SUPPLEMENTARY APPENDIX 3: Evidence Report

2023 American College of Rheumatology (ACR) and American Association of Hip and Knee Surgeons (AAHKS) Clinical Practice Guideline for the Optimal Timing of Elective Hip or Knee Arthroplasty for Patients with Symptomatic Moderate to Severe Osteoarthritis or Advanced Symptomatic Osteonecrosis with Secondary Arthritis for Whom Nonoperative Therapy is Ineffective

PICO 1. In our defined population, what is the relative impact of a 3 month "waiting period" prior to arthroplasty versus no waiting period on patient reported outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:
A systematic review of the literature identified no studies directly addressing the question; therefore, we loosened our inclusion criteria to include other studies that provided indirect evidence. We included two prospective, non-interventional studies that assessed post-operative total hip arthroplasty (THA) outcomes in patients who waited ≤6 months or >6 months. Only data for Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and EQ-5D were reported (**Table 1**). The two studies could not be pooled due to limited reporting of data in one study.[1] Two additional prospective studies, Nilsdotter, 2002 (THA)(1) with 3 month for waiting period dichotomization and Desmeules 2012 (TKA)(2) for varying waiting periods including >8 months, were included. The certainty of the overall evidence was very low.

Fielden et al. (3) evaluated patient-reported outcomes and cost effectiveness in patients who waited 6 months or less compared (n=86) to those waiting more than 6 months (n=36) for total hip arthroplasty.[2] There was no statistical difference in WOMAC or EQ-5D between the two groups at six months post-operatively, although societal and personal costs were significantly lower in patients who had surgery within six months.

Garbuz et al. (4) evaluated WOMAC outcomes in total hip arthroplasty patients comparing patients who waited 6 months or less or more than 6 months. Patients who waited 6 months or less had better functional outcomes on the WOMAC subscale (OR 0.5, confidence interval and p-value not reported), but no difference in the WOMAC pain and stiffness subscales. Garbuz was a particularly poorly reported study given the absence

of breakdown of sample size in each group, p values, confidence intervals, results tables, and difficulty interpreting which values were adjusted for and which were not.

Nilsdotter, 2002 (1) evaluated WOMAC and SF-36 scores 1 year post-THA in people who had a duration of waiting period <=3 months vs. >3 months in a non-randomized study. There were no differences in pre-operative or the 12-month post-operative WOMAC scores (pain, stiffness, and physical function), SF-36 subscale scores (including physical function and SF-36 role physical scores) in those with shorter wait time of <=3 months, compared to waiting period >3 months. In both groups, there was a significant improvement in the SF-36 subscale and the WOMAC scores from pre- to 12-month post-operative examinations.

In the case series by Desmeules 2012 (2), change scores on WOMAC and SF-36 were compared between people with different waiting periods for total knee arthroplasty (TKA) (in four categories (<=3, >3–6, >6–9, >9 months waiting period). Pre-surgery wait, defined as the time between enrollment on the pre-surgery waiting list and surgery, was considered in four categories (<=3, >3–6, >6–9, >9 months). Pain and functional limitations were measured with the WOMAC. HRQoL was measured with the SF-36. Comparing WOMAC pain scores for the operated knee 6 months after surgery, no significant differences were seen between the four groups of pre-surgery wait [$F(3, 136) = 1.88$, $P = 0.14$]. Although this difference was not significant, the group having waited >9 months presented the lowest WOMAC pain score [71.1; 95% CI: 64.8–77.5] (i.e., higher pain level) compared with the three other groups. The group that waited >3–6 months had a significantly higher contralateral knee WOMAC pain score (i.e., less pain) [86.1; 95% CI: 80.7–91.3] and significantly lower SF-36 role physical score [45.2; 95% CI: 35.4–55.0], compared with the three other groups.

Overall impression: The studies that address our question directly would compare results in patients randomized to immediate arthroplasty vs. those delayed for a 3-month period. Observational studies were included comparing these groups, but they were rated down for risk of bias, imprecision, and indirectness.
Quality of evidence: Very low

Table 1. Wait time <6 months versus >6 months. 452 Fielden 2005 (3).

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	≤6 month wait	>6 month wait	Relative (95% CI)	Absolute (95% CI)		
WOMAC at 6 months post-THA in patients waiting ≤6 months vs >6 months (follow-up: 6 months)												
1	observational studies	serious[a]	not serious	serious[b]	serious[c]	None	86	36	**OR 1.01** (0.21 to 4.79)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low	No statistically significant difference between arms
EQ-5D Outcomes at 6 months post- Total Hip Arthroplasty in patients waiting ≤6 months vs >6 months (follow-up: 6 months)												
1	observational studies	serious[a]	not serious	serious[b]	serious[c]	none	86	36	**OR 0.60** (0.19 to 1.88)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low	No statistically significant difference between arms

CI: confidence interval; **OR:** odds ratio

Explanations

a. Risk of bias deemed to be high primarily because this is a non-interventional cohort study.

b. Indirectness deemed serious given the pre-specified PICO question was concerned with waiting times of 3 months, whereas this study evaluated 6 month waits.

c. Imprecision deemed serious because the confidence interval includes the possibility of both benefit and harm.

Table 2: Wait time < 3 months vs. wait time > 3 months. 190 Desmeules 2012; 7 Nilsdotter 2002 (1).

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Wait time < 3 months	Wait time > 3 months	Relative (95% CI)	Absolute (95% CI)		
WOMAC pain at 12 months post-surgery. 7 Nilsdotter 2002												
1	observational studies	not serious	not serious	not serious	serious[a]	none	23	33	-	MD **5 lower** (12.94 lower to 2.94 higher)	⨁◯◯◯ Very low	No statistically significant difference between groups
WOMAC stiffness at 12 months post-op. 7 Nilsdotter 2002												
1	observational studies	not serious	not serious	not serious	serious[a]	none	23	33	-	MD **0.3 higher** (9.82 lower to 10.42 higher)	⨁◯◯◯ Very low	No statistically significant difference between groups
WOMAC physical function at 12 months post-op. 7 Nilsdotter 2002												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Wait time < 3 months	Wait time > 3 months	Relative (95% CI)	Absolute (95% CI)		
1	observational studies	not serious	not serious	not serious	serious[a]	none	23	33	-	MD **8.4 higher** (0.82 lower to 17.62 higher)	⨁◯◯◯ Very low	No statistically significant difference between groups

SF36 Physical function at 12 months post-op. 7 Nilsdotter 2002

1	observational studies	not serious	not serious	not serious	serious[a]	none	23	33	-	MD **6.1 higher** (5.03 lower to 17.23 higher)	⨁◯◯◯ Very low	No statistically significant difference between groups

SF36 Role physical at 12 months post-op. 7 Nilsdotter 2002

1	observational studies	not serious	not serious	not serious	serious[a]	none	23	33	-	MD **13.6 higher** (7.65 lower to 34.85 higher)	⨁◯◯◯ Very low	No statistically significant difference between groups

SF36 Bodily pain at 12 months post-op. 7 Nilsdotter 2002

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Wait time < 3 months	Wait time > 3 months	Relative (95% CI)	Absolute (95% CI)		
1	observational studies	not serious	not serious	not serious	serious[a]	none	23	33	-	MD **2.1 higher** (7.65 lower to 11.85 higher)	⨁◯◯◯ Very low	No statistically significant difference between groups

CI: confidence interval; **MD:** mean difference

Explanations

a. Low number of patients in each group and wide CI

Table 3. Additional Data from RCT and Observational Studies

Ref ID, Author, year	Study type	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results
81, Garbuz 2006 (4)	Prognostic	1 year post-THA (range not reported)	Number of patients who had waiting period prior to TJA: Of 201 eligible; 147 returned a post-operative WOMAC questionnaire	Duration of Waiting Period (Mean, Range): mean 6 months (range not reported) Defined long wait as >6 months, and short wait as ≤6 months.	**1. Patient-reported outcome scores at 12 months: waiting period v. no waiting period** For function (WOMAC subscale), logistic regression analysis indicated that wait time was negatively associated with the probability of better than expected outcome (adjusted OR 0.92 for each month of wait time). Results at 12 months included:

			Number of Patients who did not have a waiting period prior to TJA: 0 % Female: 53 Mean Age: 65 years	Note: Logistic regression analysis compared better than expected outcomes vs not better than expected outcomes based on wait time (# of months from registration on the wait list until surgery).	a. 43% shorter waiting group vs. 31% longer waiting group achieved a better than expected functional outcome b. Compared to those waiting < 6 months, waiting longer than 6 months resulted in a 50% decrease in odds of achieving a better than expected outcome. c. Each additional month spent waiting was associated with an 8% decrease in odds of a better than expected functional outcome. For pain (WOMAC subscale), wait time did not negatively influence the probability of achieving a better than expected outcome. *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
190 Desmeules 2012 (2)	Case series	6 months	141 patients who waited and were interviewed six months after TKA 93(66%) Female, Mean Age 66 (SD 9.5)	3, 3–6, 6–9, >9 months before TKA (Mean 184 (SD: 120.8) days)	Patient-reported change in scores at 6 months between enrollment on the pre-surgery waiting lists and 6 months after TKR: % (p value): WOMAC Pain: 30.6 (SD 21.8; CI 26.9–34.2) Function: 25.4 (SD 20.5; CI 22.0–28.8) Contralateral knee pain: 1.1 (SD 22.1; CI -2.6–4.8) SF-36 Physical functioning: 17.8 (SD 22.2; CI 14.1–21.5) Role physical: 18.4 (SD 33.6; CI 12.8–24.0) Bodily pain: 9.4 (SD 16.1; CI 6.7–12.1) p-value for all <0.001

References (the list of all references will be in the end of file)

1. Garbuz DS, Xu M, Duncan CP, Masri BA, Sobolev B. Delays Worsen Quality of Life Outcome of Primary Total Hip Arthroplasty. *Clin Orthop Relat Res*. 2006;447:79-84. doi:10.1097/01.blo.0000203477.19421.ed

2. Fielden JM, Cumming JM, Horne JG, Devane PA, Slack A, Gallagher LM. Waiting for Hip Arthroplasty. *J Arthroplasty*. 2005;20(8):990-997. doi:10.1016/j.arth.2004.12.060

3. Desmeules, F., Dionne, C. E., Belzile, É. L., Bourbonnais, R., & Frémont, P. (2012). The impacts of pre-surgery wait for total knee replacement on pain, function and health-related quality of life six months after surgery. Journal of evaluation in clinical practice, 18(1), 111–120. https://doi.org/10.1111/j.1365-2753.2010.01541.x

4. Nilsdotter, A. K., & Lohmander, L. S. (2002). Age and waiting time as predictors of outcome after total hip replacement for osteoarthritis. Rheumatology (Oxford, England), 41(11), 1261–1267. https://doi.org/10.1093/rheumatology/41.11.1261

PICO 2: In our defined population, what is the relative impact of physical therapy versus arthroplasty at one year on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:

A systematic review of the literature identified no studies directly addressing the question;, therefore, we loosened our inclusion criteria to include other studies. The most pertinent evidence comes from a single randomized trial comparing TKA plus non-surgical treatment to non-surgical treatment alone, which is an indirect comparison for this question. Additional studies that were included compared various exercise regimens (alone or in combination with a behavioral intervention) to usual care, an exercise regimen to other exercise regimen, or exercise regimen to control or usual care. The certainty of the overall evidence was low.

In a randomized trial of 100 patients by Skou et al. (5), patients eligible for elective, unilateral total knee arthroplasty (TKA) were randomized to undergo TKA followed by 12 weeks of nonsurgical treatment (TKA group) or to receive only the 12 weeks of nonsurgical treatment (nonsurgical-treatment group; **Table 1**). The non-surgical treatment was delivered by physiotherapists and dietitians and consisted of exercise, education, dietary advice, use of insoles, and when indicated, pain medication. The primary outcome was the change from baseline to 12 months in the mean score on four Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales, covering pain, symptoms, activities of daily living, and quality of life. In the intention-to-treat analysis, the TKA group had greater improvement in the KOOS score than did the nonsurgical-treatment group (32.5 vs. 16.0; adjusted mean difference, 15.8 [95% confidence interval, 10.0 to 21.5]).

Other studies were indirect comparisons that provided low certainty to very low certainty evidence for each outcome (**Tables 2-11)**.

(1) Behavioral grade therapy was statistically significantly better than the usual care for hip osteoarthritis for WOMAC pain and function at 9-months, but not at 60 months (**Table 2**) (6);
(2) Behavioral grade therapy was statistically significantly better than the usual care for knee osteoarthritis for WOMAC pain and function at 9-months, but not at 60 months (**Table 3**) (6);
(3) Land- vs. pool-based exercise for OA and RA patients on TJA wait list showed no statistically significant difference between the groups for WOMAC pain and function at 7 and 15 weeks (**Table 4**) (7);
(4) Intervention group included six physiotherapist-led group-based sessions (two hours/week of education, exercise, and relaxation) vs. the control group that received usual care showed statistically significant difference favoring PT arm for pain interference, pain severity, at 12 and 24 weeks (**Table 5**) (8);
(5) Intervention group included manual and supervised exercise compared to placebo showed no statistically significant difference between the groups for increase in WOMAC score, distance walked, or the rate of undergoing TKA at 1-year (**Table 6)** (9);
(6) Intervention group included health education and physical exercises compared to placebo showed no statistically significant difference between the groups for quality of life, knee extension/strength, objective assessments of **knee** function including performance tests such as timed-up-and-go (**Table 7**) (10);
(7) Intervention group included high-impact intensity exercise compared to controls showed no statistically significant difference between the groups for WOMAC pain, 6-minute walk distance, but the knee extension/strength and hip abductor strength statistically significantly favored high-impact intensity group (**Table 8**) (11);
(8) Intervention group included low-impact intensity exercise compared to controls showed no statistically significant difference between the groups for WOMAC pain, WOMAC function, 5-minute walk distance, knee extension/strength, but hip abductor strength statistically significantly favored low-impact intensity group (**Table 9**) (11);
(9) Intervention group included PT compared to standard treatment showed statistically significant difference favoring PT arm for patient global assessment, quality of life, self-efficacy, but no statistically significant difference between the groups for physical activity (**Table 10**) (12);

Intervention group included pre-habilitation compared to none showed no statistically significant difference between the groups for VAS pain, or any of the KOOS subscale scores at 3 or 6 months (**Table 11**) (13).Observational studies provided additional evidence for pre-habilitation alone, pre-habilitation vs. usual care, for people with knee or hip OA, or knee or hip awaiting TKA/THA. These studies had small sample sizes and provided indirect comparisons, sometimes with lack of precision in effect estimates. Effects of physical therapy ranged from insignificant to borderline significant with small effect sizes. High-intensity exercise group seemed to have favorable outcomes compared to sedentary (**Table 12**).

Overall impression: The studies that address our question would compare the outcomes in patients randomized to undergo PT prior to arthroplasty compared to those undergoing immediate arthroplasty, but the included RCTs either did not have a surgical arm or randomized

patients on surgical waiting lists. The first were rated down for indirectness, and the latter were rated down for indirectness, imprecision (includes less than 200 patients, wide confidence intervals), and risk of bias (includes no allocation concealment or blinding, no intention to treat or drop-out analysis).

Overall Quality of Evidence: Low

Table 1: TKR plus non-surgical treatment (included 12 weeks of exercise, supervised exercise, education, dietary advice, use of insoles, and pain medication) compared to non-surgical treatment alone. 1997 Skou 2016 (5)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TKR plus exercise	exercise alone	Relative (95% CI)	Absolute (95% CI)	
Pain											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **17.1 higher (10.4 higher to 23.8 higher)**	⊕⊕◯◯ Low
KOOS											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **15.8 higher (10 higher to 21.6 higher)**	⊕⊕◯◯ Low
Timed up-and-go (sec)											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **0.9 higher (0.2 higher to 1.6 higher)**	⊕⊕◯◯ Low
20-m walk test (sec)											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **1.5 higher (0.7 higher to 2.3 higher)**	⊕⊕◯◯ Low

Activities of daily living

1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **12.9 higher (6.8 higher to 19 higher)**	⊕⊕◯◯ Low

Serious Adverse Events (SAEs)

1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	24/50 (48.0%)	6/50 (12.0%)	**RR 4.00 (1.79 to 8.94)**	**360 more per 1,000 (from 95 more to 953 more)**	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. TKR + non-surgical treatment versus non-surgical treatment, not exercise alone; no comparison of TKA vs. exercise

b. Less than 200 patients in each group

Table 2: Behavioral graded activity vs. usual care (exercise therapy)* for Hip OA. 1381 Pisters 2010 (6).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BGA	UC, for HIP OA	Relative (95% CI)	Absolute (95% CI)	
WOMAC pain (0-20), mean change at 3 months											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	26	40	-	MD **1.47 lower** (2.78 lower to 0.16 lower)	⊕⊕◯◯ Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BGA	UC, for HIP OA	Relative (95% CI)	Absolute (95% CI)	
WOMAC pain (0-20), mean change at 9 months											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	26	36	-	MD **3.06 lower** (5 lower to 1.12 lower)	⊕⊕◯◯ Low
WOMAC pain (0-20), mean change at 60 months											
1	randomised trial	not serious	not serious	serious[a]	serious[c]	none	20	31	-	MD **1.11 lower** (3.53 lower to 1.31 higher)	⊕⊕◯◯ Low
WOMAC function (0-68), mean change at 3 months											
1	randomised trial	not serious	not serious	serious[a]	serious[c]	none	25	40	-	MD **1.27 lower** (5.24 lower to 2.7 higher)	⊕⊕◯◯ Low
WOMAC function (0-68), mean change at 9 months											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	24	34	-	MD **5.17 lower** (9.95 lower to 0.39 lower)	⊕⊕◯◯ Low
WOMAC function (0-68), mean change at 60 months											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BGA	UC, for HIP OA	Relative (95% CI)	Absolute (95% CI)	
1	randomised trial	not serious	not serious	serious[a]	serious[c]	none	21	31	-	MD **3.28 lower** (10.74 lower to 4.18 higher)	⨁⨁◯◯ Low

Number of THA, 60 months

1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	6/30 (20.0%)	18/40 (45.0%)	RR 0.44 (0.20 to 0.98)	**252 fewer per 1,000** (from 360 fewer to 9 fewer)	⨁⨁◯◯ Low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

*Usual care (exercise therapy) (UC): The physical therapists in the UC group were requested to treat the patients according to the Dutch physical therapy guideline for patients with hip and/or knee OA. This guideline consists of general recommendations, emphasizing provision of information and advice, exercise therapy, and encouragement of a positive coping with the complaints. Furthermore, it is recommended to advise patients to maintain exercising at home after discharge. The treatment consisted of a maximum of 18 sessions within a period of 12 weeks. Both BGA and UC were given individually by physical therapists in primary care.

Behavioral graded activity (BGA) is a behavioral treatment integrating the concepts of operant conditioning with exercise therapy comprising booster sessions. BGA was based on the time-contingency management as described by Fordyce23 and applied by Lindström24. In this individually tailored treatment, patients' most problematic activities were gradually increased in a time-contingent way. Furthermore, the intervention included individually tailored exercises to improve impairments limiting the performance of these activities. The treatment consisted of a 12-week period with a maximum of 18 sessions, followed by five pre-set booster moments with a maximum of seven sessions (respectively in week 18, 25, 34, 42, and 55). After the 12-week treatment period, physiotherapists advised patients to maintain exercising and performing the activities at home. The additional booster sessions consisted of evaluating, motivating (stimulating exercise adherence), and repeating the main treatment message.

Explanations

a. Only data from usual care arm of interest

b. Single study

c. Single study, 95% CI includes the possibility of no difference

Table 3. Behavioral graded activity vs. usual care (exercise therapy)* for knee OA. 1381 Pisters 2010 (6).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BGA	UC, for KNEE OA	Relative (95% CI)	Absolute (95% CI)	
WOMAC pain (0-20), mean change at 3 months											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	69	74	-	MD **0.27 higher** (0.67 lower to 1.21 higher)	⊕⊕◯◯ Low
WOMAC pain (0-20), mean change at 9 months											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	61	62	-	MD **0.57 lower** (2.07 lower to 0.93 higher)	⊕⊕◯◯ Low
WOMAC pain (0-20), mean change at 60 months											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	55	47	-	MD **0.64 lower** (2.44 lower to 1.16 higher)	⊕⊕◯◯ Low
WOMAC function (0-68), mean change at 3 months											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BGA	UC, for KNEE OA	Relative (95% CI)	Absolute (95% CI)	
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	63	74	-	MD **0.31 lower** (3.43 lower to 2.81 higher)	⊕⊕◯◯ Low

WOMAC function (0-68), mean change at 9 months

1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	60	60	-	MD **0.09 higher** (4 lower to 4.18 higher)	⊕⊕◯◯ Low

WOMAC function (0-68), mean change at 60 months

1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	51	45	-	MD **3.01 lower** (8.35 lower to 2.33 higher)	⊕⊕◯◯ Low

Number of TKA, 60 months

1	randomised trial	not serious	not serious	serious[a]	serious[c]	none	9/75 (12.0%)	9/75 (12.0%)	RR 1.00 (0.42 to 2.38)	**0 fewer per 1,000** (from 70 fewer to 166 more)	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

*Usual care (exercise therapy) (UC): The physical therapists in the UC group were requested to treat the patients according to the Dutch physical therapy guideline for patients with hip and/or knee OA. This guideline consists of general recommendations, emphasizing provision of information and advice, exercise therapy, and encouragement of a positive coping with the complaints. Furthermore, it is recommended to advise patients to maintain exercising at home after discharge. The treatment consisted of a maximum of 18 sessions within a period of 12 weeks. Both BGA and UC were given individually by physical therapists in primary care

Behavioral graded activity (BGA) is a behavioral treatment integrating the concepts of operant conditioning with exercise therapy comprising booster sessions. BGA was based on the time-contingency management as described by Fordyce23 and applied by Lindström24. In this individually tailored treatment, patients' most problematic activities were gradually increased in a time-contingent way. Furthermore, the intervention included individually tailored exercises to improve impairments limiting the performance of these activities. The treatment consisted of a 12-week period with a maximum of 18 sessions, followed by five pre-set booster moments with a maximum of seven sessions (respectively in week 18, 25, 34, 42, and 55). After the 12-week treatment period, physiotherapists advised patients to maintain exercising and performing the activities at home. The additional booster sessions consisted of evaluating, motivating (stimulating exercise adherence), and repeating the main treatment message.

