Aquatic.ti,ab.
12	Swimming.ti,ab.
13	Strength training.ti,ab.
14	Endurance training.ti,ab.
15	Cycling.ti,ab.
16	Biking.ti,ab.
17	Weight reduction.ti,ab.
18	Weight loss.ti,ab.
19	Kinesiotherapy.ti,ab.
20	Hydrotherapy.ti,ab.
21	Fitness.ti,ab.
22	Exercise therapy.ti,ab.

23	or/1-22
24	arthroplast*.ti,ab.
25	replacement.ti,ab.
26	resurfac*.ti,ab.
27	orthopedic surgery.ti,ab.
28	hip*.ti,ab.
29	knee*.ti,ab.
30	or/24-27
31	28 or 29
32	30 and 31
33	23 and 32
34	random*.mp.
35	33 and 34
36	exp animals/
37	exp human/
38	(dog or dogs or canine or canines or pig or pigs or porcine or rat or rats or cat or feline or felines or lamb or lambs or mouse or mice or rabbit or rabbits).ti,ab.
39	36 not 37
40	38 or 39
41	35 not 39
42	pre-operative.mp.
43	preoperative.mp.
44	preoperative care/

45	Preop*.mp.
46	Pre-op*.mp.
47	or/42-46
48	41 and 47

Cochrane CENTRAL

1	"exercise":ti,ab,kw (Word variations have been searched)
2	"prehabilitation":ti,ab,kw (Word variations have been searched)
3	"physical therapy":ti,ab,kw (Word variations have been searched)
4	"physiotherapy":ti,ab,kw (Word variations have been searched)
5	"therapeutic exercise":ti,ab,kw (Word variations have been searched)
6	"therapeutic activity":ti,ab,kw (Word variations have been searched)
7	"activity":ti,ab,kw (Word variations have been searched)
8	"Preoperative rehabilitation":ti,ab,kw (Word variations have been searched)
9	"weight training":ti,ab,kw (Word variations have been searched)
10	"weight lifting":ti,ab,kw (Word variations have been searched)
11	"aquatic":ti,ab,kw (Word variations have been searched)
12	"swimming":ti,ab,kw (Word variations have been searched)
13	"strength training":ti,ab,kw (Word variations have been searched)
14	"Endurance training":ti,ab,kw (Word variations have been searched)
15	"cycling":ti,ab,kw (Word variations have been searched)
16	"biking":ti,ab,kw (Word variations have been searched)
17	"weight reduction":ti,ab,kw (Word variations have been searched)

18	"weight loss":ti,ab,kw (Word variations have been searched)
19	"kinesiotherapy":ti,ab,kw (Word variations have been searched)
20	"hydrotherapy":ti,ab,kw (Word variations have been searched)
21	"fitness":ti,ab,kw (Word variations have been searched)
22	"Exercise therapy":ti,ab,kw (Word variations have been searched)
23	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 of #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
24	"arthroplasty":ti,ab,kw (Word variations have been searched)
25	"replacement":ti,ab,kw (Word variations have been searched)
26	"resurface":ti,ab,kw (Word variations have been searched)
27	"orthopedic surgery":ti,ab,kw (Word variations have been searched)
28	#24 or #25 or #26 or #27
29	"hip":ti,ab,kw (Word variations have been searched)
30	"knee":ti,ab,kw (Word variations have been searched)
31	#29 or #30
32	"preoperative":ti,ab,kw (Word variations have been searched)
33	"pre-operative":ti,ab,kw (Word variations have been searched)
34	"preop":ti,ab,kw (Word variations have been searched)
35	"pre-op":ti,ab,kw (Word variations have been searched)
36	#32 or #33 or #34 or #35
37	#28 and #31
38	#23 and #37
39	#36 and #38

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	16-21
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	13-15
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	10

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	13-15
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	11-12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13-15
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Suppl Table 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	16-21 Table 3 Table 4 Suppl Table 3 Suppl Table 4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13-15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	21-22
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22-23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23-25
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	25
FUNDING			

PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	26

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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