Explanations

a. Only data from usual care arm of interest

b. Single study, 95% CI includes the possibility of no difference

c. Single study with point estimate indicating no difference

Table 4. Land- vs. pool-based exercise* for patients with OA and RA on TJA wait list for knee or hip arthroplasty. 1359 Gill 2009 (7).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Land-based	Pool-based exercise	Relative (95% CI)	Absolute (95% CI)	
WOMAC pain, week 7											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	34	32	-	MD **0.9 lower** (2.5 lower to 0.7 higher)	⊕◯◯◯ Very low
WOMAC pain, week 15											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Land-based	Pool-based exercise	Relative (95% CI)	Absolute (95% CI)	
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	34	32	-	MD **0.3 lower** (1.71 lower to 1.11 higher)	⊕◯◯◯ Very low

WOMAC function, week 15

1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	34	32	-	MD **0.4 lower** (5.98 lower to 5.18 higher)	⊕◯◯◯ Very low

WOMAC function, week 7

1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	34	32	-	MD **3.1 lower** (8.69 lower to 2.49 higher)	⊕◯◯◯ Very low

CI: confidence interval; **MD:** mean difference

* Each 6-week program included an education session, twice-weekly exercise classes, and an occupational therapy home assessment.

Explanations

a. No intent-to-treat analysis; only indicated overall withdrawal (not withdrawal per arm) at both follow-up periods

b. Only land-based data of interest

c. Single study, 95% CI includes the possibility of no difference

Table 5. PT vs. usual care for people on TJA waiting list. 1861 Saw 2016 (8)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PT	Usual care	Relative (95% CI)	Absolute (95% CI)	
Pain severity (BPI), 24 weeks											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	35	39	-	MD **1.9 lower** (3.09 lower to 0.71 lower)	⊕◯◯◯ Very low
Pain interference (BPI), 24 weeks											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	35	39	-	MD **2.38 lower** (3.5 lower to 1.26 lower)	⊕◯◯◯ Very low
Pain severity (BPI), 12 weeks											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	35	39	-	MD **1.71 lower** (2.91 lower to 0.51 lower)	⊕◯◯◯ Very low
Pain interference (BPI), 12 weeks											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	35	39	-	MD **1.72 lower** (2.88 lower to 0.56 lower)	⊕◯◯◯ Very low

CI: confidence interval; **MD:** mean difference

Explanations

a. No allocation concealment or blinding of patients and personnel

b. Only PT data of interest

c. Single study

* 74 participants from arthroplasty waiting lists were randomly allocated to an intervention (n = 35) or control group (n = 39). The intervention included six physiotherapist-led group-based sessions (two hours/week of education, exercise, and relaxation). The control group received usual care. Data collection was conducted by blinded physiotherapists at baseline, week six, 12 and month six. The primary outcome was pain, measured by the Brief Pain Inventory.

Table 6: Manual and supervised exercise compared to Usual Care. 1002 Deyle 2000 (9).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Manual and supervised exercise	Usual Care	Relative (95% CI)	Absolute (95% CI)	
Undergone TKA after 1 year											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	2/42 (4.8%)	8/41 (19.5%)	**RR 0.24 (0.06 to 1.08)**	**148 fewer per 1,000 (from 183 fewer to 16 more)**	⊕⊕◯◯ Low
Average decrease in distance walked from 8 weeks to 1 year											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	29	22	-	MD **14.3 higher (33.04 lower to 61.64 higher)**	⊕⊕◯◯ Low
Average increase in WOMAC scores from 8 weeks to 1 year											

1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	29	22	-	MD **99.8 higher (118.46 lower to 318.06 higher)**	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Compares to Usual Care

b. Less than 200 patients in each group

Table 7. Health education and physical exercise program* for knee or hip OA patients not on a TJA waiting list compared to placebo. 1013 Hopman-Rock 2020 (10)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Health education and physical exercises	Placebo	Relative (95% CI)	Absolute (95% CI)	
IRGL pain scale (6-25), 6 months											
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **0.1 lower (1.87 lower to 1.67 higher)**	⊕⊕◯◯ Low
VAS pain intolerance (1-100), 6 months											
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **3.2 lower (12.26 lower to 5.86 higher)**	⊕⊕◯◯ Low

VAS quality of life (0-100), 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **0.9 lower (8.94 lower to 7.14 higher)**	⊕⊕◯◯ Low

Quality of life scale (7-39), 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **0.8 higher (0.84 lower to 2.44 higher)**	⊕⊕◯◯ Low

Knee extension/strength right, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **23.2 higher (11.87 lower to 58.27 higher)**	⊕⊕◯◯ Low

Knee extension/strength left, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **3.2 higher (28.71 lower to 35.11 higher)**	⊕⊕◯◯ Low

20 m walking test, s, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **0.9 lower (2.94 lower to 1.14 higher)**	⊕⊕◯◯ Low

Timed up-and-go, s, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **1.1 lower (2.51 lower to 0.31 higher)**	⊕⊕◯◯ Low

Stair climbing up, s, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **1.1 lower (2.87 lower to 0.67 higher)**	⊕⊕◯◯ Low

Stair climbing down, s, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **1.7 lower (4.45 lower to 1.05 higher)**	⊕⊕◯◯ Low

Toe reaching right, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **0.2 lower (0.61 lower to 0.21 higher)**	⊕⊕◯◯ Low

Toe reaching left, 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **0.5 lower (0.92 lower to 0.08 lower)**	⊕⊕◯◯ Low

Self-efficacy (0-100), 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	45	35	-	MD **3.4 lower (11.19 lower to 4.39 higher)**	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference

***** The program consisted of 6 weekly sessions of 2 hours and included health education by a peer and physical exercises taught by a physical therapist.

Explanations

a. No allocation concealment and blinding of patients and personnel, high-drop-out rate (12.5%)

b. Wide CI and less than 200 patients in each group

Table 8. High-impact intensity exercise compared to controls for people with knee OA. 959 Mesier 2021 (11).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High-impact intensity exercise	Controls	Relative (95% CI)	Absolute (95% CI)	
Mean change WOMAC pain, (0-20)											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	108	99	-	MD **0.3 higher (0.54 lower to 1.14 higher)**	⊕⊕⊕◯ Moderate
Mean change WOMAC function (0-68)											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	88	88	-	MD **1.4 higher (1.3 lower to 4.1 higher)**	⊕⊕⊕◯ Moderate
Mean change knee joint compressive force, Ne											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	65	63	-	MD **73 lower (281.07 lower to 135.07 higher)**	⊕⊕⊕◯ Moderate
Mean change 6-Minute walk distance,m											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	73	67	-	MD **7 lower (32 lower to 18 higher)**	⊕⊕⊕◯ Moderate
Mean change knee extensor strength,Nm											

1	randomised trials	not serious	not serious	not serious	serious[a]	none	79	75	-	MD **10 higher (3.8 higher to 16.2 higher)**	⊕⊕⊕◯ Moderate

Hip abductor strength,Nm

1	randomised trials	not serious	not serious	not serious	serious[a]	none	74	73	-	MD **5.1 higher (0.8 higher to 9.4 higher)**	⊕⊕⊕◯ Moderate

Thigh muscle volume,cm3

1	randomised trials	not serious	not serious	not serious	serious[a]	none	73	75	-	MD **2 higher (20 lower to 24 higher)**	⊕⊕⊕◯ Moderate

Joint space width, mm

1	randomised trials	not serious	not serious	not serious	serious[a]	none	83	81	-	MD **0.1 higher (0.1 lower to 0.3 higher)**	⊕⊕⊕◯ Moderate

CI: confidence interval; **MD:** mean difference

Explanations

a. Wide CI and less than 200 patients in each group

*The high-intensity group performed 3 sets of each exercise beginning at 75% of 1RM with 8 repetitions per set for 2 weeks, progressing to 80% of the 1RM with 8 repetitions per set for weeks 3 and 4, 85% of the 1RM with 6 repetitions per set for weeks 5 and 6, and 90% of the 1RM with 4 repetitions per set for weeks 7 and 8. Week 9 was a taper week with alternate exercises and establishing new 1RMs for each exercise. This 9-week block was repeated using the new 1RM values. The low-intensity group used the same 9-week block pattern but performed 3 sets of 15 repetitions at 30% to 40% 1RM of the exercises described above. The target workload per total volume performed during these 9-week cycles was the same regardless of whether the participant was assigned to the high-intensity or low-intensity group. To improve adherence and retention, interventionists were trained in standardized behavioral techniques developed in a social cognitive framework.

Attention Control Group: Participants attended 60-minute group workshops biweekly for the first 6 months and monthly thereafter (total of 24 sessions over 18 months). Details of the control intervention are included in Supplement 1 and the design publication.

Table 9. Low-impact intensity exercise compared to controls for people with knee osteoarthritis (OA) with K-L grade 2-3 and with self-reported disability due to knee osteoarthritis. 959 Mesier 2021 (11).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low-impact intensity exercise	Controls	Relative (95% CI)	Absolute (95% CI)	
Mean change WOMAC pain, (0-20)											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	104	99	-	MD **0.6 lower (1.45 lower to 0.25 higher)**	⨁⨁⨁◯ Moderate
Mean change knee joint compressive force, Ne											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	65	63	-	MD **46 lower (254.07 lower to 162.07 higher)**	⨁⨁⨁◯ Moderate
Mean change WOMAC function (0-68)											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	89	88	-	MD **1.5 lower (4.19 lower to 1.19 higher)**	⨁⨁⨁◯ Moderate
Mean change 6-Minute walk distance,m											
1	randomised trials	not serious	not serious	not serious	serious[a]	none	73	67	-	MD **1 lower (26 lower to 24 higher)**	⨁⨁⨁◯ Moderate
Mean change knee extensor strength,Nm											

1	randomised trials	not serious	not serious	not serious	serious[a]	none	79	75	-	MD **4.7 higher (1.5 lower to 10.9 higher)**	⊕⊕⊕◯ Moderate

Hip abductor strength,Nm

1	randomised trials	not serious	not serious	not serious	serious[a]	none	77	73	-	MD **5.1 higher (0.84 higher to 9.36 higher)**	⊕⊕⊕◯ Moderate

Thigh muscle volume,cm3

1	randomised trials	not serious	not serious	not serious	serious[a]	none	76	75	-	MD **9 higher (12.78 lower to 30.78 higher)**	⊕⊕⊕◯ Moderate

Joint space width, mm

1	randomised trials	not serious	not serious	not serious	serious[a]	none	84	81	-	MD **0 (0.2 lower to 0.2 higher)**	⊕⊕⊕◯ Moderate

CI: confidence interval; **MD:** mean difference

Explanations

a. Wide CI and less than 200 patients in each group

Table 10. PT compared to standard treatment for people with knee osteoarthritis (OA) with K-L grade 2-3 and with self-reported disability due to knee osteoarthritis. 955 Johnson 2018 (12).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PT	Standard	Relative (95% CI)	Absolute (95% CI)	

Physical activity, sedentary, mean change in minutes at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	112	28	-	MD **9 higher (11.67 lower to 29.67 higher)**	⊕⊕◯◯ Low

Physical activity, low, mean change in minutes at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	112	28	-	MD **3 higher (10.76 lower to 16.76 higher)**	⊕⊕◯◯ Low

Physical activity, moderate-vigorous, mean change in minutes at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	112	28	-	MD **3.8 higher (5.26 lower to 12.86 higher)**	⊕⊕◯◯ Low

Patient global assessment (VAS/pain), mean change in scores at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	169	49	-	MD **13 lower (20.07 lower to 5.93 lower)**	⊕⊕◯◯ Low

Quality of life (EQ-5D), mean change in scores at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	168	49	-	MD **0.17 higher (0.11 higher to 0.23 higher)**	⊕⊕◯◯ Low

Selfefficacy (ASES/pain), mean change in scores at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	168	49	-	MD **7 higher (1.29 higher to 12.71 higher)**	⊕⊕◯◯ Low

Selfefficacy (ASES/other), mean change in scores at 3 months from baseline

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	168	49	-	MD **5 higher (0.48 higher to 9.52 higher)**	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference

Explanations

a. Non-blinded non-randomized prospective controlled study

b. Wide CI and less than 200 patients in each group

Table 11. Prehabilitation compared to none. 931 Aytekin 2019 (13).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prehabilitation	None	Relative (95% CI)	Absolute (95% CI)	
VA rest 3 months											
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **0.1 lower (0.72 lower to 0.52 higher)**	⊕⊕◯◯ Low
VA rest 6 months											
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **0.4 lower (0.99 lower to 0.19 higher)**	⊕⊕◯◯ Low
VA activity 3 months											

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **0.9 lower (2.1 lower to 0.3 higher)**	⊕⊕◯◯ Low

VA activity 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **0.8 lower (1.94 lower to 0.34 higher)**	⊕⊕◯◯ Low

KOOS 3 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **5.7 lower (13.76 lower to 2.36 higher)**	⊕⊕◯◯ Low

KOOS 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **3.3 lower (11.21 lower to 4.61 higher)**	⊕⊕◯◯ Low

KOOS ADL 3 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **6.5 lower (14.8 lower to 1.8 higher)**	⊕⊕◯◯ Low

KOOS ADL 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **3.9 lower (12.58 lower to 4.78 higher)**	⊕⊕◯◯ Low

KOOS QOL 3 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **5.7 lower (18.03 lower to 6.63 higher)**	⊕⊕◯◯ Low

KOOS QOL 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **3.3 higher (8.02 lower to 14.62 higher)**	⊕⊕◯◯ Low

KOOS pain 3 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **3.3 lower (11.2 lower to 4.6 higher)**	⊕⊕◯◯ Low

KOOS pain 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **4.8 lower (12.21 lower to 2.61 higher)**	⊕⊕◯◯ Low

KOOS sports 3 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **5.7 lower (17.45 lower to 6.05 higher)**	⊕⊕◯◯ Low

KOOS sports 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **3.3 lower (15.03 lower to 8.43 higher)**	⊕⊕◯◯ Low

KOOS stiffness 3 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **9.3 lower (17.28 lower to 1.32 lower)**	⊕⊕◯◯ Low

KOOS stiffness 6 months

1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	21	23	-	MD **4.3 lower (11.73 lower to 3.13 higher)**	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference

Explanations

a. Non-blinded non-randomized prospective controlled study

b. Wide CI and less than 200 patients in each group

Table 12: Exercise compared to Control (no exercise). 2225 Vasileiadis 2022.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise	Control	Relative (95% CI)	Absolute (95% CI)	
WOMAC, 12 weeks											
1	observational studies	not serious	not serious	not serious	serious[a]	none	44	44	-	MD **5.11 lower** (10.55 lower to 0.33 higher)	⊕◯◯◯ Very low
SF-36, 12 weeks											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise	Control	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[a]	none	44	44	-	MD **5.19 higher** (0.23 lower to 10.61 higher)	⊕◯◯◯ Very low

KOOS, 12 weeks

1	observational studies	not serious	not serious	not serious	serious[a]	none	44	44	-	MD **2.58 higher** (3.07 lower to 8.23 higher)	⊕◯◯◯ Very low

20 meters walk test, 12 weeks

1	observational studies	not serious	not serious	not serious	serious[a]	none	44	44	-	MD **0.21 higher** (0.33 lower to 0.75 higher)	⊕◯◯◯ Very low

30-sec chair stand test, 12 weeks

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exercise	Control	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[a]	none	44	44	-	MD **0.75 higher** (0.28 higher to 1.22 higher)	⊕◯◯◯ Very low

Quadriceps strength, 12 weeks

1	observational studies	not serious	not serious	not serious	serious[a]	none	44	44	-	MD **0.08 higher** (0.04 higher to 0.12 higher)	⊕◯◯◯ Very low

CI: confidence interval; **MD:** mean difference

Explanations

a. Wide CI crosses no-effect and significant effect thresholds and less than 200 patients in each group

Table 13. Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan for PICO 2

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results (if not reported indicate so)

1002 Deyle 2000 (9)	RCT	Follow-up at 4 weeks, 8 weeks, 1 year	83 patients with osteoarthritis of the knee referred by physicians to physical therapy	Description of PT: Type, duration, frequency A combination of manual physical therapy and supervised exercise (n = 42; 15 men and 27 women [mean age, 60+-11 years]) or placebo (n = 41; 19 men and 22 women [mean age, 62+-10 years])	Patient-reported outcome scores at X months: PT % v. TJA % (p value): **WOMAC** Treatment group at baseline 1046.7 (891.4±1202.0), week 4: 505.2 (438.0±572.4), week 8: 462.4 (312.9±611.9), Placebo group at baseline: 1093.5 (931.1±1255.9), week 4: 921.2 (730.8±1112.1), week 8: 934.3 (720.8±1147.8). **Distance walked in 6 minutes**: Mean distance walked in 6 minutes (95%CI), Treatment group at baseline 431.0 (390.0±472.0), week 4: 484.0 (442.7±525.3), week 8: 487.4 (447.6±527.2), Placebo group at baseline 402.9 (368.8±437.0), week 4: 402.1 (359.9±444.3), week 8: 409.7 (366.0±453.4) At 4 weeks, average WOMAC scores were 51.8% lower in the treatment group (P=0.05) and 15.8% lower in the placebo group (P=0.05). At 8 weeks, the reduction in WOMAC scores from baseline was 55.8% in the treatment group (P=0.05) and 14.6% in the placebo group (P value not significant). After controlling for potential confounding variables with multiple regression analysis, on average, 8-week WOMAC scores were 599 mm (CI, 197 to 1002 mm) better in the treatment group than in the placebo group and the average distance walked in 6 minutes was 170 m (CI, 71 to 270 m) more. Despite increase from 8 weeks to 1 year, compared with scores collected at baseline, average WOMAC scores in the treatment group were still reduced at 1 year by 371.9 mm (CI, 211.5 to 532.3 mm).

					*The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
955 Jonsson 2018 (12)	Controlled trial	12 months	Number of patients who had PT: 195 Number of patients who underwent TJA (specify TKA or THA or both): 22 both PT cohort (n=195) 64% Female Mean Age 60 Reference cohort (n=69) 58% Female Mean Age 66	Description of PT: Type, duration, frequency Intervention group: education and supervised exercise 2x/wk for 6 weeks (BOA protocol). Program tailored to patient needs. No strength training. Reference group: standard care, no lifestyle change Patient reported outcomes were assessed at baseline, 3 months, and at 12 months for the intervention group only.	1. Patient-reported outcome scores at baseline (median, IQR): PT v. standard therapy a. Physical activity (daily minutes) **Sedentary**: 562 (523-605) vs 572 (505-599) **Low**: 180 (150-214) vs 169 (130-218) **Moderate-vigorous**: 34 (22-52) vs 20 (11-30) b. Patient global assessment (VAS/pain): 51 (36-62) vs 60 (50-70) c. Health quality of life (EQ-5D): 0.725 (0.62-0.796) vs 0.656 (0.159-0.727) d. Self-efficacy (ASES/pain): 60 (46-76) vs 46 (38-62) e. Self-efficacy (ASES/other): 68 (53-80) vs 61 (48-70) 2. Mean difference in outcome scores at 3 months from baseline (mean, 95%CI, p value): mean change (95% CI) PT vs. mean change (95% CI) standard therapy a. Physical activity (daily minutes) **Sedentary**: -2 (-12-8) vs -11 (-30-8); **diff**. -9 (31-12), p=0.401 **Low**: -8 (-15 to -2) vs -11 (-24-2); **diff**. -3 (-17-12), p=0.707 **Moderate-vigorous**: 4 (-0.6-8) vs 0.2 (-8-9); diff. -4 (-14-6), p=0.460 b. Patient global assessment (VAS/pain): -9 (-13 to -6) vs 4 (-2-9); **diff**. 13 (7-19), p<0.001

					c. QOL (EQ-5D): 0.03 (-0.004-0.07) vs -0.14 (-0.19 to -0.08); **diff**. -0.17 (-0.24 to -0.1), p<0.001 d. Self-efficacy (ASES/pain): 5 (2-8) vs -2 (-7-3); **diff**. -7(-13 to -2), p=0.01 e. Self-efficacy (ASES/other): 2 (-0.3-5) vs -3 (-7-1); **diff**. -5(-10 to -0.3), p=0.04 *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1849 Williamson 2007 (14)	Assessor-blind, randomized controlled trial	Outcomes measured at 12 weeks prior to surgery	Patients awaiting knee arthroplasty.	19 patients received PT; 26 controls.	Changes in means as compared to control group, mean (CI): 1. OKS -2 (5.04 to1.03); 2. 50-minute walk test (s) -5.66(13.93 to 2.61); 3. VAS (cm) -0.88(-1.72 to –0.04); 4. WOMAC score -3(-9.08 to 3.13); 5. HAD score anxiety 0.54(-1.11 to 2.19); 6. HAD score depression -0.38(-1.71 to 0.95) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1033 Dash 2015 (15)	RCT	3 months	2054 (72%) patients had OA (male:female-1.9:1) with mean age of 63 (SD 8). Of 2054 patients, 226 patients were randomly	Group 1 (113 patients) with KOA was assigned a 12-week hip strengthening exercise program and group 2 (113 patients) was assigned a 12-week leg strengthening exercise program.	Posttherapeutic (n=226) Group 1 (hipex), n=113, mean(range): WOMAC 30 (26-38), VAS 2(0-4), Friedman-WymanScore(%) good 22, fair 73, poor 5, 30-SecondTimed ChairTest, Range 8-15, Group 2 (legex), n=113, mean(range): WOMAC 31(24-36), VAS 2(0-4), Friedman-WymanScore(%) good 24, fair 71, poor 5, 30-SecondTimed ChairTest, Range 9-15

			selected for therapeutic study.	274 patients had arthroplasty	Surgical population (n=274) Postoperative mean(range): WOMAC 28 (22-32), VAS 2(0-4), Friedman-WymanScore(%) good 20, fair 75, poor 5, Walking ability IV 65, III 29, II 4, I 2; 30-SecondTimed ChairTest, Range 8-13
705 Kolisek 2018 (16)	RCT	3 months	Patients presenting with degenerative OA of the knee, where surgery is not yet recommended. 16 patients had exercise only, 19 had brace only, 14 had exercise+brace.	16 patients had exercise	Changes from baseline at 12 weeks in Exercise group: 1. VAS pain: -17.96; 2. Lower Extremity Function Scale: 12.86; 3. MCS 3.26; 4. PCS 3.89 *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1036 Czyzewska 2014 (17)	Non-randomized trial	1 year prior to TJR	45 patients admitted for total hip replacement (THR) surgery	27 patients received PT, 18 controls	Average values after 1 year: 1. HOOS activity daily living: PT group 39.98, non-PT group 26.47, p=0.024 2. SF-36 vitality: PT group 46.48, non-PT group 35.55, p=0.024 3. SF-36 mental health: PT group 60.59, non-PT group 46.89, p= 0.023 4. SF-36 social functioning: PT group 48.15, non-PT group 31.94, p=0.044 5. Difference: functional limb – length: PT group 2.00, non-PT group –0.67, p=0.005; 6. Difference: active internal rotation rom: PT group 11.48, non-PT group 4.16, p=0.017; 7. Difference: passive internal rotation rom: PT group 12.22, non-PT group 3.61, p=0.007

1571 Gwynne-Jones 2020 (18)	Observational study	2012-2014	OA patients awaiting 186 TKR and 151 THR surgery	All patients received outpatient physiotherapy OA program, occupational therapy, dietitian advice, or orthotic management	Health-related quality of life scales: 1. Oxford Hip/Knee Score: Knee group 0.77(0.58-1.01), Hip group 0.74(0.63-0.86) 2. SF-12 PCS score Knee group 0.79(0.64-0.98), Hip group 1.01(0.89-1.15); 3. SF-12 MCS score: Knee group 0.98(0.85-1.13), Hip group 1.14(1.03-1.26)

PICO 3: In our defined population, what is the relative impact of NSAIDs versus arthroplasty in patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:

A systematic review of the literature identified one study directly addressing the question, therefore, we loosened our inclusion criteria to include other studies including those that compared various NSAIDs to each other that provided indirect evidence. The overall certainty of evidence was very low.

In two randomized trials reported as a single study by Skou et al. (19), the authors compared 2-year outcomes of total knee arthroplasty (TKA) followed by non-surgical treatment to that of non-surgical treatment alone and outcomes of the same non-surgical treatment to that of written advice (**Table 1**). In two randomized trials, 200 (mean age 66) adults with moderate to severe knee osteoarthritis (OA), 100 eligible for TKA and 100 not eligible for TKA, were randomized to TKA followed by non-surgical treatment, non-surgical treatment alone, or written advice. Non-surgical treatment consisted of 12 weeks of exercise, patient education, and insoles, while weight loss and/or pain medication were prescribed if indicated. In the two groups for patients eligible for TKA, 67% in TKA plus non-surgical treatment and 58% in the non-surgical treatment group alone were treated with NSAIDs. The primary outcome was the mean score of the Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales, including pain, symptoms, activities of daily living (ADL), and quality of life (QOL). Patients randomized to TKA plus non-surgical treatment had greater improvements than patients randomized to nonsurgical treatment alone (difference of 18.3 points (95% CI; 11.3 to 25.3)), who in turn improved more than patients randomized to written advice (difference of 7.0 points (95% CI; 0.4 to 13.5)).

One knee OA RCT by Adams (20) that could not be abstracted into Revman (reason: no direct comparison), compared the mean improvement with NSAIDs, hyaluronic acid injections+NSAIDs, or hyaluronic acid injections alone were all statistically significantly improved from baseline in patient reported outcomes at 12 weeks (**Table 2**). While at 12 weeks all groups showed statistically significant improvements from baseline but

did not differ from each other. A statistical test for equivalence, the q-statistic, demonstrated that viscosupplementation with hylan G-F 20 was at least as good or better than continuous NSAID therapy for all outcome measurements except activity restriction. At 26 weeks both groups receiving hylan G-F 20 were significantly better than the group receiving NSAIDs alone.

Other studies compared various NSAIDs to each other in people with knee OA (Table 3) (21) and people with hip OA (Tables 4 and 5) (22, 23). Therefore, these provide indirect evidence for this PICO.

Overall Impression: The studies that would directly address our question would compare outcomes in patients receiving NSAIDs prior to arthroplasty vs. immediate arthroplasty. None of the included studies made this direct comparison, so all were graded down for indirectness. Other included studies did not include a surgical group. Studies were graded down for indirectness and imprecision (low numbers, wide confidence intervals) or risk of bias (no intention to treat analysis).

Overall Quality of Evidence: Very low

Table 1: TKA followed by non-surgical treatment compared to non-surgical treatment alone. 1988 Skou 2018 (19).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TKA followed by non-surgical treatment	Non-surgical treatment alone	Relative (95% CI)	Absolute (95% CI)	
KOOS											
1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **18.5 higher (9.45 higher to 27.55 higher)**	⨁⨁◯◯ Low
Timed up-and-go test(s)											

1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **1.6 lower (2.5 lower to 0.7 lower)**	⊕⊕◯◯ Low

20-minutes walk test

1	randomised trials	not serious	not serious	serious[a]	serious[b]	none	50	50	-	MD **2.2 lower (3.31 lower to 1.09 lower)**	⊕⊕◯◯ Low

CI: confidence interval; **MD:** mean difference

Explanations

a. Indirect comparison

b. Less than 200 patients in each group

Table 2: Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan.

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results (if not reported indicate so)
1834, Adams 1995 (20)	Multicenter RCT for 26 weeks, no placebo injection. Placebo group was effectively	All received 26 week telephone interview (mean and	Number of patients who had Viscosupplementation Injections: 61	3 groups NSAID with three weekly arthrocenteses (mean age 63)	Adverse effects not reported. Does not compare TJA vs viscosupplementation. NO TJA performed Patient-reported outcome scores at 3 months and 26 weeks:

	an aspiration group.	range not reported)	Number of patients who underwent TJA (specify TKA or THA or both): 0 % Female: 65% Mean Age: 61 Additional details: Men (35%) and women (65%) aged 18-75 with osteoarthritis of the knee (Kellgren Lawrence 1-3 in </= 2 compartments and not 3 or more in patellofemoral joint).	2.0mL hylan G-F 20 intra-articular injections (mean age 61) NSAID with three weekly 2.0 mL G-F 20 intra-articular injections (mean age 61)	Purely survey data reported. No KOOS/HOOS/WOMAC At 3 months: 1. Mean improvement with NSAIDs, hylan+NSAIDs or Hylan alone were all statistically significantly improved in terms of VAS ($p<0.01$), but not different from each other. 2. Mean improvement in VAS pain (0-100 point scale) with motion were all statistically significantly improved (19 NSAID, 23 Hylan, 26 Hylan +NSAID), 3. pain with rest (9 NSAID, 19 Hylan, 12 Hylan + NSAID), 4. pain at night (13 NSAID, 21 Hylan, 10 Hylan + NSAID), restriction of activity (14 NSAID, 13 Hylan, 14 Hylan+ NSAID), 5. overall assessment of pain (19 NSAID, 24 Hylan, 26 Hylan + NSAID) **At 26 weeks** the hylan G-F 20 + NSAID group was statistically superior to the NSAID only group. The hylan +NSAID group was statistically superior to the Hylan only group in pain at rest and night pain. These demonstrate mean VAS scores as follows: 1. pain with motion (52 NSAID, 40 Hylan, 37 Hylan +NSAID), 2. pain with rest (22 NSAID, 25 Hylan, 11 Hylan + NSAID), 3. pain at night (28 NSAID, 25 Hylan, 9 Hylan + NSAID), restriction of activity (52 NSAID, 41 Hylan, 38 Hylan+ NSAID), 4. overall assessment of pain (52 NSAID, 47 Hylan, 37 Hylan + NSAID) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.

Table 3: Licofelone (NSAID) compared to naproxen for knee OA. 1821 Raynauld 2011 (21).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Licofelone	Naproxen	Relative (95% CI)	Absolute (95% CI)	
TKA, 2 years											
1	Post-hoc analysis (data from a 2-year clinical trial (RCT) comparing licofelone vs. naproxen)	not serious	not serious	serious[a]	serious[b]	none	7/18 (38.9%)	11/18 (61.1%)	**RR 0.64** (0.32 to 1.26)	**220 fewer per 1,000** (from 416 fewer to 159 more)	⊕⊕◯◯ Low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Indirect comparison

b. Single study with 95% CI including the possibility of no difference

Table 4: **NSAIDS (Celecoxib vs Diclofenac) for Hip OA. 535 Emery 2008 (22).**

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Celecoxib	Diclofenac	Relative (95% CI)	Absolute (95% CI)	
Global assessment of arthritis pain on walking (VAS, mm), week 6, mean change from baseline											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	69	72	-	MD **15 higher** (6.64 higher to 23.36 higher)	⊕⊕◯◯ Low
Arthritis pain on walking (VAS, mm), week 12, mean change from baseline											
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	50	48	-	MD **13 higher** (3.11 higher to 22.89 higher)	⊕⊕◯◯ Low
Death, 29-day post study completion, medication partially responsible											
1	randomized trial	not serious	not serious	serious[a]	serious[b]	none	1/125 (0.8%)	0/123 (0.0%)	**RR 2.95** (0.12 to 71.78)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕◯◯ Low
Infections and infestations, week 12											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Celecoxib	Diclofenac	Relative (95% CI)	Absolute (95% CI)	
1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	14/125 (11.2%)	19/123 (15.4%)	**RR 0.73** (0.38 to 1.38)	**42 fewer per 1,000** (from 96 fewer to 59 more)	⨁⨁◯◯ Low

Treatment-related complications, week 12

1	randomised trial	not serious	not serious	serious[a]	serious[b]	none	40/125 (32.0%)	31/123 (25.2%)	**RR 1.27** (0.85 to 1.89)	**68 more per 1,000** (from 38 fewer to 224 more)	⨁⨁◯◯ Low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Indirect comparison

b. Single study, 95% CI includes the possibility of no difference

Table 5: Piroxicam vs. Naproxen for OA patients awaiting THR. 1651 Alho 1988 (23).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Piroxicam (20 mg/day)	Naproxen (750 mg/day)	Relative (95% CI)	Absolute (95% CI)	
Pain (modified Harris hip score), mean change at 1 month											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	118	115	-	MD **1.7 lower** (3.42 lower to 0.02 higher)	⊕◯◯◯ Very Low
Pain (modified Harris hip score), mean change at 2 to 5 months											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	109	100	-	MD **1.9 lower** (3.96 lower to 0.16 higher)	⊕◯◯◯ Very Low
Adverse events, 1 month											
1	randomised trial	serious[a]	not serious	serious[b]	serious[c]	none	27/118 (22.9%)	39/115 (33.9%)	**RR 0.67** (0.44 to 1.02)	**112 fewer per 1,000** (from 190 fewer to 7 more)	⊕◯◯◯ Very Low
Adverse events, 2 to 5 months											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Piroxicam (20 mg/day)	Naproxen (750 mg/day)	Relative (95% CI)	Absolute (95% CI)	
1	randomised trial	serious[a]	not serious	serious[b]	Serious[c]	none	25/109 (22.9%)	23/100 (23.0%)	**RR 1.00** (0.61 to 1.64)	**0 fewer per 1,000** (from 90 fewer to 147 more)	⨁⨁◯◯ Low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. No intent-to-treat analysis (27 individuals discontinued before 1st follow up, and 21 additional individuals discontinued before 2nd follow up; N per arm not reported)

b. indirect comparison

c. Single study, 95% CI includes the possibility of no difference

PICO 4: In our defined population, what is the relative impact of braces/ambulatory aides versus arthroplasty on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:

A systematic review of the literature did not identify any evidence that directly answered this PICO question;, therefore, we loosened our inclusion criteria to include other studies evaluating braces and ambulatory aides that provided indirect evidence. No study directly addressed our question by comparing outcomes after a delay for bracing vs. proceeding directly to arthroplasty, and none compared bracing directly to surgery. There were five studies overall, three randomized controlled trials and two observational studies. The overall certainty of evidence was very low due to indirectness.

The results from the five studies included suggested that bracing was probably beneficial for pain relief and possibly beneficial in some functional measures. The randomized controlled trial by Cherian et al. (24) was rated as very low quality due to its indirectness, bias, not blinded, and imprecision due to small numbers. The results from this study showed an improvement in multiple outcomes in the bracing group, but numbers overall were small and functional improvements varied over multiple tests. For instance, muscle strength improved significantly in the brace group, and although timed up-and-go improved significantly, stair climb did not. The randomized controlled trial by Brower et al. (25) included 57 and 60 patients per group, and the randomized controlled trial by Kolisek et al. (16) included 19 patients only and were of very low quality due to indirectness. No direct comparison to arthroplasty was made. Mintzlaff (prospective cohort (26)) and Morgan (retrospective case series (27)) showed minimal benefits of bracing- in Morgan as a co-variate in their analysis and not as a primary intervention. Both were graded down to very low quality due to indirectness.

Overall impression: These 5 studies provide very low certainty evidence for our question as none examined outcomes comparing delay for bracing/ambulatory aides vs. proceeding to arthroplasty, or simply show an association with outcomes such as pain relief and improvement in function. The quality of evidence was therefore rated down for imprecision (small numbers), indirectness, and risk of bias (no blinding).

Overall Quality of Evidence: Very low

Table 1: Brace compared to standard care. 1888 Cherian 2015 (24)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Brace	Standard care	Relative (95% CI)	Absolute	

										(95% CI)	
Strength Change quadriceps at 90 days											
1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **11.65 higher (4.37 higher to 18.93 higher)**	⊕◯◯◯ Very Low
Strength Change hamstrings at 90 days											
1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **5.9 higher (1.57 higher to 10.23 higher)**	⊕◯◯◯ Very Low
Timed up-and-go											
1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **2.3 higher (0.7 higher to 3.9 higher)**	⊕◯◯◯ Very Low
Timed stair climb											
1	randomized trials	serious[a]	not serious	serious	serious[a]	none	26	26	-	MD **6.1 higher (1.19 lower to 13.39 higher)**	⊕◯◯◯ Very Low

6-inch step

1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **8.8 higher (4.58 lower to 22.18 higher)**	⊕◯◯◯ Very Low

2-minute walk

1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **16.3 higher (39.18 lower to 71.78 higher)**	⊕◯◯◯ Very Low

VAS pain score

1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **1.8 higher (0.36 higher to 3.24 higher)**	⊕◯◯◯ Very Low

SF-36 mental

1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **6.3 lower (17.41 lower to 4.81 higher)**	⊕◯◯◯ Very Low

SF-36 functional

1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **3.8 lower (15.3 lower to 7.7 higher)**	⊕◯◯◯ Very Low

Lower extremity functional scale

1	randomized trials	serious[a]	not serious	serious	serious[b]	none	26	26	-	MD **4.8 higher (2.48 lower to 12.08 higher)**	⊕◯◯◯ Very Low

CI: confidence interval; **MD:** mean difference

Explanations

a. Blinding was not done for patients, personnel, and assessors

b. Less than 200 patients in each group

Table 2. Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan for PICO 4.

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results (if not reported indicate so)

2076 Minzlaff, 2015 (26)	Prospective cohort	1 year – but they do not give range or loss to follow-up numbers	57 patients with symptomatic varus malalignment	Patients were treated with valgus producing unloading knee brace for 6-8 weeks. Pain monitored using VAS.	Mean VAS score decreased from 6.7 (SD 1.6) to 2.5 points (SD 1.7) p<0.001 following brace test. *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1224 Morgan, 2015 (27)	Case series Retrospective	6 months (range not reported)	Number of patients who had Ambulatory Aides or Braces: 110/207 Number of patients who underwent TJA (specify TKA or THA or both) 57% Female Mean Age 65	Description of Ambulatory Aides or Braces: Type, duration, frequency Non-customized single-hinged medial off-loading knee brace (V/Q OrthoCare)	Patient-reported outcome scores at 6 months: BRACES (outcome: regression parameter for pain [10-point scale]) -- grade 2 OA: 0.94 (p= 0.25) -- grade 3 OA: 0.3 (p=0.67) -- grade 4 OA: 1.81 (p=0.1) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.

628 Brouwer 2006 (25)	RCT	Follow-up at 3, 6, and 12 months	117 patients with unicompartmental OA of the knee. Female 58 (50%)	Intervention group (n=60) comprising conservative treatment with additional brace treatment and a control group (n=57) comprising conservative treatment alone	Patient-reported outcome scores: **Differences between the intervention and control groups:** **3 months follow-up**: Pain severity (VAS,0-10): -0.73(CI -1.62;0.16), p-value 0.3; Knee function (HSS,0-100): 3.5 (CI -0.24;7.24), p-value 0.3; Walking distance (km): 1.21(CI 0.12;2.28), p-value 0.3; Quality of life (EQ-5D,0-1): 0.03 (CI -0.05;0.12), p-value 0.1 **6 months follow-up:** Pain severity (VAS,0-10): -0.58 (CI -1.48;0.32), p-value 0.3; Knee function (HSS,0-100): 3.2 (CI -0.58;6,98), p-value 0.3; Walking distance (km): 0.79 (CI -0.40;1.98), p-value 0.2; Quality of life (EQ-5D,0-1): 0.01 (CI -0.08;0.10), p-value 0.01 **12 months follow-up:** Pain severity (VAS,0-10): -0.81 (CI -1.76;0.14), p-value 0.4; Knee function (HSS,0-100): 3.0 (CI -1.05;7.05), p-value 0.3; Walking distance (km): 1.34 (CI 0.05;2.63), p-value 0.4; Quality of life (EQ-5D,0-1): 0.01 (CI -0.08;0.10), p-value 0.0 **Overall:** Pain severity (VAS,0-10): -0.63 (CI -1.38;0.12), p-value 0.3; Knee function (HSS,0-100): 3.0 (CI -0.41;6.41), p-value 0.3; Walking distance (km): 1.25 (CI 0.15;2.35), p-value 0.4; Quality of life (EQ-5D,0-1): 0.02 (CI -0.05;0.09), p-value 0.1 **Explorative subgroup analyses** showed better outcomes in patients with severe OA (n=43) for pain severity (estimate VAS 1.31; P=0.10) compared to the effect of the brace in patients with mild OA (n=74) (estimate VAS 0.21; P=0.65), as well for in patients younger than 60 years (n=60) for knee function (estimate HSS 3.38; P=0.13) compared to the effect of the brace inpatients aged 60 years and older (n=57) (estimateHSS2.48;P=0.38).

					*The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
705 Kolisek 2018 (16)	RCT	3 months	Patients presenting with degenerative OA of the knee, where surgery is not yet recommended. 16 patients had exercise only, 19 had brace only, 14 had exercise+brace.	19 patients had braces only	Changes from baseline at 12 weeks in Braces group: VAS pain: -42.6 Lower Extremity Function Scale: 9.0 MCS 4.54 PCS -0.03 *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.

PICO 5: In our defined population, what is the relative impact of corticosteroid injections versus arthroplasty at one year on patient important outcomes including pain, function, infection, hospitalization, and death at one year in patients with KL grade 3-4 OA?

Summary of Evidence:

A systematic review of the literature did not identify any evidence directly addressing the question; therefore, we loosened our inclusion criteria to include other studies. None of the studies directly compared arthroplasty to intra-articular glucocorticoids. We identified four studies, one randomized controlled trial and three observational studies, that evaluated and compared intra-articular glucocorticoids to placebo or to other nonsurgical treatments and used these studies as indirect evidence. The overall certainty of evidence was very low.

The randomized controlled trial by Jurgenmeister et al. (28) showed a statistically significant decrease in pain and function one week after triamcinolone injection in the knee (as measured by VAS, KOOS Jr, KOOS Conversion) and hip (VAS, HOOS Jr, HOOS Conversion) and hip. A qualitative attenuation of this effect was observed after injection and a statistically significant attenuation was observed comparing 1 week post-injection to 3 months post-injection for KOOS Jr and KOOS conversion scores. Global joint health did not significantly change. The single trial has low risk of bias, no demonstrable inconsistency, no serious precision concerns for outcomes at 1 week but does have serious imprecision beyond 1 week for most outcomes, and has very serious indirectness with respect to the question asked.

The three remaining studies were observational studies (29-31). In each of these studies, either a majority of patients had moderate to severe osteoarthritis or results were reported stratified by severity of arthritis. These studies demonstrated improvement with corticosteroid injections, but the duration or magnitude of effect decreased as the severity of osteoarthritis increased.

Overall impression: A study directly examining our question would compare those receiving a trial of corticosteroid injections prior to arthroplasty vs. those proceeding immediately to arthroplasty. Our single trial provides very low certainty evidence that intra-articular triamcinolone is beneficial for pain and function in the knee and hip at one week, and less certainty evidence of benefit thereafter, in a non-surgical population. This was graded down for indirectness as well as imprecision.

Overall quality of evidence: Very low

Table 1: Triamcinolone injection in the knee. 1301 Jurgenmeister (28)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			Relative (95% CI)	Absolute (95% CI)	
Knee Pain VAS (follow-up: mean 1 weeks; Scale from: 0 to 10)											
1	randomised trials	not serious[a]	not serious	Very serious[b]	Not serious	Search bias[d].		N= 30 (single arm)	-	MD **2.4 VAS lower than baseline** (p < 0.05)	⊕◯◯◯ Very Low
Knee Pain VAS (follow-up: mean 3 months; Scale from: 0 to 10)											
1	randomised trials	not serious	not serious	Very serious	serious[c]	Search bias.		N= 30 (single arm)	-	MD **1.11 VAS lower than baseline** (p > 0.05)	⊕◯◯◯ Very Low
KOOS Jr (follow-up: mean 1 weeks; Scale from: 0 to 10)											
1	randomised trials	not serious	not serious	Very serious	Not serious	Search bias.		N= 30 (single arm)	-	MD **2.65 VAS lower than baseline** (p < 0.05)	⊕◯◯◯ Very Low
KOOS Jr (follow-up: mean 3 months; Scale from: 0 to 10)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			Relative (95% CI)	Absolute (95% CI)	
1	randomised trials	not serious	not serious	Very serious	serious	Search bias.		N= 30 (single arm)	-	MD **1.11 VAS lower than baseline** (p > 0.05)	⊕◯◯◯ Very Low

Hip pain VAS (follow-up: mean 1 weeks; Scale from: 0 to 10)

1	randomised trials	not serious	not serious	Very serious	Not serious	Search bias.		N= 26 (single arm)	-	MD **2.65 VAS lower than baseline** (p < 0.05)	⊕◯◯◯ Very Low

Hip Pain VAS (follow-up: mean 3 months; Scale from: 0 to 10)

1	randomised trials	not serious	not serious	Very serious	serious	Search bias.		N= 26 (single arm)	-	MD **1.11 VAS lower than baseline** (p > 0.05)	⊕◯◯◯ Very Low

HOOS Jr (follow-up: mean 1 weeks; Scale from: 0 to 10)

1	randomised trials	not serious	not serious	Very serious	Not serious	Search bias.		N= 26 (single arm)	-	MD **2.65 VAS lower than baseline** (p < 0.05)	⊕◯◯◯ Very Low

HOOS Jr (follow-up: mean 3 months; Scale from: 0 to 10)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			Relative (95% CI)	Absolute (95% CI)	
1	randomised trials	not serious	not serious	Very serious	serious	Search bias.		N= 26 (single arm)	-	MD **1.11 VAS lower than baseline** (p > 0.05)	⊕◯◯◯ Very Low

a = Risk of bias was deemed low given blinding of patients and physicians (an independent physician provided the injection), randomization via accepted technique. Recruitment strategy unclear, but likely mitigated by randomization. Minimal loss to follow-up.
b = This data is very indirect given it does not address the question, similar to other PICOS (e.g., 1-3).
c = The p-value is >0.05, indicating imprecise confidence intervals. The trial does not provide a confidence interval of change.
d = Given there are over 50 randomized trials in recent meta-analyses evaluating intra-articular glucocorticoids, we should suspect search and selection bias.

CI: confidence interval; MD: mean difference; RR: risk ratio

Table 2. Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan.

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results
1301, Jurgensmeier 2021 (28)	Double-blind randomized, noninferiority	Range 1 to 3 months	Number of patients who had Corticosteroid Injections: 120 patients with moderate to severe radiographic primary OA of the hip (n=58), or knee (n=62)	1 intraarticular injection of ketorolac 30 mg or triamcinolone 80 mg	Patient-reported outcome scores at 1 and 3 months: **Ketorolac versus Triamcinolone**: Triamcinolone inj. Hip: pre-injection, 1 week, 1 mo, 3 mo 1. HOOS Jr: 11.35 -> 6.15 -> 7.69 -> 9.65 (p<0.05 from pre-injection to 1 week) 2. HOOS Conversion: 55.4 -> 71.1 -> 67.2 -> 60.8 (p<0.05 from pre-injection to 1 week) 3. VAS: 5.42 -> 2.77 -> 3.96 -> 4.31 (p<0.05 from pre-injection to 1 week)

			Number of patients who underwent TJA (specify TKA or THA or both): 0 % Female: 64 Mean Age: 65.28±12.6		4. Hip global health: 3.38 -> 3.67 -> 3.47 -> 3.45 Non-significant Triamcinolone Knee inj: pre-injection, 1 week, 1 mo, 3 mo 5. KOOS Jr: 15.1 -> 8.1 -> 9.2-> 11.3 (p<0.05 from pre-injection to 1 week and 1mo) 6. KOOS Conversion: 49.4 -> 66.7 -> 64.1 -> 58.4 (p<0.05 from pre-injection to 1 week) 7. VAS: 5.3 -> 2.9 -> 2.9 -> 4.2 (p<0.05 from pre-injection to 1 week and 1mo) 8. Knee global health: 3.2 -> 3.58 -> 3.34 -> 3.32 Non-significant <u>Hip injections:</u> no significant difference between drugs at 1 month and 3 months. 1 mo. (HOOS Jr): mean score 7.65 vs 7.69 3 mos (HOOS Jr.): mean score 9.50 vs 9.65 1 mo. (HOOS Conversion): mean score 67.0 vs 67.2 3 mos (HOOS Conversion): mean score 61.5 vs 60.8 1 month (VAS): mean score 4.19 vs 3.96 3 months (VAS): mean score 4.19 vs 4.31 <u>Knee injections</u>: no significant difference between drugs at 1 month and 3 months, p>0.05 for all outcomes 1 mo. (KOOS Jr): mean score 10.9 vs 9.2 3 mos (KOOS Jr.): mean score 11.4 vs 11.3 1 mo. (KOOS Conversion): mean score 59.7 vs 64.1 3 mos (KOOS Conversion): mean score 59.0 vs 58.4 1 month (VAS): mean score 4.1 vs 2.9

					3 months (VAS): mean score 4.1 vs 4.2 *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1391, Steer K, 2020 (29)	Observational Cohort study, single arm	Follow-up interval at least 1 year (range 1.1–3.3 years) for TJA; 8 weeks for PROs and physical impairment/ function outcomes.	97 patients included in the study (received CSI) N=94/97 -> age 59 +/- SD 12.7; N=94 -> Female 44 patients; N=91--> BMI 29.6 +/- SD 5.8 (certain demographic variables were missing in some patients). 37/97 patients proceeded to THA within the f/u interval (1.1-3.3 years after CSI).	-CSI: Intra-articular injection of 40 mg triamcinolone + 5 mg bupivacaine at the end of the baseline visit, by experienced interventional musculoskeletal radiologists under fluoroscopic guidance.	**PRO at baseline and 8 weeks post-CSI:** **1. WOMAC pain** a. Week 0 (baseline) (N=96): mean 223.35 +/- SD 99.02 b. Change Week 8-0 (N=90): mean –31.63 +/- SD 89.27 c. % change = –14.2% p = 0.001 **2. WOMAC function** a. Week 0 (baseline) (N=96): mean 714.79 +/- SD 291.36 b. Change Week 8-0 (N=91): mean –92.54 +/- SD 286.13 c. % change = –12.9% p = 0.003 **3. WOMAC stiffness** a. Week 0 (baseline) (N=96): mean 111.94 +/- SD 45.63 b. Change Week 8-0 (N=91): mean –23.12 +/- SD 45.28 c. % change = –20.7% p <0.001 -**Physical impairment/Function at baseline and 8 weeks post-CSI:** 1. **Timed Up and Go test** - **Pre-test pain** (NPRS) a. Week 0 (baseline) (N=95): mean 2.511 +/- SD 2.03

					b. Change Week 8-0 (N=88): mean –0.59 +/- SD 1.84 c. % change = –23.3% p = 0.004 2. **Timed Up and Go test** - **Post-test pain** (NPRS) a. Week 0 (baseline) (N=95): mean 2.86 +/- SD 2.29 b. Change Week 8-0 (N=88): mean –0.82 +/- SD 2.15 c. % change = –28.6% p = 0.001 3. **6 minute walk test** - **Pre-test pain** (NPRS) a. Week 0 (baseline) (N=89): mean 2.55 +/- SD 1.98 b. Change Week 8-0 (N=79): mean –0.70 +/- SD 1.78 c. % change = –27.6% p < 0.001 4. **6 minute walk test** - **Post-test pain** (NPRS) a. Week 0 (baseline) (N=91): mean 4.12 +/- SD 2.29 b. Change Week 8-0 (N=82): mean –0.70 +/- SD 2.20 c. % change = –17.0% p = 0.005 **-Total hip arthroplasty at 1 year or later (post-injection) on injected hip = 37/97 patients** Subjects who proceeded to arthroplasty within the follow-up interval (1.1–3.3 years after injection) had: 1. More severe radiographic OA than others, as measured by smaller JSW (mean 0.173 mm vs. 0.086, p = 0.001) and higher KL Grade ($\chi 2$ = 9.79, p = 0.044) 2. Significantly lower active ROM in flexion (89.0 vs. 96.7, p = 0.027) and internal rotation (14.4 vs. 20.9, p = 0.006). 3. Those without objective stiffness at baseline were less likely to proceed to arthroplasty ($\chi 2$ = 3.89, p = 0.048).

					*The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
674 Walter 2019 (30)	Retrospective, cohort, single arm study	Follow-up period of up to 6 months (range not reported)	113 patients (68% women, 77/113); overall mean age 59 years (SD ±13.7 years). The mean patient BMI was 28.2 (SD ±6.1).	-CSI: intra-articular therapeutic hip steroid injections under direct visualization with ultrasound or fluoroscopy. A 5-mL mixture containing 80 mg (or 40 mg) of triamcinolone (40 mg/mL) and 3 mL or 4 mL of 0.5% ropivacaine.	**Patient Reported Outcomes** **Short-term (<8 weeks) follow-up interval post-CSI (within-patient change), n=34:** 1. EuroQol-5 domain (EQ5D) = mean 0.01 +/- SD 0.22; median 0.00 and IQR 0.21; p=0.770 2. EuroQol-5 domain visual analog scale (EQ5D-VAS) = mean 1.00 +/- SD 18.32; median 0.50 and IQR 20.25; p=0.915 3. Average HOOS = mean –0.32 +/- SD 18.05; median –1.80 and IQR 24.90; p=0.696 4. Total HOOS = mean –11.46 +/- SD 103.33; median –11.0 and IQR 119.25; p=0.517 **Long-term (≥8 weeks) follow-up interval post-CSI (within-patient change, n=79:** 1. EQ5D = mean 0.02 +/- SD 0.2; median 0.00 and IQR 0.14; p=0.493 2. EQ5D-VAS = mean 0.25 +/- SD 20.58; median –1.00 and IQR 21.00; p=0.455 3. Average HOOS = mean 0.7 +/- SD 16.77; median –2.60 and IQR 12.90; p=0.443 4. Total HOOS = mean 3.22 +/- 83.24; median –13.5 and IQR 65.25; p=0.423 **Frequency of hip arthroplasty post-CSI:**

					49 patients (43.3%) had ipsilateral hip arthroplasty at a mean time to surgery of 229 days (SD±135 days) following injection. *No significant change in patient-reported outcomes measured at short- and long-term intervals up to6 months after therapeutic steroid hip injections. "No significant change in patient-reported outcomes measured at short- and long-term intervals up to 6 months after therapeutic steroid hip injections." *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1060, Lai W, 2018 (31)	Retrospective cohort study, single arm	F/u for 2 years for hip surgery (all included patients) (range not reported)	82 hip injections in 78 patients. 75.6% (59/78) were female, average age at time of injection was 64.4 years (range, 41–94 years old).	-CSI: Intraarticular joint injection under fluoroscopic guidance: 1 cc of 80 mg of methylprednisolone and 5 to 10 cc of 0.5% ropivacaine.	1. **Pain:** **Self-reported pain relief post-CSI** (documented in the electronic medical records at follow-up clinic visits): 19.5% (16/82) showed no relief 47.6% (39/82) showed immediate response (≤2 weeks of pain relief) 32.9% (27/82) showed continued response (>2 weeks of pain relief) 2. **Rate of TJA or resurfacing post-hip CSI:** 48.7% (38/78) of patients had hip resurfacing or replacement within 2 years after initial injection for OA (13.2% or 5/38 underwent hip resurfacing and 86.8% or 33/38 underwent TJA). *The outcomes of mortality, complications, hospital readmissions, emergency department visits, infection, deep vein thrombosis, admission to higher level of care,

					length of hospital stay, and discharge to long-term care facility all are not reported.

CSI = corticosteroid injection

PICO 6: In our defined population, what is the relative impact of viscosupplementation versus arthroplasty at one year on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:

A systematic review of the literature did not identify evidence directly addressing the question; therefore, we loosened our inclusion criteria to include other studies. No studies directly compared viscosupplementation versus arthroplasty in our defined population. We identified two randomized controlled trials (RCT) and eight observational studies that compared viscosupplementation to placebo or to other nonsurgical treatments and used these studies as indirect evidence. The overall certainty of evidence was very low.

One RCT was a multicenter double-blind randomized, placebo-controlled trial that randomized patients to either a 4mL single injection of Monovisc (viscosupplementation) or 4mLs of saline (32). At 26 weeks, more patients who received hylauronic acid had 50% improvement and > 20 improvement from baseline on the WOMAC physical function test than placebo. However, there was no difference in the absolute WOMAC physical function mean WOMAC physical function or VAS scores at 26 weeks between groups (Table 1).

All but one observational study analyzed patient-reported outcomes after viscosupplementation injections and found improvement. However, none of the studies directly compared these outcome measures to arthroplasty. In their study of 97 patients with severe hip arthritis, Eymard et al. (33) found improved WOMAC scores out to 90 days. Kearey et al. (34) similarly found improved WOMAC scores as well as SF-36 scores from baseline at 52 weeks in patients who received viscosupplementation. Goorman et al. (35) looked at functional outcomes in the SF-36 and found improved physical functioning and bodily pain at 6 months compared to baseline. Saturveithan et al. (36) compared patients who received viscosupplementation alone versus viscosupplementation with platelet rich plasma and found improved IKDC scores at 6 months with the viscosupplementation and PRP, but both groups improved over baseline. Morgan et al. (27) found improved pain with viscosupplementation based on the Likert scale. Neustadt et al. (37) also found improved VAS pain with viscosupplementation, with a reduction in improvement over 24 months. Adams et al. (20) compared patients who received NSAIDs versus viscosupplementation injections versus both treatments. They found improvement in all three groups at 3 months in pain, but at 26 weeks improved pain in patients who received both viscosupplementation injections as well as NSAIDs compared to both treatments alone.

One observational cohort study looking at TJA patients found that TKA and THA patients who received viscosupplementation injections before surgery had increased time from first presentation to surgery compared to patients that did not receive viscosupplementation injections (38).

Overall Impression: The studies that address our question would compare the results of those who went to total joint arthroplasty (TJA) directly versus those in whom TJA was delayed for a trial of viscosupplementation. None of the papers examined the outcomes in those who underwent surgery immediately versus those who were delayed. As a result, we rated all of the quality of evidence as very low due to indirect evidence.

Overall Quality of Evidence: Very low

Table 1: Monovisc vs. saline for moderate knee OA. 1867 Petterson and Plancher 2019 (32).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Monovisc	Saline	Relative (95% CI)	Absolute (95% CI)	
WOMAC physical function, mean scores at 26 weeks											
1	67andomized trial	not serious	not serious	serious	serious[a]	none	181	184	-	MD **0.6 lower** (5.73 lower to 4.53 higher)	⨁⨁⨁◯ Moderate
Patient global assessment (VAS), mean scores at 26 weeks											
1	67andomized trial	not serious	not serious	serious	serious[a]	none	181	184	-	MD **0.3 higher** (5.06 lower to 5.66 higher)	⨁⨁⨁◯ Moderate
Evaluator global assessment (VAS), mean scores at 26 weeks											
1	67andomized trial	not serious	not serious	serious	serious[b]	none	181	184	-	MD **1 higher** (3.61 lower to 5.61 higher)	⨁⨁⨁◯ Moderate
Total Serious AEs											
1	67andomized trial	not serious	not serious	serious	serious[a]	none	9/181 (5.0%)	5/184 (2.7%)	RR 1.83 (0.63 to 5.35)	**23 more per 1,000** (from 10 fewer to 118 more)	⨁⨁⨁◯ Moderate
Device-related AEs											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Monovisc	Saline	Relative (95% CI)	Absolute (95% CI)	
1	68andomized trial	not serious	not serious	serious	serious[a]	none	24/181 (13.3%)	14/184 (7.6%)	RR 1.74 (0.93 to 3.26)	**56 more per 1,000** (from 5 fewer to 172 more)	⨁⨁⨁◯ Moderate

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Single study, 95% CI includes the possibility of no difference

b. Single study, point estimate indicates no difference

Table 2. Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan.

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results
878, Tang A, 2021 (38)	Observational cohort study; two arms: intervention vs control	90 days post TJA (range not reported)	3400 consecutive primary TJA cases (1770 THA and 1570 TKA). Only 1 THA patient had hyaluronic acid injection (HAI) prior to THA, so	Sodium hyaluronate (10 mg/mL, 30 mg/mL, 16 mg/2 mL, or 48 mg/6 mL) or cross-linked hyaluronate acid (30 mg/3 mL or 88 mg/4 mL) were classified as HAI therapy + local anesthetic (lidocaine or ropivacaine).	TKA group (all patients who received CSI, CSI + HAI combination, or HAI are analyzed together in a single group = intervention) n = 1570 (intervention group n=192; control 1378) 1. Overall complications at 3 months (90 days): Exp/intervention 5/192 (2.6%) Vs Control 39/1378 (2.8%). 2. Deep Infection (i.e., PJI) at 3 months (90 days): Exp/intervention 0/192 Vs Control 7/1378 (0.5%)

			this group was only used for PICO5. 141 TKA patients received HAI and 28 received combination of CSI and HAI prior to surgery. TKA patients (n=192). Age 67.0+/-8.6; BMI 32.3 +/- 5.9; Female 136 (29%). TKA Controls (n=1378): Age 66.9 +/- 9.7; BMI 32.3 +/- 6.3; 934/1378 female gender (68%).		3. Superficial infection (e.g., abscess) at 3 months (90 days): Exp/intervention 0/192 Vs Control 2/1378 (0.1%) 4. Wound complications (e.g., dehiscence, drainage) at 3 months (90 days): Exp/intervention 0/192 Vs Control 8/1378 (0.6%) *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
1684, Eymard 2017 (33)	Prospective, observational multicenter study of 25 centers in France	Mean and range of follow up NR. 47% completed 90 day follow up	Number of patients who had Viscosupplementation Injections: 97 Number of patients who underwent TJA (specify TKA or	Single intra-articular hip fluoroscopically guided or US guided injection of HAnox-M-XL	Mortality at 90 days: 0 with viscosupplementation Overall complications at 90 days: With HA injections there were adverse effects in 9% of patients (9 events) with 90 day follow up. 3 increased hip pain following injections. 2 resolved within 24h, 1 resolved by 7d. Remaining complications were 2 cases of low back pain, 1 sciatica, 1 case of knee pain with knee OA, 1 dizziness Patient-reported outcome scores at 90 days: VISCOSUPPLEMENTATION INJECTIONS

			THA or both): 1 THA % Female 58% Mean Age: 63 Kellgren Lawrence grade 1 (10%), II (41%), III (34%), IV (12%)		For viscosupplementation WOMAC scores all improved (p<0.001) at 90 days compared to baseline WOMAC pain improved from 26 (7-42) to 16.5 (0-46) WOMAC stiffness improved from 10 (0-18) to 6 (0-17) WOMAC Function improved from 84 (23-134) to 58 (0-133) PGA improved from 7(3-10) to 5 (0-10). *The outcomes of hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1238, Kearey 2017 (34)	Prospective single-arm observational multi-center study in Australia	Mean and range NR but time points assessed were week 12, Month 6 and Week 52	Number of patients who had Viscosupplementation Injections: 131 Number of patients who underwent TJA (specify TKA or THA or both): At least 1 TKA, 12 underwent "knee surgery" within 52 weeks 66.4% females, Mean age 60.2 years with	Single intra-articular knee injection with hylan G-F20 for knee OA	Mortality at 52 weeks: HA no mortality Overall complications at 52 weeks: HA with 40 adverse events in 37 patients, 33 considered unrelated to HA. 7 considered treatment related and were MSK related. Remainder included CVS (2), Respiratory (4), GI (1), Renal (1), Dental (2), Oncologic (3), Bruising (1), Vasc (1), Miscellaneous (4) 1 "vascular" complication in HA group up to 52 weeks but type not denoted. Patient-reported outcome scores up to 52 weeks: WOMAC AND SF36 REPORTED AS IMPROVEMENT IN % FROM BASELINE. No values for scores reported Womac ITT analysis (% improvement) (P all <0.001)

			92.4% with Kellgren-Lawrence II or III		Pain improvement: -37.83 (12 weeks), -34.71 (6 mos), -32.73 (52 weeks) Stiffness improvement: -38.52 (12 weeks), -35.41 (6 mos), -30.39 (52 weeks) Function improvement: -32.32 (12 weeks), -30.69 (6 mos), -29.63 (52 weeks) Total improvement: -34.01 (12 weeks), -31.82 (6 mos), -29.63 (52 weeks) SF36 outcomes below in terms of percent improvement from baseline PCS: 7.25 (12 weeks), 10.32 (6 mos), 7.72 (52 weeks) MCS: 7.54 (12 weeks), 3.37 (6 mos), -0.3 (52 weeks) *The outcomes of hospital readmissions, emergency department visits, reoperations, revisions, infection, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1291, Saturveithan 2016 (36)	Cross-sectional retrospective review of a knee injection registry at a single site with 2 groups: PRP + hyaluronic acid vs hyaluronic acid alone in grade III and IV knee OA	Mean and range of follow up NR. Outcomes reported at 2 and 6 mos	Number of patients who had Viscosupplementation Injections: HA only 47 knees HA+PRP: 56 knees Number of patients who underwent TJA	Group one received 4mL High molecular weight HA (22mg/mL) Group 2 received the same concentration of HA with added PRP (30cc of patient's blood to produce 2.5-3mL PRP with platelet concentration of 1.4-1.6mill/microL	Improvement in IKDC score was reported at 2 and 6 mos post injection. For HA group at 2 mos this improved 7 points (SD 7.8) and at 6 months 12.1 points (8.2) For HA+PRP group at 2 mos this improved 16.3 points (11.9 SD) and at 6 months 24.3 points (13.7). The p value <0.05 demonstrated statistically sig improvement in IKDC score for both groups. *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations,

			(specify TKA or THA or both): NR % Female: 62.5% Mean Age: 66 (50-87)		revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1224, Morgan, 2015 (27)	Case series	6 months (range not reported)	Number of patients who had Viscosupplementation Injections: 207 Number of patients who underwent TJA (specify TKA or THA or both): 0 60% Female Mean Age: 63	Description of Viscosupplementation Injections: Medication, Dose, Frequency HA (Euflexxa, 1 % Sodium Hyaluronate) injections administered fluoroscopically, 3 doses with 1-week intervals	Patient-reported outcome scores at 6 months: VISCOUS SUPPLEMENTATION (outcome: mean improvement for pain (SD) [10 point scale]) customized pain (scored 0–10) and function (scored 0–120) assessment based on the Likert scale -- grade 2 OA: 1.66 (2.1) -- grade 3 OA: 2.74 (2.5) -- grade 4 OA: 2.3 (2.8) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1383, Neustadt 2003 (37)	Prospective single arm cohort study	Mean and range of follow up not reported: Goals was 24 mos. At 6 mos 37% were lost to follow up or TKA, at 12 mos 55% lost to	Number of patients who had Viscosupplementation Injections: 76 patients, 92 knees Number of patients who	5 intra-articular injections of 20mg sodium hyaluronate administered at weekly intervals	Overall complications up to 24 months: VISCOSUPPLEMENTATION INJECTIONS v. TJA: for injection 20% of patients experienced injection site pain, 9% experienced bruising, 7.5% headache, 3% nausea. Otherwise no major adverse effects Patient-reported outcome scores up to 24 months:

		follow up or TKA, at 24 mos 74% lost to follow up or TKA	underwent TJA (specify TKA or THA or both): 15 TKA % Female 21% Mean Age: 64 (+/- 7.4)		VAS pain score was outcome. At baseline 31% of patients reported moderate (4-6), 59% reported severe (7-9), 11% experienced extreme (9 or more). At 6 mos: 6 no pain, 32 (35%) reported slight, 16 (18%) reported moderate, 4 reported severe. At 12 mos: 5 no pain, 25 (28%) reported slight, 9 mod, 3 severe. At 24 mos: 4 no pain, 12 (13%) slight, 7 mod, 1 severe *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1808, Barrett 2002	Retrospective single center study examining 18 month period with minimum 6 month follow up.	Mean and range of follow up: NR. 25.6% of those injected were lost to follow up within 6 months	Number of patients who had Viscosupplementation Injections: 248 Number of patients who underwent TJA (specify TKA or THA or both): 20.3% underwent TKA % Female 51.2% Mean Age: 72 (30-97)	Single intra-articular injection with Hyalgan into the knee	Overall complications up to 18 months: “no serious adverse effects reported following HA injection” Reoperations up to 18 months: 50 (20.3%) went on to TKA within 6 months of injection Patient-reported outcome scores up to 18 months: VISCOSUPPLEMENTATION INJECTIONS No formal outcome scoring was collected. 196 of 218 knees were analyzed for QOL metrics and of these the score improved by the following (on a scale of 1-10): Mean improvement in quality of life was 2.1, pain on walking 2.3, pain under load 2.4, pain at night 1.6. These were collected “after treatment” but time of collection not denoted. *The outcomes of mortality, hospital readmissions, emergency department visits, revisions, infection, deep vein thrombosis, admission to higher level of care, length

					of hospital stay, and discharge to long-term care facility all are not reported.
1834, Adams 1995 (20)	Multicenter RCT for 26 weeks, no placebo injection. Placebo group was effectively an aspiration group.	All received 26 week telephone interview (mean and range not reported)	Number of patients who had Viscosupplementation Injections: 61 Number of patients who underwent TJA (specify TKA or THA or both): 0 % Female: 65% Mean Age: 61 Additional details: Men (35%) and women (65%) aged 18-75 with osteoarthritis of the knee (Kellgren Lawrence 1-3 in </= 2 compartments and not 3 or more in patellofemoral joint).	3 groups NSAID with three weekly arthrocenteses (mean age 63) 2.0mL hylan G-F 20 intra-articular injections (mean age 61) NSAID with three weekly 2.0 mL G-F 20 intra-articular injections (mean age 61)	*Adverse effects not reported. Does not compare TJA vs viscosupplementation. NO TJA performed Patient-reported outcome scores at 3 months and 26 weeks: Purely survey data reported. No KOOS/HOOS/WOMAC At 3 months Mean improvement with NSAIDs, hylan+NSAIDs or Hylan alone were all statistically significantly improved in terms of VAS ($p<0.01$), but not different from each other. Mean improvement in VAS pain (0-100 point scale) with motion were all statistically significantly improved (19 NSAID, 23 Hylan, 26 Hylan +NSAID): 1. pain with rest (9 NSAID, 19 Hylan, 12 Hylan + NSAID), 2. pain at night (13 NSAID, 21 Hylan, 10 Hylan + NSAID), 3. restriction of activity (14 NSAID, 13 Hylan, 14 Hylan+ NSAID), 4. overall assessment of pain (19 NSAID, 24 Hylan, 26 Hylan + NSAID) At 26 weeks the hylan G-F 20 + NSAID group was statistically superior to the NSAID only group. The hylan +NSAID group was statistically superior to the Hylan only group in pain at rest and night pain. These demonstrate mean VAS scores as follows: 1. pain with motion (52 NSAID, 40 Hylan, 37 Hylan +NSAID), 2. pain with rest (22 NSAID, 25 Hylan, 11 Hylan + NSAID), 3. pain at night (28 NSAID, 25 Hylan, 9 Hylan + NSAID), 4. restriction of activity (52 NSAID, 41 Hylan, 38 Hylan+ NSAID),

					5. overall assessment of pain (52 NSAID, 47 Hylan, 37 Hylan + NSAID) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
1141, Goorman S, 2000 (35)	Prospective case series with 6-month follow-up.	6 months	Patients with knee OA (one or both knees). n =61; mean age 65.8 +/- SD 11.65; female 35 (57.4%)	3 weekly injections of Hylan G-F 20 into one or both (if bilaterally symptomatic) knees.	Functional categories SF-36 health survey (pre = baseline; post = 6 months after injection): 1. Physical Functioning pre 38.8 vs post 60.1, p <0.001 2. Role–Physical Pre 29.1 vs post 64.3, p <0.001 3. Bodily Pain Pre 42.4 vs post 55.2, p <0.001 4. General Health Pre 66.1 vs post 65.9, p 0.92 5. Vitality Pre 49.8 vs post 50.6, p 0.60 6. Social Functioning Pre 70.5 vs post 79.2, p 0.01 7. Role–Emotional Pre 52.5 vs post 94, p <0.001 8. Mental Health Pre 47.1 vs post 42.7, p 0.01 *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
483 Miller and Block 2014 (39), and 1380 Miller et al. 2017 (40)	Case series	1 and 2 years (2014 study) Mean 3.7 years (range 2.7 to 4.9 years; 2017 study)	Number of patients who had viscosupplementation Injections: 336 at 1 year and 217 at 2 years mostly receiving Hyalgan and Supartz (2014	Weekly HA injections for 3 or 5 weeks, depending on HA product (57% received Hyalgan, 43% received Supartz, and <1% received Synvisc or Euflexxa). NSAIDS (routine users): 50% at 1 year, 61% at 2 years (2014	1. Mortality: NR 2. Overall complications: NR 3. Hospital Readmissions: NR 4. Emergency Department Visits: NR 5. Reoperations: NR 6. Revisions: NR 7. Infection: NR 8. Deep vein thrombosis: NR 9. Admission to higher level of care: NR 10. Length of hospital stay: NR 11. Discharge to long-term care facility: NR

			study), 218 received Hyalgan (2017 study) Number of patients who underwent TKA: 10.4% at 1 year, 18% at 2 year (2014 study); 22.8% up to 4.9 years (81/356; 2017 study) % Female: 49% (2014 study), 47% (2017 study) Mean Age (years): 71±10 (2014 study), 70.5±9.2 (2017 study) K-L grade 3 and 4: >70%	study); 48.7% up to 4.9 years (2017 study) Patients participated in an 8-week multimodal intervention (including viscosupplementation, deliberate PT, rehabilitation, and an education program provided by licensed physical therapists 2 to 3x/week. Knee bracing was prescribed when clinically indicated (% prescribed NR). Regular low-impact aerobic activity and functional exercises at home were encouraged. 158/3569 patients in the original cohort participated in a subsequent 8-week treatment cycle and were not eligible for the 2014 and 2017 studies.	12. Patient-reported outcome scores at 2 years, and up to 4.9 years (multimodal treatments including viscosupplemetation, NSAIDS, PT, and bracing): Index knee pain severity at 2 years Baseline (n=553): 5.8±2.8; results at 2 years (n=217): Severity <4: 68 (18 (26.5%) underwent TKA) Severity 4 to 6: 69 (8 (11.6%) underwent TKA) Severity ≥7: 80 (13 (16.3%) underwent TKA) Pain at mean 3.7 years (range 2.7 to 4.9 years) WOMAC pain at baseline (mean±SD): 48±20 WOMAC pain at follow-up: 42% reduction (statistically significant difference vs baseline; data figuratively displayed) Percent of responders (≥20% improvement vs baseline in WOMAC pain): 69% NPRS at baseline (mean): 5.5±2.8 NPRS at follow-up: 60% reduction (statistically significant difference vs baseline; data figuratively displayed) Percent of responders (≥30% improvement vs baseline in NPRS): 75% Function at mean 3.7 years (range 2.7 to 4.9 years) WOMAC function at baseline: 49±19

					WOMAC function at follow-up: 41% reduction (statistically significant difference vs baseline; data figuratively displayed) Percent of long-term responders (≥20% improvement vs baseline) in WOMAC function: 71% *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.

NPRS: Numeric Pain Rating Scale; PT: physical therapy

PICOs 7-9

PICO 7: In our defined population with BMI between 35-39, what is the relative impact of delaying arthroplasty to achieve weight reduction to BMI <35 versus proceeding to arthroplasty on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

PICO 8: In our defined population with BMI between 40-49, what is the relative impact of delaying arthroplasty to achieve weight reduction to BMI <40 versus proceeding to arthroplasty on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

PICO 9: In our defined population with BMI between >50, what is the relative impact of delaying arthroplasty to achieve weight reduction to BMI <50 versus proceeding to arthroplasty on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:

A systematic review of the literature did not identify any evidence that directly answered this PICO question; therefore, we loosened our inclusion criteria to include other studies evaluating bariatric surgery and outcomes of total joint arthroplasty (TJA) stratified by body mass index (BMI) that provided indirect evidence. There were 14 observational studies that provided indirect evidence (41-54). The only evidence used to compare patients with elevated BMIs who pursued weight loss prior to total joint arthroplasty (TJA) versus those who proceeded directly to arthroplasty was in studies evaluating bariatric surgery. There were no other methods of weight loss evaluated in those studies with direct evidence. The overall certainty of evidence was very low due to indirectness and bias.

Eight of the studies published were database studies. In these studies, the reduction in BMI from bariatric surgery was not provided. Nickel et al. (41) conducted a claims-based review of the Medicare database and compared patients who underwent bariatric surgery prior to THA versus those that did not with a BMI > 40 as well as BMI < 25. Patients who underwent bariatric surgery prior had increased overall complications as well as revisions at 2 years compared to patients with BMI > 40. Compared to patients with BMI < 25, the patients who had bariatric surgery had increased risk of all complications, revisions, and infections at both 90 days and 2 years. Nickel et al. utilized the same methodology comparing patients who underwent bariatric surgery prior to TKA versus those that did not with a BMI > 40 as well as BMI < 25. They again found increased risk of mortality, DVT, infection, and revision at 90 days as well as infection and revision at 2 years in patients who underwent bariatric surgery prior to TJA. Lee et al. (48) analyzed Medicare 5% Part B data and found increased risk of revision and infection at 1, 2, and 5 years. In the New York Statewide Planning and Research Cooperative System Database, Liu et al. (54) found no difference in nonelective readmissions after TJA out to 1 year between obese patients who underwent bariatric surgery prior to TJA and obese patients who proceeded directly to TJA.

In contrast to the above studies, Kulkarni et al. (43) compared patients in the English NHS who underwent bariatric surgery then arthroplasty and vice versa; bariatric surgery was performed first in 53 and arthroplasty first in 90 patients, and found no difference in outcomes between

groups. Wang et al. (44) also did a database study with the Nationwide Inpatient Sample and found no difference in most outcomes between morbid obese patients (BMI > 40 kg/m^2) who underwent TKA and THA patients and those who underwent bariatric surgery prior to THA or TKA. The only difference found was in the rate of pulmonary embolism among TKA patients favoring patients who underwent bariatric surgery first. Werner et al. (47) analyzed the PearlDiver database and compared non-obese TKA patients to morbidly obese TKA patients to morbidly obese patients who underwent bariatric surgery prior to TKA. They found a significantly decreased risk of major and minor complications as well as infections at 90 days.

In a case-control study matching patients based on demographics and BMI who underwent bariatric surgery prior to TKA and those that went directly onto TKA, Martin et al. (45) found increased rates of reoperation and revision at 5 years. In the bariatric surgery group, the mean reduction in BMI was 14 kg/m^2. In a similar case-control study of 102 patients by Nearing et al (46), patients who underwent bariatric surgery prior to TKA or THA had decreased length of stay compared to patients who had bariatric surgery after their TJA.

Several studies looked at early postoperative complications after THA and TKA stratified by BMI. A study of 750 patients stratified complications in the first 45 days postoperatively based on BMI and found no difference in infection or overall complications. Hung et al. (50) looked at 1565 THAs and found those with BMIs > 35 had increased overall complications and hospital stays. Keulen (51) looked at a series of 525 TJAs at their institution and found no difference in overall complications or hospital readmission within 90 days of surgery. Reeves et al. (53) found increased rates of complications after TJA in patients with BMI > 50 compared to those with BMI of 40-49.9.

Overall impression: Studies directly addressing our question would compare patients randomized to weight reduction prior to arthroplasty to those proceeding immediately to arthroplasty without weight reduction, and none of the included studies followed that methodology. Furthermore, a majority of these studies compared outcomes in those who underwent bariatric surgery prior to arthroplasty to those who did not, further introducing bias. The included studies show an association between BMI and outcomes, so the studies were rated down for indirectness as well as risk of bias.

Overall Quality of Evidence: Very low.

Table 1: THA, bariatric surgery (BS) compared to no BS (BMI>40) for OA undergoing THA_2647 Nickel 2017 (41)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, bariatric surgery (BS)	No BS (BMI>40)	Relative (95% CI)	Absolute (95% CI)	
Pneumonia, 30 days											
1	observational studies	serious[a]	not serious	not serious	not serious	none	36/1545 (2.3%)	168/6918 (2.4%)	**RR 0.96** (0.67 to 1.37)	**1 fewer per 1,000** (from 8 fewer to 9 more)	⊕◯◯◯ Very low
UTI, 30 days											
1	observational studies	serious[a]	not serious	not serious	not serious	none	211/1545 (13.7%)	974/6918 (14.1%)	**RR 0.97** (0.84 to 1.11)	**4 fewer per 1,000** (from 23 fewer to 15 more)	⊕◯◯◯ Very low
Venous thromboembolic events (DVT and PE), 30 days											
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	58/1545 (3.8%)	326/6918 (4.7%)	**RR 0.80** (0.61 to 1.05)	**9 fewer per 1,000** (from 18 fewer to 2 more)	⊕◯◯◯ Very low
Overall complications, 30 days											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, bariatric surgery (BS)	No BS (BMI>40)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	not serious	none	529/1545 (34.2%)	2978/6918 (43.0%)	**RR 0.80** (0.74 to 0.86)	**86 fewer per 1,000** (from 112 fewer to 60 fewer)	⊕◯◯◯ Very low

Periprosthetic infection, 90 days

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	41/1545 (2.7%)	235/6918 (3.4%)	**RR 0.78** (0.56 to 1.08)	**7 fewer per 1,000** (from 15 fewer to 3 more)	⊕◯◯◯ Very low

Revision, 90 days

1	observational studies	serious[a]	not serious	not serious	not serious	none	49/1545 (3.2%)	234/6918 (3.4%)	**RR 0.94** (0.69 to 1.27)	**2 fewer per 1,000** (from 10 fewer to 9 more)	⊕◯◯◯ Very low

Overall complications, 90 days

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, bariatric surgery (BS)	No BS (BMI>40)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	not serious	none	153/1545 (9.9%)	718/6918 (10.4%)	**RR 0.95** (0.81 to 1.13)	**5 fewer per 1,000** (from 20 fewer to 13 more)	⊕◯◯◯ Very low

Periprosthetic infection, 2 years

1	observational studies	serious[a]	not serious	not serious	not serious	none	98/1545 (6.3%)	462/6918 (6.7%)	**RR 0.95** (0.77 to 1.17)	**3 fewer per 1,000** (from 15 fewer to 11 more)	⊕◯◯◯ Very low

Revisions, 2 years

1	observational studies	serious[a]	not serious	not serious	not serious	none	125/1545 (8.1%)	334/6918 (4.8%)	**RR 1.68** (1.37 to 2.04)	**33 more per 1,000** (from 18 more to 50 more)	⊕◯◯◯ Very low

Overall complications, 2 years

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, bariatric surgery (BS)	No BS (BMI>40)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	not serious	none	367/1545 (23.8%)	1288/6918 (18.6%)	**RR 1.28** (1.15 to 1.41)	**52 more per 1,000** (from 28 more to 76 more)	⨁◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Observational study

b. Wide CI crosses no-effect and significant effect lines

Table 2: THA, BS with average weight reduction of 15 BMI units compared to no BS (BMI<25) for OA undergoing THA_2647 Nickel 2017 (41)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, BS	No BS (BMI<25)	Relative (95% CI)	Absolute (95% CI)	
Pneumonia, 30 days											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, BS	No BS (BMI<25)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	not serious	none	36/1545 (2.3%)	55/3697 (1.5%)	**RR 1.57** (1.03 to 2.37)	**8 more per 1,000** (from 0 fewer to 20 more)	⊕◯◯◯ Very low

UTI, 30 days

1	observational studies	serious[a]	not serious	not serious	not serious	none	211/1545 (13.7%)	338/3697 (9.1%)	**RR 1.49** (1.27 to 1.76)	**45 more per 1,000** (from 25 more to 69 more)	⊕◯◯◯ Very low

VTE (DVT and PE), 30 days

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	58/1545 (3.8%)	130/3697 (3.5%)	**RR 1.07** (0.79 to 1.45)	**2 more per 1,000** (from 7 fewer to 16 more)	⊕◯◯◯ Very low

Overall complications, 30 days

1	observational studies	serious[a]	not serious	not serious	not serious	none	529/1545 (34.2%)	745/3697 (20.2%)	**RR 1.70** (1.55 to 1.87)	**141 more per 1,000** (from 111 more to 175 more)	⊕◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, BS	No BS (BMI<25)	Relative (95% CI)	Absolute (95% CI)	
Periprosthetic infection, 90 days											
1	observational studies	serious[a]	not serious	not serious	not serious	none	41/1545 (2.7%)	21/3697 (0.6%)	**RR 4.67** (2.77 to 7.88)	**21 more per 1,000** (from 10 more to 39 more)	⨁◯◯◯ Very low
Revisions, 90 days											
1	observational studies	serious[a]	not serious	not serious	not serious	none	49/1545 (3.2%)	62/3697 (1.7%)	**RR 1.89** (1.31 to 2.74)	**15 more per 1,000** (from 5 more to 29 more)	⨁◯◯◯ Very low
Overall complications, 90 days											
1	observational studies	serious[a]	not serious	not serious	not serious	none	153/1545 (9.9%)	149/3697 (4.0%)	**RR 2.46** (1.98 to 3.05)	**59 more per 1,000** (from 39 more to 83 more)	⨁◯◯◯ Very low
Periprosthetic infection, 2 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	THA, BS	No BS (BMI<25)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	not serious	none	98/1545 (6.3%)	52/3697 (1.4%)	**RR 4.51** (3.24 to 6.28)	**49 more per 1,000** (from 32 more to 74 more)	⊕◯◯◯ Very low

Revision, 2 years

1	observational studies	serious[a]	not serious	not serious	not serious	none	125/1545 (8.1%)	148/3697 (4.0%)	**RR 2.02** (1.60 to 2.55)	**41 more per 1,000** (from 24 more to 62 more)	⊕◯◯◯ Very low

Overall complications, 2 years

1	observational studies	serious[a]	not serious	not serious	not serious	none	367/1545 (23.8%)	337/3697 (9.1%)	**RR 2.61** (2.28 to 2.98)	**147 more per 1,000** (from 117 more to 180 more)	⊕◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Observational study

b. Wide CI crosses no-effect and significant effect lines

Table 3: TKA, BS compared to no BS (BMI >40) for OA undergoing THA_3338 Nickel 2016 (42)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TKA, BS	No BS (BMI > 40)	Relative (95% CI)	Absolute (95% CI)	
Periprostetic infection, 2 years											
1	observational studies	serious	not serious	not serious	not serious	none	343/5918 (5.8%)	1286/26616 (4.8%)	**RR 1.20 (1.07 to 1.35)**	**0 fewer per 1,000 (from 0 fewer to 0 fewer)**	⊕⊕◯◯ Low
Revision, 2 years											
1	observational studies	serious	not serious	not serious	not serious	none	437/5918 (7.4%)	1286/26616 (4.8%)	**RR 1.53 (1.38 to 1.70)**	**26 more per 1,000 (from 18 more to 34 more)**	⊕⊕◯◯ Low
Mortality, 30 days											
1	observational studies	serious	not serious	not serious	not serious	none	1302/5918 (22.0%)	1597/26616 (6.0%)	**RR 3.67** (3.43 to 3.92)	**160 more per 1,000** (from 146 more to 175 more)	⊕⊕◯◯ Low
Deep vein thrombosis, 30 days											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TKA, BS	No BS (BMI > 40)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious	not serious	not serious	not serious	none	295/5918 (5.0%)	796/26616 (3.0%)	**RR 1.67** (1.46 to 1.90)	**20 more per 1,000** (from 14 more to 27 more)	⊕⊕◯◯ Low

Periprosthetic infection, 90 days

1	observational studies	serious	not serious	not serious	not serious	none	104/5918 (1.8%)	460/26616 (1.7%)	**RR 1.02** (0.82 to 1.26)	**0 fewer per 1,000** (from 3 fewer to 4 more)	⊕⊕◯◯ Low

Revision, 90 days

1	observational studies	serious	not serious	not serious	not serious	none	61/5918 (1.0%)	184/26616 (0.7%)	**RR 1.49** (1.12 to 1.99)	**3 more per 1,000** (from 1 more to 7 more)	⊕⊕◯◯ Low

CI: confidence interval; **RR:** risk ratio

Table 4: Bariatric first compared to THR first (BMI > 40) for OA undergoing THA. 2677 Kulkarni 2011 (43)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric first	THR first (BMI > 40)	Relative (95% CI)	Absolute (95% CI)	
DVT, 90-day											
1	observational studies	serious	not serious	not serious	serious[a]	none	0/37 (0.0%)	1/22 (4.5%)	**RR 0.20** (0.01 to 4.75)	**36 fewer per 1,000** (from 45 fewer to 170 more)	⨁◯◯◯ Very low
Mortality, 90-day											
1	observational studies	serious	not serious	not serious	serious[a]	none	1/22 (4.5%)	1/22 (4.5%)	**RR 1.00** (0.07 to 15.00)	**0 fewer per 1,000** (from 42 fewer to 636 more)	⨁◯◯◯ Very low
Return to reoperation for infection, 30-day											
1	observational studies	serious	not serious	not serious	serious[a]	none	1/37 (2.7%)	0/22 (0.0%)	**RR 1.82** (0.08 to 42.73)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low
30-day readmission											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric first	THR first (BMI > 40)	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious	not serious	not serious	serious[a]	none	1/37 (2.7%)	0/22 (0.0%)	**RR 1.82** (0.08 to 42.73)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Less than 200 patients in each group

Table 5: Bariatric first compared to TKR first (BMI > 40) for OA undergoing THA. 2677 Kulkarni 2011 (43)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric first	TKR first (BMI > 40)	Relative (95% CI)	Absolute (95% CI)	
DVT, 90-day											
1	observational studies	serious	not serious	not serious	serious[a]	none	1/53 (1.9%)	0/31 (0.0%)	**RR 1.78** (0.07 to 42.35)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric first	TKR first (BMI > 40)	Relative (95% CI)	Absolute (95% CI)	
Mortality, 90-day											
1	observational studies	serious	not serious	not serious	serious[a]	none	1/53 (1.9%)	0/31 (0.0%)	**RR 1.78** (0.07 to 42.35)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low
Return to reoperation for infection, 30-day											
1	observational studies	serious	not serious	not serious	serious[a]	none	0/53 (0.0%)	2/31 (6.5%)	**RR 0.12** (0.01 to 2.39)	**57 fewer per 1,000** (from 64 fewer to 90 more)	⊕◯◯◯ Very low
30-day readmission											
1	observational studies	serious	not serious	not serious	serious[a]	none	0/53 (0.0%)	4/31 (12.9%)	**RR 0.07** (0.00 to 1.18)	**120 fewer per 1,000** (from -- to 23 more)	⊕◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI and less than 200 patients in each group

Table 6: Bariatric surgery compared to morbid obesity for OA undergoing THA. 3080 Wang 2019 (44)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery	Morbid obesity	Relative (95% CI)	Absolute (95% CI)	
Length of hospital stay, THA patients											
1	observational studies	serious[a]	not serious	serious	not serious	none	2540	2540	-	MD **0.2 lower** (1.52 lower to 1.12 higher)	⊕◯◯◯ Very low
Length of hospital stay, TKA patients											
1	observational studies	serious[a]	not serious	serious	not serious	none	9803	9803	-	MD **0.19 lower** (0.23 lower to 0.15 lower)	⊕◯◯◯ Very low
Infection, THA patients											
1	observational studies	serious[a]	not serious	serious	not serious	none	0/2540 (0.0%)	2/2540 (0.1%)	**RR 0.20** (0.01 to 4.16)	**1 fewer per 1,000** (from 1 fewer to 2 more)	⊕◯◯◯ Very low
Infection, TKA patients											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery	Morbid obesity	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	serious	serious[b]	none	14/9803 (0.1%)	20/9803 (0.2%)	**RR 0.70** (0.35 to 1.39)	**1 fewer per 1,000** (from 1 fewer to 1 more)	⊕◯◯◯ Very low

Death, THA patients

1	observational studies	serious[a]	not serious	serious	serious[b]	none	0/2540 (0.0%)	2/2540 (0.1%)	**RR 0.20** (0.01 to 4.16)	**1 fewer per 1,000** (from 1 fewer to 2 more)	⊕◯◯◯ Very low

Death, TKA patients

1	observational studies	serious[a]	not serious	serious	not serious	none	1/9803 (0.0%)	15/9803 (0.2%)	**RR 0.07** (0.01 to 0.50)	**1 fewer per 1,000** (from 2 fewer to 1 fewer)	⊕◯◯◯ Very low

Deep vein thrombosis, THA patients

1	observational studies	serious[a]	not serious	serious	serious[b]	none	2/2540 (0.1%)	7/2540 (0.3%)	**RR 0.29** (0.06 to 1.37)	**2 fewer per 1,000** (from 3 fewer to 1 more)	⊕◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery	Morbid obesity	Relative (95% CI)	Absolute (95% CI)	
Deep vein thrombosis, TKA patients											
1	observational studies	serious[a]	not serious	serious	serious[b]	none	33/9803 (0.3%)	38/9803 (0.4%)	**RR 0.87** (0.55 to 1.38)	**1 fewer per 1,000** (from 2 fewer to 1 more)	⊕◯◯◯ Very low
Pulmonary embolism, THA patients											
1	observational studies	serious[a]	not serious	serious	serious[b]	none	2/2540 (0.1%)	9/2540 (0.4%)	**RR 0.22** (0.05 to 1.03)	**3 fewer per 1,000** (from 3 fewer to 0 fewer)	⊕◯◯◯ Very low
Pulmonary embolism, TKA patients											
1	observational studies	serious[a]	not serious	serious	not serious	none	19/9803 (0.2%)	56/9803 (0.6%)	**RR 0.34** (0.20 to 0.57)	**4 fewer per 1,000** (from 5 fewer to 2 fewer)	⊕◯◯◯ Very low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Observational study

b. Wide CI crosses no-effect and significant effect thresholds

Table 7: BMI 35+ bariatric surgery or not before TKA compared to placebo for OA undergoing THA. 2297 Martin 2015 (45)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI 35+ bariatric surgery or not before TKA	Placebo	Relative (95% CI)	Absolute (95% CI)	
5 year complications											
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	26/91 (28.6%)	25/91 (27.5%)	**RR 1.04** (0.65 to 1.66)	**11 more per 1,000** (from 96 fewer to 181 more)	⊕◯◯◯ Very low
5 year infection/wound healing											
1	observational studies	serious[a]	not serious	not serious	not serious	none	7/91 (7.7%)	7/91 (7.7%)	**RR 1.00** (0.37 to 2.74)	**0 fewer per 1,000** (from 48 fewer to 134 more)	⊕◯◯◯ Very low
5 year DVT											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI 35+ bariatric surgery or not before TKA	Placebo	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	1/91 (1.1%)	3/91 (3.3%)	**RR 0.33** (0.04 to 3.15)	**22 fewer per 1,000** (from 32 fewer to 71 more)	⊕◯◯◯ Very low

5 year reoperation

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	21/91 (23.1%)	10/91 (11.0%)	**RR 2.10** (1.05 to 4.21)	**121 more per 1,000** (from 5 more to 353 more)	⊕◯◯◯ Very low

5 year revision

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	7/91 (7.7%)	6/91 (6.6%)	**RR 1.17 (0.41 to 3.34)**	**11 more per 1,000** (from 39 fewer to 154 more)	⊕◯◯◯ Very low

CI: confidence interval; **HR:** hazard Ratio; **RR:** risk ratio

Explanations

a. Observational study

b. Wide CI crosses no-effect and significant effect thresholds

Table 8: Bariatric surgery or not before TJA compared to placebo for OA undergoing THA_ RefID 2307 Nearing 2017 (46)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery or not before TJA	No Bariatric surgery before TJA	Relative (95% CI)	Absolute (95% CI)	
30 day complications											
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	11/66 (16.7%)	5/36 (13.9%)	**RR 1.20** (0.45 to 3.18)	**28 more per 1,000** (from 76 fewer to 303 more)	⊕◯◯◯ Very low
30 day SSI											
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	3/66 (4.5%)	0/36 (0.0%)	**RR 3.87** (0.21 to 72.82)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low
30 day Venous thromboembolism											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery or not before TJA	No Bariatric surgery before TJA	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	2/66 (3.0%)	1/36 (2.8%)	**RR 1.09** (0.10 to 11.62)	**3 more per 1,000** (from 25 fewer to 295 more)	⨁◯◯◯ Very low

30 day periprosthetic infection

2	observational studies	serious[a]	not serious	not serious	not serious	none	10/1544 (0.6%)	99/60295 (0.2%)	**RR 4.12** (2.15 to 7.88)	**5 more per 1,000** (from 2 more to 11 more)	⨁◯◯◯ Very low

Proportion discharged to inpatient facility

1	observational studies	serious[a]	not serious	not serious	not serious	none	16/66 (24.2%)	2/36 (5.6%)	**RR 4.36** (1.06 to 17.92)	**187 more per 1,000** (from 3 more to 940 more)	⨁◯◯◯ Very low

Mean acute care length of stay

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery or not before TJA	No Bariatric surgery before TJA	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious[a]	not serious	not serious	not serious	none	66	36	-	MD **0.9 lower** (1.39 lower to 0.41 lower)	⊕◯◯◯ Very low

Overall reoperation rate

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	3/66 (4.5%)	4/36 (11.1%)	**RR 0.41** (0.10 to 1.73)	**66 fewer per 1,000** (from 100 fewer to 81 more)	⊕◯◯◯ Very low

Overall revision rate

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	1/66 (1.5%)	4/36 (11.1%)	**RR 0.14** (0.02 to 1.17)	**96 fewer per 1,000** (from 109 fewer to 19 more)	⊕◯◯◯ Very low

30-day readmission

1	observational studies	serious	not serious	not serious	not serious	none	83/1478 (5.6%)	2748/60259 (4.6%)	**RR 1.23 (1.00 to 1.52)**	**10 more per 1,000 (from 0**	⊕⊕◯◯ Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery or not before TJA	No Bariatric surgery before TJA	Relative (95% CI)	Absolute (95% CI)	
										fewer to 24 more)	
90-day readmission											
1	observational studies	serious	not serious	not serious	serious[a]	none	104/1478 (7.0%)	3863/60259 (6.4%)	**RR 1.10 (0.91 to 1.32)**	**6 more per 1,000 (from 6 fewer to 21 more)**	⊕◯◯◯ Very low
1-year readmission											
1	observational studies	serious	not serious	not serious	serious[a]	none	205/1478 (13.9%)	7472/60259 (12.4%)	**RR 1.12 (0.98 to 1.27)**	**15 more per 1,000 (from 2 fewer to 33 more)**	⊕◯◯◯ Very low
Revision, 30 days											
1	observational studies	serious	not serious	not serious	serious[a]	none	5/1478 (0.3%)	211/60259 (0.4%)	**RR 0.97 (0.40 to 2.34)**	**0 fewer per 1,000 (from 2 fewer to 5 more)**	⊕◯◯◯ Very low
Revision, 90 days											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery or not before TJA	No Bariatric surgery before TJA	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious	not serious	not serious	serious[a]	none	6/1478 (0.4%)	307/60259 (0.5%)	**RR 0.80 (0.36 to 1.78)**	**1 fewer per 1,000 (from 3 fewer to 4 more)**	⨁◯◯◯ Very low

Revision, 1 year

1	observational studies	not serious	not serious	not serious	serious[a]	none	14/1478 (0.9%)	633/60259 (1.1%)	**RR 0.90 (0.53 to 1.53)**	**1 fewer per 1,000 (from 5 fewer to 6 more)**	⨁◯◯◯ Very low

90-day periprosthetic infection

1	observational studies	serious	not serious	not serious	serious[a]	none	12/1478 (0.8%)	115/20629 (0.6%)	**RR 1.46 (0.81 to 2.63)**	**3 more per 1,000 (from 1 fewer to 9 more)**	⨁◯◯◯ Very low

1-year periprosthetic infection

1	observational studies	serious	not serious	not serious	serious[a]	none	12/1478 (0.8%)	362/60259 (0.6%)	**RR 1.35 (0.76 to 2.39)**	**2 more per 1,000 (from 1 fewer to 8 more)**	⨁◯◯◯ Very low

Infection and inflammatory reaction due to internal joint prosthesis, 30 days

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric surgery or not before TJA	No Bariatric surgery before TJA	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	serious	not serious	not serious	serious[a]	none	7/1478 (0.5%)	223/60259 (0.4%)	**RR 1.28 (0.60 to 2.70)**	**1 more per 1,000 (from 1 fewer to 6 more)**	⊕◯◯◯ Very low
Infection and inflammatory reaction due to internal joint prosthesis, 90 days											
1	observational studies	not serious	not serious	not serious	serious[a]	none	7/1478 (0.5%)	283/60259 (0.5%)	**RR 1.01 (0.48 to 2.13)**	**0 fewer per 1,000 (from 2 fewer to 5 more)**	⊕◯◯◯ Very low
Infection and inflammatory reaction due to internal joint prosthesis, 1 year											
1	observational studies	not serious	not serious	not serious	serious[a]	none	11/1478 (0.7%)	368/60259 (0.6%)	**RR 1.22 (0.67 to 2.21)**	**1 more per 1,000 (from 2 fewer to 7 more)**	⊕◯◯◯ Very low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Observational study

b. Wide CI crosses no-effect and significant effect thresholds

Table 9: Bariatric surgery before TKA vs TKA only. 2301 Werner 2015 (47)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric before TKA	TKA only	Relative (95% CI)	Absolute (95% CI)	
Major complications at 90 days											
1	observational study	serious[a]	not serious	not serious	serious[b]	none	21/219 (9.6%)	2147/11294 (19.0%)	**RR 0.50** (0.34 to 0.76)	**95 fewer per 1,000** (from 125 fewer to 46 fewer)	⊕◯◯◯ Very low
Minor complications at 90 days											
1	observational study	serious[a]	not serious	not serious	serious[b]	none	33/219 (15.1%)	2556/11294 (22.6%)	**RR 0.67** (0.49 to 0.91)	**75 fewer per 1,000** (from 115 fewer to 20 fewer)	⊕◯◯◯ Very low
VTE at 90 days											
1	observational study	serious[a]	not serious	not serious	serious[b]	none	14/219 (6.4%)	675/11294 (6.0%)	**RR 1.07** (0.64 to 1.78)	**4 more per 1,000** (from 22 fewer to 47 more)	⊕◯◯◯ Very low
Infections at 90 days											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bariatric before TKA	TKA only	Relative (95% CI)	Absolute (95% CI)	
1	observational study	serious[a]	not serious	not serious	serious[b]	none	4/219 (1.8%)	560/11294 (5.0%)	**RR 0.37** (0.14 to 0.98)	**31 fewer per 1,000** (from 43 fewer to 1 fewer)	⨁◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Retrospective, nonrandomized, no blinding

b. Single study

Table 10: Weight loss vs BMI>40.

Bibliography: 4756 Middleton 2022.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Weight loss	BMI>40	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[a]	none	3/106 (2.8%)	4/96 (4.2%)	**RR 0.68** (0.16 to 2.96)	**13 fewer per 1,000** (from 35 fewer to 82 more)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Weight loss	BMI>40	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[a]	none	5/106 (4.7%)	1/96 (1.0%)	**RR 4.53** (0.54 to 38.07)	**37 more per 1,000** (from 5 fewer to 386 more)	⨁◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds

Table 11: BMI comparisons in OA patients undergoing TJR

Bibliography: 4798 Gritsyuk 2021; 4835 Goh 2022; 4850 Mukka 2020; 5016 Tabalabai 2021; 4848 Dowsey 2022; 5053 Wu 2022; 5098 Kim 2022.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
Total post-surgical complications, prospective, BMI 35-39 vs 30-35											
1	observational studies	not serious	not serious	not serious	serious[a]	none	2/29 (6.9%)	1/16 (6.3%)	**RR 1.10** (0.11 to 11.25)	**6 more per 1,000** (from 56 fewer to 641 more)	⨁◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
Total post-surgical complications, prospective, BMI 40-49 vs 35-39											
1	observational studies	not serious	not serious	not serious	serious[a]	none	14/37 (37.8%)	4/29 (13.8%)	**RR 2.74** (1.01 to 7.45)	**240 more per 1,000** (from 1 more to 890 more)	⊕◯◯◯ Very low
Prosthesis dislocations, prospective, BMI>40 vs BMI 35-39											
1	observational studies	not serious	not serious	not serious	serious[a]	none	2/37 (5.4%)	0/29 (0.0%)	**RR 3.95** (0.20 to 79.16)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low
Late aseptic loosening, prospective, BMI>40 vs BMI<35											
1	observational studies	not serious	not serious	not serious	serious[a]	none	2/37 (5.4%)	0/29 (0.0%)	**RR 3.95** (0.20 to 79.16)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low
Periprosthetic fractures, prospective, BMI>40 vs 35-39											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[a]	none	3/37 (8.1%)	0/29 (0.0%)	**RR 5.53** (0.30 to 102.90)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low

HHS score, BMI>40 vs BMI 35-39, prospective, 12 months

1	observational studies	not serious	serious[a]	not serious	not serious	none	47	183	-	MD **6.7 lower** (11.79 lower to 1.61 lower)	⨁◯◯◯ Very low

HHS score, retrospective, BMI>40 vs BMI 35-39, 12 months

1	observational studies	not serious	serious[a]	not serious	serious[b]	none	47	183	-	MD **1.3 lower** (86.84 lower to 84.24 higher)	⨁◯◯◯ Very low

Physical functioning by SF-36, BMI>40 vs BMI 35-39, retrospective, 12 months

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	serious[a]	not serious	serious[b]	none	47	183	-	MD **1.5 lower** (26.94 lower to 23.94 higher)	-

Physical functioning by SF-36, BMI 35-39 vs BMI 26-34, prospective, 12 months

1							29	16	-	MD **1.7 lower** (7.87 lower to 4.47 higher)	-

Total post-surgical complications, retrospective, BMI 35-39 vs 30-35

1	observational studies	not serious	not serious	not serious	not serious	none	24/183 (13.1%)	5/450 (1.1%)	**RR 11.80** (4.57 to 30.46)	**120 more per 1,000** (from 40 more to 327 more)	⊕⊕◯◯ Low

Total post-surgical complications, retrospective, BMI 40-49 vs 35-39

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[a]	none	45/47 (95.7%)	24/183 (13.1%)	**RR 7.30** (5.00 to 10.65)	**826 more per 1,000** (from 525 more to 1,000 more)	⨁◯◯◯ Very low

Deep SSI, BMI 35-39 vs BMI 30-35, retrospective

1	observational studies	not serious	not serious	not serious	serious[a]	none	3/183 (1.6%)	2/450 (0.4%)	**RR 3.69** (0.62 to 20.56)	**12 more per 1,000** (from 2 fewer to 87 more)	⨁◯◯◯ Very low

Deep SSI, BMI 35-39 vs BMI 30-35, prospective

1	observational studies	not serious	not serious	not serious	serious[a]	none	4/29 (13.8%)	1/16 (6.3%)	**RR 2.21** (0.27 to 18.10)	**76 more per 1,000** (from 46 fewer to 1,000 more)	⨁◯◯◯ Very low

Deep SSI, BMI 40-49 vs BMI 35-39, retrospective

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	not serious	none	4/47 (8.5%)	3/183 (1.6%)	**RR 5.19** (1.20 to 22.40)	**69 more per 1,000** (from 3 more to 351 more)	⊕⊕◯◯ Low

Deep SSI, BMI 40-49 vs BMI 35-39, prospective

1	observational studies	not serious	not serious	not serious	serious[a]	none	3/37 (8.1%)	2/29 (6.9%)	**RR 1.18** (0.21 to 6.58)	**12 more per 1,000** (from 54 fewer to 385 more)	⊕◯◯◯ Very low

Prosthesis dislocations, retrospective, BMI>40 vs BMI 35-39

1	observational studies	not serious	not serious	not serious	not serious	none	5/47 (10.6%)	3/183 (1.6%)	**RR 6.49** (1.61 to 26.18)	**90 more per 1,000** (from 10 more to 413 more)	⊕⊕◯◯ Low

Aseptic loosening, retrospective, BMI >40 vs BMI 35-39

1	observational studies	not serious	not serious	not serious	not serious	none	12/47 (25.5%)	7/183 (3.8%)	**RR 6.67** (2.78 to 16.02)	**217 more per 1,000** (from 68 more to 575 more)	⊕⊕◯◯ Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
Superficial SSI, prospective, BMI >40 vs BMI 35-39											
1	observational studies	not serious	not serious	not serious	serious[a]	none	3/37 (8.1%)	1/29 (3.4%)	**RR 2.35** (0.26 to 21.44)	**47 more per 1,000** (from 26 fewer to 705 more)	⊕◯◯◯ Very low
Superficial SSI, retrospective, BMI 35-39 vs BMI 30-35											
1	observational studies	not serious	not serious	not serious	serious[a]	none	3/183 (1.6%)	1/450 (0.2%)	**RR 7.38** (0.77 to 70.46)	**14 more per 1,000** (from 1 fewer to 154 more)	⊕◯◯◯ Very low
Prosthesis dislocations, prospective, BMI>35-39 vs BMI 30-35											
1	observational studies	not serious	not serious	not serious	serious[a]	none	3/183 (1.6%)	0/450 (0.0%)	**RR 17.16** (0.89 to 330.52)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low
Late aseptic loosening, prospective, BMI 35-39 vs BMI 30-35											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	not serious	none	7/183 (3.8%)	0/450 (0.0%)	**RR 36.77** (2.11 to 640.44)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕◯◯ Low

Periprosthetic fractures, prospective, BMI 35-39 vs 30-35

1	observational studies	not serious	not serious	not serious	serious[a]	none	3/183 (1.6%)	0/450 (0.0%)	**RR 17.16** (0.89 to 330.52)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low

Superficial SSI, retrospective, BMI 40-49 vs BMI 35-39

1	observational studies	not serious	not serious	not serious	not serious	none	5/47 (10.6%)	3/183 (1.6%)	**RR 6.49** (1.61 to 26.18)	**90 more per 1,000** (from 10 more to 413 more)	⊕⊕◯◯ Low

Superficial SSI, prospective, BMI 35-39 vs BMI 30-35

1	observational studies	not serious	not serious	not serious	serious[a]	none	1/29 (3.4%)	1/16 (6.3%)	**RR 0.55** (0.04 to 8.24)	**28 fewer per 1,000** (from 60 fewer to 453 more)	⊕◯◯◯ Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
KOOS-JR, BMI 35-39 vs 26-34, 6 months											
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	258	423	-	MD **1.4 lower** (5.31 lower to 2.51 higher)	⨁◯◯◯ Very low
KOOS-JR, BMI > 40 vs 35-39, 6 months											
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	115	258	-	MD **4.9 higher** (0.16 lower to 9.96 higher)	⨁◯◯◯ Very low
SF-12 physical, BMI 35-39 vs 26-34, 6 months											
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	258	423	-	MD **0.5 lower** (1.99 lower to 0.99 higher)	⨁◯◯◯ Very low
SF-12 physical, BMI >40 vs 35-39, 6 months											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	115	258	-	MD **0.9 higher** (1.11 lower to 2.91 higher)	⊕◯◯◯ Very low

SF-12 mental, BMI 35-39 vs 26-34, 6 months

1	observational studies	not serious	not serious	serious[a]	not serious	none	258	423	-	MD **2.3 lower** (3.64 lower to 0.96 lower)	⊕◯◯◯ Very low

SF-12 mental, BMI >40 vs 35-39, 6 months

1	observational studies	not serious	not serious	not serious	serious[b]	none	115	258	-	MD **1.3 higher** (0.6 lower to 3.2 higher)	⊕◯◯◯ Very low

Hip pain, 12 months, BMI 35-39 vs BMI 26-34

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	not serious	serious[b]	none	2899	12036	-	MD **0.01 higher** (0.02 lower to 0.04 higher)	⨁◯◯◯ Very low

Hip pain, 12 months, BMI>40 vs BMI 35-39

1	observational studies	not serious	not serious	not serious	serious[a]	none	612	2899	-	MD **0.01 lower** (0.07 lower to 0.06 higher)	⨁◯◯◯ Very low

EQ-5D-3Lindex, 12 months, BMI 35-39 vs BMI 26-34

1	observational studies	not serious	not serious	serious[a]	not serious	none	2899	12036	-	MD **0.03 lower** (0.04 lower to 0.02 lower)	⨁◯◯◯ Very low

EQ-5D-3Lindex, 12 months BMI>40 vs BMI 35-39

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	serious[a]	not serious	none	612	2899	-	MD **0.02 lower** (0.04 lower to 0)	⨁◯◯◯ Very low

EQ VAS, 12 months, BMI 35-39 vs BMI 26-34

1	observational studies	not serious	not serious	serious[a]	not serious	none	2899	12036	-	MD **2.9 lower** (3.76 lower to 2.04 lower)	⨁◯◯◯ Very low

EQ VAS, 12 months, BMI >40 vs BMI 35-39

1	observational studies	not serious	not serious	serious[a]	not serious	none	612	2899	-	MD **2.4 lower** (4.1 lower to 0.7 lower)	⨁◯◯◯ Very low

HHS score, retrospective, BMI 35-39 vs BMI 26-34, 12 months

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	183	450	-	MD **0.6 lower** (121.8 lower to 120.6 higher)	⊕◯◯◯ Very low

HHS score, BMI 35-39 vs BMI 26-34, prospective, 12 months

1	observational studies	not serious	not serious	serious[a]	serious[b]	none	29	16	-	MD **1.4 lower** (84.5 lower to 81.7 higher)	⊕◯◯◯ Very low

Physical functioning by SF-36, BMI 35-39 vs BMI 26-34, retrospective, 12 months

1	observational studies	not serious	not serious	serious[a]	serious[b]	none	183	450	-	MD **2.6 lower** (40.52 lower to 35.32 higher)	⊕◯◯◯ Very low

Physical functioning by SF-36, BMI>40 vs BMI 35-39, prospective, 12 months

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BMI	BMI	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	37	29	-	MD **1.5 lower** (26 lower to 23 higher)	⨁◯◯◯ Very low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. No weight reduction, just a comparison of outcomes in patients with different BMI

b. Wide CI crosses no-effect and significant effect thresholds

Table 12. Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan for PICOs 7 – 9.

PICO 7

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results (if not reported indicate so)
2706 Lee 2018 (48)	Retrospective case-control (Medicare 5% Part B data)	3 years	Patients who underwent primary THA (n = 47,895) and	0.1% of patients underwent prior bariatric surgery within 24 months of primary THA/TKA 0.1%	5. At 1, 2, and 5 years of follow-up, primary TKA patients who previously underwent bariatric surgery had a 4.3 (SD or range not provided, p = 0.003), 3.6 (SD or range not provided, p = 0.004), and 3.4 (SD or range not provided, p

			primary TKA (n = 86,609)		=0.003) times greater risk of revision for any reason. 6. Bariatric surgery prior to THA was positively correlated with increased risk for postoperative infections. Bariatric surgery patients were associated with 12.8 (SD or range not provided, p = 0.009) 0.5 years, 10.1 (SD or range not provided, p = 0.017) at 1 year, and 7.7 (SD or range not provided, p =0.038) times greater risk of periprosthetic joint infection at 2 years than the nonbariatric surgery patients. *A study provides outcomes after bariatric surgery, no weight loss *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
4101 Correa-Valderrama 2019 (49)	Retrospective cohort	45 days	Number of patients who underwent weight loss prior to TJA: **None** Number of patients who underwent TJA (specify TKA or THA or both): 750	Description of Weight Loss Intervention: Provide Details Regarding Intervention, Mean Weight Loss, Cohort Mean BMI pre- and post-intervention No intervention Patients stratified into groups by BMI <25 (n=187, 24.9%) 25-29.9 (n=313, 41.7%)	1. Infection (Peri- and post-operative) 45 days: HR 6.08 (0.75-49.16) p=0.090 [infectious: type not specified] 45 days: HR 2.81 (0.32-24.51) p=0.349 [wound: type not specified] 2. Overall complications: Weight Loss v. Immediate TJA (%) at 45 days: HR 1.49 (0.72-3.06) p=0.282

			THA: 268, TKA: 482 FOR EACH COHORT % Female, Mean Age, Mean BMI (range) THA: 60.2y (+/- 14.6), 61.6% female, 26.4kg/m2 (+/- 4.0) TKA: 67.6y (+/- 10.1), 75.7% female, 28.9 mg/m2 (+/- 4)	30-39.9 (n=250, 33.4%)	*The outcomes of mortality, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care are not reported.
3898 Hung 2019 (50)	Retrospective cohort	30 days	Number of patients who underwent weight loss prior to TJA: None Number of patients who underwent TJA (specify TKA or THA or both) 1565 THA	Description of Weight Loss Intervention: Provide Details Regarding Intervention, Mean Weight Loss, Cohort Mean BMI pre- and post-intervention No intervention Patients stratified into groups by BMI <18.5 (n=56) 18.5-24.99 (n=697)	1. Overall complications at 30 days: Weight Loss vs. Immediate TJA (%) 30 days: 8.9% vs 2.4% (p>0.05, specific value not reported) 30 days: OR 2.415 (0.742-7.862) p=0.143 2. Length of hospital stay: Weight Loss v. Immediate TJA (mean or median, IQR, CI or range, p value) Mean 3.69 vs 3.58 days (p>0.05, specific value not reported)

			BMI <18.5 47.0y (+/-16.8) 58.9% female 17.35kg/m2(+/-1.28) BMI 18.5-25 54.6y (+/-14.6) 58.5% female 22.57kg/m2(+/-1.66) BMI 25-29.99 57.5y (+/- 13.2) 46.3% female 27.21 mg/m2 (+/- 1.41) BMI 30-34.99 56.0y (+/- 14.0) 49.4% female 31.95 mg/m2 (+/- 1.29) BMI 35+ 57.2y (+/- 12.2) 64.4% female	25-29.99 (n=609) 30-34.99 (n=158) 35+ (n=45)	*The outcomes of mortality, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care are not reported.

			37.60 mg/m2 (+/- 2.94)		
4069 Keulen 2021 (51)	Retrospective cohort	90 days	Number of patients who underwent weight loss prior to TJA: None Number of patients who underwent TJA (specify TKA or THA or both): 525 TKA=277 (53%) THA=90 (17%) UKA=158 (30%) Not stratified by procedure type or BMI 63y (+/-7.6) 49% female 28 kg/m2(+/- 4.1)	Description of Weight Loss Intervention: Provide Details Regarding Intervention, Mean Weight Loss, Cohort Mean BMI pre- and post-intervention No weight loss intervention All patients were planned for same day discharge, stratified into those that did vs did not get discharged same day On multivariable analysis, investigated association between BMI and 90-day complication and readmission rates	1. Overall complications: Weight Loss vs. Immediate TJA (%): 90 days: OR 0.39 (0.11-1.5) 2. Hospital Readmissions: Weight Loss vs. Immediate TJA (%): 90 days: OR 0 (no readmissions occurred) *The outcomes of mortality, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care are not reported.
1040 Roos 2016 (52)	Retrospective study	All patients had > 90 days' follow-up	Non-obese (BMI < 30 kg/m2, n = 512); obese (BMI 30 kg/m2	All patients had TKA	BMI 30 to 39 kg/m2 (n = 748): Mean LOS, days (SD) 2.5 (1.0) 1. Mean procedure time, mins (SD) 73.2 (20.2)

			to 39.9 kg/m2, n = 748); and morbidly obese (BMI > 40 kg/m2, n=354		2. Mean in- room time, mins (SD) 126.7 (33.3) 3. Unexpected ICU admission, n (%) 7 (0.9) 4. Discharge to facility, n (%) 256 (34.2) 5. Transfusion, n (%) 23 (3.1) 6. DVT or PE during admission, n (%) 5 (0.7) 7. ED visit within 90 days, n (%) 77 (10.3) 8. Readmission in 90 days, n (%) 30 (4.0) 9. Return to operating room in 90 days, n (%) 25 (3.3) 10. Aseptic revision in 1 yr, n (%) 0 11. Septic revision in 1 yr, n (%) 2 (0.3) 12. Mortality in 1 yr, n (%)2 (0.3)
5016 Tabalabai 2021	Cohort study	Length of stay at least 2 days	1262 patients aged 65+ Obesity Class 1 (BMI 30-35), Obesity Class 2 (BMI 35-40), Obesity Class 3 (BMI >40)	Hip 311 (24.64%) Knee 290 (22.98%) Spine 661 (52.38%) surgery	1. Postoperative complications incident risk ratio (IRR): BMI 30-35 1.11 [0.83,1.46], BMI 35-40; 1.21 [0.80,1.78]; BMI >40: 1.86 [1.16,2.86] 2. Length of stay (IRR): BMI 30-35: 1.04 [0.96-1.13]; BMI 35-39: 1.15 [1.02-1.29]; BMI >40: 1.08 [0.92-1.27]
5053 Wu 2022 (some outcomes reported in gradepro)	Retrospective study	90 days	Class 2 [BMI: 35.0-39.9] n=346, Class 3 [BMI: 40.0-67.0] n=90. BMI loss>5% n=90, BMI change<5% n=242, BMI gain >5% n=99	Total hip arthroplasty BMI loss>5% (does not specify BMI group)	Predictors of Postoperative Clinical Outcomes: 1. 90-d emergency room visit in Preoperative BMI loss>5% OR 1.10(0.50-2.56), p=0.817 2. 90-d hospital readmission in Preoperative BMI loss>5% OR 0.59(0.23-1.57), p=0.274 3. PJI Preoperative BMI gain>5% in Preoperative BMI loss>5% OR 0.37(0.11-1.24), p=0.097 4. Revision in Preoperative BMI loss>5% OR 0.94(1.32-3.17), p=0.914 5. Facility discharge Preoperative BMI loss>5% OR 0.71(0.34-1.45), p=0.363
5098 Kim 2022	Retrospective study	1 year	3058 patients who had primary TKA,	Total knee arthroplasty	1. Postoperative results as OR of BMI loss >5% relative to No change in weight: All-Cause

(some outcomes reported in gradepro)			384 had preoperative weight loss >5%, 1999 had no change	BMI loss>5% (does not specify BMI group)	Revision: 1.38 (0.64-2.75), p=0.378; Prosthetic Joint Infection 1.45 (0.57-3.27), p=0.398 2. Adjusted Multivariable Logistic Regression for Predictors of 90-d Hospital Returns for BMI loss >5% in relation to No-change group (OR(CI))::: 90-d ED Visit 1.99(1.41-2.79), p<0.001; 90-d Readmission 1.43(0.94-2.13), p=0.088 3. Adjusted Multivariable Logistic Regression for Predictors of All-Cause Revision and PJI for BMI loss >5% in relation to No-change group (OR(CI)): All-Cause Revision 1.38 (0.64-2.75), p=0.378; Prosthetic Joint Infection 1.45 (0.57-3.27), p=0.398

PICO 8

Ref ID, Author, year	**Study type (e.g., RCT)**	**Mean Follow-Up (Range)**	**Population Description**	**Treatment given to relevant population**	**Results (if not reported indicate so)**
3080 Wang 2019 (44)	Retrospective case-control (**data in revman**)	3 years	THA patients, 2540 patients with morbid obesity are paired with the same number of patients with bariatric surgery by formula A (consists of age, gender, income,	Bariatric surgery	For THA patients, most outcomes between the morbid obesity group and the bariatric surgery group showed no statistical difference after matching by formula A, except for: 1. pulmonary embolism (OR 0.22, 95% CI 0.05-1.03, P =.0346), 2. blood transfusion (OR 1.76, 95% CI 1.52-2.03, P < 0.0001), 6. anemia (OR 1.16, 95% CI 1.031.31, P = 0.0147), and length of stay (morbid obesity: 3.34 days vs bariatric surgery: 3.14 days, P =0.0079).

			primary payer, and race). for TKA patients, 9803 pairs of patients with morbid obesity and patients with bariatric surgery were matched by formula A.		Similarly, after matching by formula B, incidences of 7. blood transfusion (OR 1.63, 95% CI 1.421.88, P < .0001) and 8. anemia (OR 1.23, 95% CI 1.09-1.39, P =0.0008) were more prevalent in the bariatric surgery group, but 9. length of stay was higher in the morbid obesity group (morbid obesity: 3.26 days vs bariatric surgery:3.14 days, P = 0.0278). * For THA patients, most outcomes between the morbid obesity group and the bariatric surgery group showed no statistical difference after matching by formula A *A study provides outcomes after bariatric surgery, no weight loss *Data for mortality, length of hospital stay after surgery, infection, deep vein thrombosis, pulmonary embolism were used in Review Manager *The outcomes of complications, hospital readmissions, emergency department visits, reoperations, revisions, admission to higher level of care, and discharge to long-term care facility all are not reported.

2931 Reeves 2021 (53)	Retrospective cohort	Min 3 months (no mean or range reported	Number of patients who underwent weight loss prior to TJA: Unknown 52% (n=26) of BMI 50+, 21.7% (n=50) of BMI 40-49.9 received weight management referral Number of patients who underwent TJA (specify TKA or THA or both) TJA = 106 (TKA/THA not reported separately) Mean BMI (range) <u>BMI 40-49.9</u> Age mean/range not reported	Description of Weight Loss Intervention: Provide Details Regarding Intervention, Mean Weight Loss, Cohort Mean BMI pre- and post-intervention No specific weight loss intervention. Variable proportion of patients received 'weight loss referral'. unclear exactly what that involved, or impact of this intervention. But authors did say that 'only one patient with clinically meaningful weight loss attended their weight management referral' Comparison was between patients with BMI 40-49.9 vs those with BMI 50+ (means not reported)	1. Venous thromboembolic disease (within 30 days, within 90 days): Time range not reported: 10% vs 0% (for PE only, p value not reported) 2. Overall complications at X months: Weight Loss v. Immediate TJA (%): Time range not reported: 10% vs 4.2% (p=0.423) 3. Infection at X months: Weight Loss v. Immediate TJA (%): Time range not reported: 0% vs 3.1% (type of infection not specified, p value not reported) *The outcomes of mortality, complications, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care are not reported.

			76.5% female BMI mean not reported <u>BMI 50+</u> Age mean/range not reported 86% female BMI mean not reported		
1040 Roos 2016 (52)	Retrospective study	All patients had > 90 days' follow-up	Non-obese (BMI < 30 kg/m2, n = 512); obese (BMI 30 kg/m2 to 39.9 kg/m2, n = 748); and morbidly obese (BMI > 40 kg/m2, n=354	All patients had TKA	1. BMI ≥ 40 kg/m2 (n = 354): 2. Mean LOS, days (SD) 2.8 (2.0) 3. Mean procedure time, mins (SD) 81.8 (20.4) 4. Mean in- room time, mins (SD) 139.6 (26.6) 5. Unexpected ICU admission, n (%) 6 (1.7) 6. Discharge to facility, n (%) 170 (48.0) 7. Transfusion, n (%) 16 (4.5) 8. DVT or PE during admission, n (%) 2 (0.6) 9. ED visit within 90 days, n (%) 37 (10.5) 10. Readmission in 90 days, n (%) 18 (5.1) 11. Return to operating room in 90 days, n (%) 11 (3.1) 12. Aseptic revision in 1 yr, n (%) 2 (0.5) 13. Septic revision in 1 yr, n (%) 0 14. Mortality in 1 yr, n (%) 0
4745 DeMik 2022	Retrospective study	8 years	234,334 patients who underwent THA and 16,979 (7.8%)	THA	Patients with BMI 40 kg/m2 were at significantly higher odds for readmission, reoperation, and infectious complications. 1. Readmission: BMI<40 uOR=0.78 (0.68-0.9), p=0.0005 aOR=0.74(0.64-0.85), p<.0001;

			had BMI 40 kg/m2.		2. BMI>40 uOR=0.71 (0.48-1.05), p=.0902; aOR 0.65(0.44-0.96), p=0.0283; Change BMI<40 vs BMI>40 uOR=0.91(0.60-1.38), p=0.6645; aOR=0.87(0.58-1.32), p=0.5253. 3. Reoperation: BMI<40 uOR=0.82(0.68-0.99), p=0.0375, aOR=0.79(0.66-0.95), p=0.0121; BMI>40 uOR=0.92(0.58-1.47), p=0.7287; aOR=0.86(0.54-1.37), p=0.5234; Change BMI<40 vs BMI>40 uOR=1.12(0.68-1.85), p=0.6547; aOR=1.09(0.66-1.80), p=0.7384. 4. Wound complications BMI<40 uOR=0.97(0.78-1.22), p=0.8088, aOR=0.94(0.75-1.17), p=0.5787; BMI>40 uOR=1.07(0.66-1.73), p=0.7980, aOR=1.01(0.62-1.64), p=0.9597; Change BMI<40 vs BMI>40 uOR=1.10(0.64-1.86), p=0.7387; aOR=1.08(0.63-1.84),p=0.7812 5. Deep infection BMI<40: uOR=1.07(0.70-1.64), p=0.7620, aOR=0.87(0.43-1.80), p=0.7195; BMI>40: uOR=0.93(0.45-1.91), p=0.8461, aOR=1.03(0.67-1.58), p=0.8861; Change BMI<40 vs BMI>40 uOR=0.87(0.38-2.01), p=0.7477, aOR=0.85(0.37-1.96), p=0.7024 6. Any complication BMI<40: uOR=0.22(0.21-0.24), p=0<.0001; aOR=0.20(0.19-2.22), p=<.0001; BMI>40 uOR=0.36(0.29-0.46), p<0.0001; aOR=0.32(0.26-0.41), p<0.0001; Change BMI<40 vs BMI>40 uOR=1.65(1.30-2.09), p<0.0001; aOR=1.61(1.27-2.05), p=0.0001 7. Any complication (excluding transfusion) BMI<40 uOR=1.19(1.05-1.34), p=0.0070; aOR=1.12(0.99-1.27), p=0.0737; BMI>40 uOR=1.09(0.77-1.55), p=0.6406; aOR=1.00(0.70-1.43), p=0.9994; Change BMI<40 vs BMI>40 0.92(0.63-1.33), p=0.6472; aOR=0.89(0.61-1.30), p=0.5512

4834 Ryan 2022	Retrospective review	90 days	Bariatric (n = 142) BMI <40 units (n = 142) BMI > 40 units (n = 142)	TKA	1. For bariatric surgery patients, the 1-year survivorship free of reoperation for infection was 97.7% (95.1-100) compared to 100% (100-100) in the low BMI group and 99.3% (97.8-100) in the high BMI group. 2. For bariatric surgery patients, the 1-year survivorship free of reoperation for instability was 98.4% (96.2-100) compared to 100% (100-100) in both the low and high BMI groups. 3. The hazard ratios for complications of bariatric patients relative to low BMI (HR 2.1, 95% CI 0.8-5.7, p=0.16) and high BMI (HR 1.1, 95% CI 0.5-2.7, p=0.77) patients were not significantly different at 90 days of their TKA. 4. The 10-year survivorship free of any revision was 74% (95% confidence interval [CI] 64-85%) in the bariatric group vs 92% (95% CI 86-98%) in the low BMI and 95% (95% CI 89-100%) in the high BMI group. 5. Patients with persistent BMI 40 were not at significantly higher risk of any revision (HR 0.5, 95% CI 0.2-1.3, p =0.10), or any reoperation (HR 0.7, 95% CI 0.3-1.4, p =0.30). 6. Bariatric surgery patients had a greater reoperation risk than the low BMI (HR 2.2, 95% CI 1.2-4.0, P < .01) and high BMI (HR 6.4, 95% CI 2.7-15.6, P < .01) cohorts. 7. Risk of reoperation for instability was higher in the bariatric surgery patients than the low (HR 14.8, 95% CI 0.7-316.3, p=0.01) and high BMI (HR 16.7, 95% CI 0.8-356.4, p < .01) groups.
4904 Ryan 2022	Retrospective study	1 year	88 primary THA procedures in 71 patients who previously	THA	1. Survivorship free of reoperation at 1 year: BS group 92.8% (86.2-99.9), BMI<40 98.3% (95-100); BMI>40 93% (86.6-99.9). 2. Survivorship free of revision at 1 year: BS group 90.8% (83.4-98.9), BMI<40 100% (100-100), BMI>40 96.4% (81.7-100)

			underwent bariatric surgery		The 90-Day Complication-Free Rates After Total Hip Arthroplasty: 3. DVT Bariatric 100%, BMI<40 97.7% (94.5-100), BMI<40 100% 4. PE Bariatric 100%, BMI<40 100%, BMI<40 100%. 5. Dehiscence Bariatric 100%, BMI<40 95% (90.4-99.9), BMI<40 96.1% (91.9-100). 6. Dislocation Bariatric 95.1% (89.7-100), BMI<40 100%, BMI<40 100%. 7. Delayed healing Bariatric 97.4% (93.9-100), BMI<40 92.7% (87.2-98.5), BMI<40 98.8% (96.5-100). 8. Superficial infection Bariatric 98.6% (95.9-100), BMI<40 96.3% (92.2-100), BMI<40 100% 9. Deep infection Bariatric 97.4% (94-100), BMI<40 97.5% (94.1-100), BMI<40 98.4% (95.4-100)
5012 Dowsey 2022	Retrospective study	1 year follow-up	2177 patients who had undergone THR between 2012 and 2019	THR	Compared to BMI <40kg/m^2 as a reference, a BMI >40kg/m^2 had unadjusted OR=1.87 (CI 1.18-2.98), p=0.008, and adjusted OR=1.89 (CI 1.16-3.07), p=0.010 as a predictor of non-response to surgery

PICO 9

Ref ID, Author, year	**Study type (e.g., RCT)**	**Mean Follow-Up (Range)**	**Population Description**	**Treatment given to relevant population**	**Results (if not reported indicate so)**
3928 Liu 2018 (54)	Retrospective cohort analysis	1 year	Patients with obesity and BS Prior to TJA (N=1478)	Bariatric Surgery (no additional details provided)	1. Complications: Total Infections at 30 days 1.15%; at 90 days 1.28%; 1 year 10%; Infection and inflammatory reaction due to internal joint prosthesis at 30 days 0.47%; at 90 days 0.47%; at 1 year 0.74%

			Female 10.10%		Other postoperative infection at 30 days 0.68%; at 90 days 0.81%; at 1 year 0.81% Other complications due to internal joint prosthesis at 30 days 0.14%; 90 days 0.14%, 1 year 0.2% 2. Non-elective readmission rates at 30 days: 5.62%; 90 days: 7.05%; 1 year: 13.9% All-cause Hospital Readmissions at 30 days: 6.5%; 90 days: 9.61%; 1-year: 22.6% 3. Revisions at 30 days 0.34%; at 90 days 0.41%; at 1 year 0.95% 4. Bariatric surgery prior to THA was positively correlated with increased risk for postoperative infections. Bariatric surgery patients were associated with 12.8 (P = 0.009) 0.5 years, 10.1 (P = 0.017) at 1 year, and 7.7 (P =0.038) times greater risk of periprosthetic joint infection at 2 years than the nonbariatric surgery patients. *A study provides outcomes after bariatric surgery, no weight loss *The outcomes of mortality, emergency department visits, reoperations, deep vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.

PICO 10: In our defined population with poorly controlled diabetes mellitus, what is the relative impact of delaying arthroplasty to improve glycemic control versus proceeding to arthroplasty on patient-important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of evidence:

A systematic review of the literature did not identify any evidence that directly answered this PICO question; therefore, we loosened our inclusion criteria to include other studies evaluating outcomes after total joint arthroplasty in diabetics stratified by markers of severity (e.g., HbA1c). There were 23 observational studies (55-77) that were used as indirect evidence; there were no randomized trials. The overall certainty of evidence was very low due to indirectness.

The definition of controlled vs. uncontrolled diabetes mellitus was not homogenous across studies. Controlled diabetes mellitus vs. uncontrolled diabetes mellitus was defined as HbA1c<7% vs. HbA1c≥7% in 4 studies (Harris 2013 (55), Marchant, 2009 (56), Na 2020 (57), McVey 2020 (58)), preoperative blood glucose <110 vs. 110-199 in 1 study (Mraovic 2010 (59)), preoperative blood glucose <110 vs. >199 in 1 study (Mraovic 2010 (59)), HbA1c<7% vs. HbA1c7%-8% in 1 study (Godshaw 2018 (60)), HbA1c<7% vs. HbA1c >8% in 1 study (Godshaw 2018 (60)), HbA1c<7.5% vs. HbA1c>7.5% in 1 study (Kavin 2021 (61)), HbA1c<7% vs. HbA1c≥7% in 1 study (Shohat 2017 (62)), HbA1c<7%vs. HbA1c>7% at 12 weeks in 1 study (Shohat 2019 (63)) and fructosamine <293umol/l vs. >293umol/l at 12 weeks in 1 study (Shohat 2019 (63)). These studies were all suitable for RevMan analysis. In the group of studies utilizing HbA1c to define controlled vs. uncontrolled diabetes mellitus, there were statistically significant differences favoring the controlled group for readmissions and overall complications in most studies. There was one paper that demonstrated no statistically significant differences between the groups for all outcome measures (Shohat 2019 (63)). In the studies that utilized preoperative blood glucose levels, it was demonstrated that patients with a blood glucose >200 had statistically significant increased risk of in-hospital pulmonary embolism, however, this was independent of the diagnosis of diabetes mellitus. The paper utilizing fructosamine as a marker, demonstrated that patients with fructosamine levels <293umol/l had favorable statistically significant differences for PJI, readmission, reoperation, and mortality.

Of those studies not suitable for RevMan abstraction, there were 4 observational/cohort studies (Chrastil 2015 (64), Cancienne 2017 (65), Cancienne 2017 (66), Jamsen 2012 (67)), 7 restrospective studies (Han 2013 (68), Lavernia 2016 (69), Adams 2013 (70), Chun 2014 (71), Kallio 2015 (72), Kremers 2017 (73), Webb 2017 (74)), 4 prospective studies (Rajamaki 2015 (75), Shohat 2019 (63), Tarabichi 2017 (76), Tew 2019 (77)). These papers demonstrated significant heterogeneity of markers, thresholds, and outcomes measures limiting their overall utility.

Overall impression: The observational studies that address our question would compare the results in uncontrolled diabetes who went to surgery directly versus those in whom surgery was delayed. None of the papers examined the outcomes in those who underwent surgery immediately versus those who were delayed, they simply show an association between glucose level and outcome. This is the reason we rate down for indirectness in each case.

Overall Quality of Evidence: Very low

Table 1: Controlled DM compared to uncontrolled DM (HbA1c<7% vs HbA1c≥7%). 5589 Harris 2013 (55), 5686 Marchant, 2009 (56), 5680 Na 2020 (57), 5424 McVey 2020 (58)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Controlled DM	Uncontrolled DM	Relative (95% CI)	Absolute (95% CI)	
Mortality, 90 days											
2	observational studies	not serious	not serious	serious[a]	not serious	none	268/109446 (0.2%)	56/6100 (0.9%)	**RR 0.33 (0.24 to 0.44)**	**6 fewer per 1,000 (from 7 fewer to 5 fewer)**	⊕⊕◯◯ Very Low
Infection											
2	observational studies	not serious	not serious	serious[a]	not serious	none	880/183668 (0.5%)	81/7140 (1.1%)	**RR 0.43 (0.34 to 0.53)**	**6 fewer per 1,000 (from 7 fewer to 5 fewer)**	⊕◯◯◯ Very low
Deep vein thrombosis											

1	observational studies	not serious	not serious	serious[a]	serious[b]	none	40/105485 (0.0%)	3/3973 (0.1%)	**RR 0.50 (0.16 to 1.62)**	**0 fewer per 1,000 (from 1 fewer to 0 fewer)**	⊕◯◯◯ Very low

Length of hospital stay

1	observational studies	not serious	not serious	serious[a]	not serious	none	105485	3973	-	MD **0.86 lower (0.98 lower to 0.73 lower)**	⊕◯◯◯ Very low

Overall complications, 30 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	281/3961 (7.1%)	185/2127 (8.7%)	**RR 0.82 (0.68 to 0.97)**	**16 fewer per 1,000 (from 28 fewer to 3 fewer)**	⊕◯◯◯ Very low

TKA Hospital readmissions, 90 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	77137/78183 (98.7%)	3126/3167 (98.7%)	**RR 1 (1 to 1)**	**0 fewer per 1,000 (from**	⊕◯◯◯ Very low

										0 fewer to 0 fewer)	

TKA Overall complications, 90 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	1931/78183 (2.5%)	137/3167 (4.3%)	**RR 0.57 (0.48 to 0.68)**	**19 fewer per 1,000 (from 22 fewer to 14 fewer)**	⊕◯◯◯ Very low

TKA Pulmonary embolism at 30 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	504/78183 (0.6%)	35/3167 (1.1%)	**RR 0.58 (0.41 to 0.82)**	**5 fewer per 1,000 (from 7 fewer to 2 fewer)**	⊕◯◯◯ Very low

THA Hospital readmissions, 90 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	26956/27227 (99.0%)	931/940 (99.0%)	**RR 1.00 (0.99 to 1.01)**	**0 fewer per 1,000 (from 10 fewer**	⊕◯◯◯ Very low

										to 10 more)	

THA Overall complications, 90 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	1006/27227 (3.7%)	53/940 (5.6%)	**RR 0.66 (0.50 to 0.86)**	**19 fewer per 1,000 (from 28 fewer to 8 fewer)**	⊕◯◯◯ Very low

THA Infection, 90 days

1	observational studies	not serious	not serious	serious[a]	serious[b]	none	240/27227 (0.9%)	14/940 (1.5%)	**RR 0.59 (0.35 to 1.01)**	**6 fewer per 1,000 (from 10 fewer to 0 fewer)**	⊕◯◯◯ Very low

THA Pulmonary embolism at 30 days

1	observational studies	not serious	not serious	serious[a]	not serious	none	83/27227 (0.3%)	10/940 (1.1%)	**RR 0.29 (0.15 to 0.55)**	**8 fewer per 1,000 (from 9 fewer to 5 fewer)**	⊕◯◯◯ Very low

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Indirectly answers the PICO question
b. Wide CI crosses no-effect and significant effect thresholds

Table 2: Preop BG <110 compared to 110-199. 6347 Mraovic 2010 (59)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Preop BG 110-189	Preop BG <110	Relative (95% CI)	Absolute (95% CI)	
In-hospital pulmonary embolus											
1	observational studies	not serious	serious	not serious	serious[a]	none	31/1797 (1.7%)	69/5347 (1.3%)	**RR 1.34 (0.88 to 2.04)**	**4 more per 1,000 (from 2 fewer to 13 more)**	⨁◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds

Table 3: Preop BG <110 compared to >199. 6347 Mraovic 2010 (59)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Preop BG >199	Preop BG <110	Relative (95% CI)	Absolute (95% CI)	

In-hospital pulmonary embolus (length of follow up not specified)

1	observational studies	not serious	not serious	serious	serious[a]	none	7/138 (5.1%)	69/5347 (1.3%)	**RR 3.93 (1.84 to 8.40)**	**38 more per 1,000 (from 11 more to 95 more)**	⊕◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Less than 200 patients in one group

Table 4: A1c >7 compared to 7-8. 6389 Godshaw 2018 (60)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A1c >7	7-8	Relative (95% CI)	Absolute (95% CI)	
PJI - unknown timeframe											
1	observational studies	not serious	not serious	serious	serious[a]	none	3/151 (2.0%)	12/534 (2.2%)	**RR 0.88 (0.25 to 3.09)**	**3 fewer per 1,000 (from 17 fewer to 47 more)**	⊕◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds

Table 5: A1c >7 compared to >8. 6389 Godshaw 2018 (60)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A1c >7	>8	Relative (95% CI)	Absolute (95% CI)	
PJI - unknown timeframe											
1	observational studies	not serious	not serious	serious	serious[a]	none	4/88 (4.5%)	12/534 (2.2%)	**RR 2.02 (0.67 to 6.13)**	**23 more per 1,000 (from 7 fewer to 115 more)**	⨁◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds

Table 6: A1c > or < 7.5%. 6390 Kavin 2021 (61)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A1c > 7.5%	A1c < 7.5%	Relative (95% CI)	Absolute (95% CI)	
Complications at 3 months											
1	observational studies	not serious	not serious	serious	serious[a]	none	8/111 (7.2%)	23/779 (3.0%)	**RR 2.44 (1.12 to 5.32)**	**43 more per 1,000 (from 4 more to 128 more)**	⊕◯◯◯ Very low
90-day readmission											
1	observational studies	not serious	not serious	serious	serious[a]	none	12/111 (10.8%)	39/779 (5.0%)	**RR 2.16 (1.17 to 4.00)**	**58 more per 1,000 (from 9 more to 150 more)**	⊕◯◯◯ Very low

CI: confidence interval; **RR:** risk ratio

Explanations

a. Less than 200 patients in one group

Table 7: A1c>7 compared to A1c </= 7%. 6710 Shohat 2017 (62)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A1c>7%	</= 7%	Relative (95% CI)	Absolute (95% CI)	
PJI at 3 months											
1	observational studies	not serious	not serious	serious	serious[a]	none	1/50 (2.0%)	13/779 (1.7%)	**RR 1.20 (0.16 to 8.98)**	**3 more per 1,000 (from 14 fewer to 133 more)**	⊕◯◯◯ Very low
Superficial infection at 3 months											
1	observational studies	not serious	not serious	serious	serious[b]	none	8/50 (16.0%)	10/779 (1.3%)	**RR 12.46 (5.15 to 30.19)**	**147 more per 1,000 (from 53 more to 375 more)**	⊕◯◯◯ Very low
All infection at 3 months											
1	observational studies	not serious	not serious	serious	serious[b]	none	12/50 (24.0%)	23/779 (3.0%)	**RR 8.13 (4.30 to 15.37)**	**211 more per 1,000 (from**	⊕◯◯◯ Very low

										97 more to 424 more)	

Medical complications at 3 months

1	observational studies	not serious	not serious	serious	serious[b]	none	12/50 (24.0%)	45/779 (5.8%)	**RR 4.15 (2.35 to 7.34)**	**182 more per 1,000 (from 78 more to 366 more)**	⊕◯◯◯ Very low

Readmission at 3 months

1	observational studies	not serious	not serious	serious	serious[b]	none	8/50 (16.0%)	31/779 (4.0%)	**RR 4.02 (1.95 to 8.28)**	**120 more per 1,000 (from 38 more to 290 more)**	⊕◯◯◯ Very low

Reoperation at 3 months

1	observational studies	not serious	not serious	serious	serious[b]	none	8/50 (16.0%)	29/779 (3.7%)	**RR 4.30 (2.07 to 8.91)**	**123 more per 1,000 (from 40 more**	⊕◯◯◯ Very low

										to 294 more)	

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds and less than 200 patients in one group

b. Less than 200 patients in one group

Table 8: Patients with HbA1c > 7% compared to HbA1c < 7% at 12 weeks. Study 4740 Shohat 2019 (63).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Patients with HbA1c > 7%**	**HbA1c < 7%**	**Relative (95% CI)**	**Absolute (95% CI)**	
PJI											
1	observational studies	not serious	not serious	serious	serious[a]	none	2/69 (2.9%)	10/1050 (1.0%)	**RR 3.04 (0.68 to 13.62)**	**19 more per 1,000 (from 3 fewer to 120 more)**	⊕◯◯◯ Very low
Wound complication											
1	observational studies	not serious	not serious	serious	serious[a]	none	0/69 (0.0%)	8/1050 (0.8%)	**RR 0.88 (0.05 to 15.15)**	**1 fewer per 1,000**	⊕◯◯◯ Very low

										(from 7 fewer to 108 more)	

Readmission

1	observational studies	not serious	not serious	serious	serious[a]	none	4/69 (5.8%)	31/1050 (3.0%)	**RR 1.96 (0.71 to 5.40)**	**28 more per 1,000 (from 9 fewer to 130 more)**	⊕◯◯◯ Very low

Reoperation

1	observational studies	not serious	not serious	serious	serious[a]	none	2/69 (2.9%)	20/1050 (1.9%)	**RR 1.52 (0.36 to 6.38)**	**10 more per 1,000 (from 12 fewer to 102 more)**	⊕◯◯◯ Very low

Mortality

1	observational studies	not serious	not serious	serious	serious[a]	none	0/69 (0.0%)	2/1050 (0.2%)	**RR 3.00 (0.15 to 61.95)**	**4 more per 1,000 (from 2 fewer**	⊕◯◯◯ Very low

										to 116 more)	

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds

Table 9: Patients with high fructosamine > 293 µmol/l (n = 60) compared to low fructosamine < 293 µmol/l (n = 1059) at 12 weeks. Study ID 4740 Shohat 2019 (63).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Patients with high fructosamine > 293 µmol/l (n = 60)**	**Low fructosamine < 293 µmol/l (n = 1059)**	**Relative (95% CI)**	**Absolute (95% CI)**	
PJI											
1	observational studies	not serious	not serious	serious[a]	not serious	none	4/60 (6.7%)	6/1059 (0.6%)	**RR 11.77 (3.41 to 40.58)**	**61 more per 1,000 (from 14 more to 224 more)**	⊕◯◯◯ Very low
Wound complication											

1	observational studies	not serious	not serious	serious[a]	serious[a]	none	0/60 (0.0%)	8/1059 (0.8%)	**RR 1.02 (0.06 to 17.50)**	**0 fewer per 1,000 (from 7 fewer to 125 more)**	⊕◯◯◯ Very low

Readmission

1	observational studies	not serious	not serious	serious[a]	not serious	none	6/60 (10.0%)	25/1059 (2.4%)	**RR 4.24 (1.81 to 9.93)**	**76 more per 1,000 (from 19 more to 211 more)**	⊕◯◯◯ Very low

Reoperation

1	observational studies	not serious	not serious	serious[a]	not serious	none	4/60 (6.7%)	16/1059 (1.5%)	**RR 4.41 (1.52 to 12.79)**	**52 more per 1,000 (from 8 more to 178 more)**	⊕◯◯◯ Very low

Mortality

1	observational studies	not serious	not serious	serious[a]	serious[a]	none	1/60 (1.7%)	1/1059 (0.1%)	**RR 17.65 (1.12 to 278.75)**	**16 more per 1,000**	⊕◯◯◯ Very low

										(from 0 fewer to 262 more)	

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses significant effect and non-significant effect thresholds

Table 10. Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan for PICOs 10

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results (if not reported indicate so)
5823,Chrastil, 2015 (64)	Observational/ cohort	2 years (2y follow up part of the study)	VA (VINCI) database, primary TKA and primary THA with diabetes Total (THA and TKA combined): 13272 (median age 64.0, 4% female, mean BMI 35.4) THA: 3582 (27%), TKA 9690 (73%), age, gender, BMI not reported based on THA vs TKA	Descriptive study of PJI risk, no delays related to A1C	1. Mortality at 2 years: 4.4% overall (589) a. A1C>7 HR 1.3 (CI 1.083-1.564, p=0.01) vs A1C<7 b. Preop glucose >194 HR 1.371 (CI 1.103-1.703, p=0.004) vs preop glucose <194 2. Infection at 2 years: 2.5% overall (328) a. A1C>7 HR 0.860 (CI 0.677-1.1, p=0.230) vs A1C<7 b. Preop glucose >194 HR 1.443 (CI 1.099-1.894, p=0.018) vs preop glucose <194 *The outcomes of hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5835, Cancienne 2017 (65)	Observational/ cohort	1 year (per database)	PearlDiver database primary THA with a diagnosis of DM	Stratified 1y postop deep infection following THA requiring surgical intervention by A1C	Deep infection requiring surgical intervention at 1 year: a. Low of 0.7% for A1C 5.9 to 5.9% for A1C >11.5, curve included below if it is useful

			7736 THA pts with DM and A1C preop (%female, mean age, mean BMI not reported)		b. Infection rate for A1C over 7.5 was 2.4% (21) vs. below 7.5 at 1.0% (69), AUC 0.68, CI 0.59-0.76, p=0.001. *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5836 Cancienne, 2017 (66)	Observational/ cohort	1 year	Primary TKA from PearlDiver database, with database vs without Diabetes: 17435 (62.1% female, most common age 70-79 years 43.85%, mean age not reported, mean BMI not reported) Non-diabetes: 25,105 (61.42% female, most common age 70-79 years 42.53%, mean age not reported, mean BMI not reported)	Compare deep infection requiring surgical intervention at 1 year	Deep infection requiring surgical intervention at 1 year: a. Low of 0.8% for A1C 5.49 to 3.5% for A1C >11.5, graph included below if it is useful b. Infection rate for A1C over 8 was 1.6% (41) vs. below 8 at 0.98% (147), AUC 0.548, CI 0.5-0.59, p=0.025. *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6124, Jamsen, 2012 (67)	observational/c ohort	1 year	7181 primary THA and TKAs at single institution in Finland THA 3266 (median age 68.7, 26.4-95.0; 43.4% of patients with BMI 25-29, 53.9% female) TKA 3915 (median age 72.2, 38.3-97.1; 39.6% of patients with BMI 25-29, 72.2% female)	Stratified infection risk by preop glucose levels and diabetes medication	Periprosthetic infection at 1 year: a. Overall rate 0.64% THA (16), 0.79% (31) TKA (p=0.459) i. THA infection with preop DM: 2.19% vs without 0.48%, adjusted OR 3.49 (CI 1.06-11.47)-*unable to calculate number since THA with preop DM not reported* ii. TKA infection with preop DM: 1.59% vs without 0.66%, adjusted OR 1.85 (CI 0.75-4.58)- *unable to calculate number since TKA with preop DM not reported* b. Stratified by preop glucose level TKA and THA combined: p=.073 iii. <6.1mmol/L: 0.27% (9)

					iv. 6.1-6.8: 0.28% (4) v. >6.9: 0.77% (8) *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6525, Han 2013 (68)	Retrospective cohort (logistic regression)	3 months	115 diabetic patients with 167 TKR 91% F, mean age 68	TKR No treatment for diabetics	Infection (Peri- and post-operative) – HgA1c ≥ 8% was independent risk factor for risk of postoperative wound complication after TKA after adjusting for BMI, hypertension, volume of blood transfusion, use of antibiotic cement though it was not associated with risk of deep infection. Adjusted odds ratio of 6.07 (1.12-33) *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6388 Lavernia 2016 (69)	Retrospective study of prospectively collected data	5.9 years (range, 2.1-10.7 years	120 primary TJAs (33 hips and 87 knees) were performed by the senior author in 105 type 2 diabetic patients stratified by A1c < or ≥ 7% A1c <7: 61 joints, avg age of 71.6, 70% F, 100% white, BMI avg 32.9, avg A1c 6.3 A1c≥7: 59 joints, avg age of 73, 64%F, 98% white, avg BMI 32.1, A1c avg 8.0	TKR/THR No treatment for diabetics	Length of hospital stay: nonsignificant difference between A1c <7 and >7 (5.12 days and 4.7 days respectively) Arthroplasty outcomes – No significant difference was detected in any of the outcomes (WOMAC pain, stiffness, function, total) for follow up mean 5.9 years, range from 2-10 *The data provided only in graphs with no numbers *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6813 Adams 2013 (70)	Retrospective cohort study	8 years (range not reported)	40,491 patients underwent total knee arthroplasty, 7567 (18.7%) had diabetes (5042 had HbA1c<7%, 2525 had	TKA	**No significant differences in any of the outcomes studied** **1. Revision**: No diabetes OR 1.00;

			HbA1c<7%). Females 64% in non-diabetes, 57.3% in HbA1c<7%, 57% in HbA1c<7% group.		Diabetes HbA1c<7% 1.32, CI 0.99-1.76; Diabetes HbA1c≥7% 1.03, CI 0.68-1.54; **2. Deep infection**: No diabetes 1.00; Diabetes, HbA1c<7% OR 1.31, CI 0.92-1.86; Diabetes, HbA1c≥7% OR 0.55, CI 0.29-1.06; **3. DVT or PE**: No diabetes OR 1.00, Diabetes, HbA1c<7% OR 0.84, CI 0.60-1.17; Diabetes, HbA1c≥7% OR 0.70, CI 0.43-1.13; **4. Incident myocardial infarction**: No diabetes OR 1.00, Diabetes, HbA1c<7% OR 1.92, CI 1.46-2.54 Diabetes,HbA1c≥7% OR 1.40, CI 0.93-2.11 **5. All-cause rehospitalization**: No diabetes1.00, Diabetes, HbA1c<7% OR 1.08, CI 1.00-1.16, Diabetes, HbA1c≥7% OR 0.98, CI 0.88-1.08 *The outcomes of mortality, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

5042 Chun 2014 (71)	Retrospective case-control	26 months after THA	Unilateral primary THA	Evaluated Harris hip score, postoperative complications such as wound problem, surgical site infection, other medical complication, and length of stay in hospital as clinical parameters. Radiographic evaluations were also included to determine loosening, dislocation and osteolysis.	1. Age, DM, waiting days for operation after hospitalization and total days in hospital) were found to have a statistically significant association 2. Dx of DM (P=0.001; odds ratio [OR], 15.13; 95% confidence interval [CI], 3.11-73.67) and total days in hospital (P=0.005; OR, 1.04; 95% CI, 1.01-1.07) were found to be significantly associated with the development of orthopedic complications *The outcomes of mortality, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
4806 Kallio 2015 (72)	retrospective, observational	7.5 mo (3—12mo) after TJA	Two hundred and three patients with and without diabetes (n = 103 and n = 100, respectively) undergoing elective joint arthroplasty were randomly chosen from this cohort. threshold value HbA1c ≥ 8%	Adverse events and LOS quantified during the immediate postoperative period and at the three-, six-, and twelve-month orthopedic surgery follow-up appointment	1. Serum creatinine was significantly greater in DM (P = 0.00121). 2. DM with uncontrolled HbA1c and those with HbA1c < 10%, but not <8%, had higher incidence CAD, hypercholesterolemia, more likely receive ACE inhibitors, ARB. 3. An increase in complication rate was observed in diabetic pts with uncontrolled HbA1c versus pts without DM (P < 0.0001), but this elevated complication rate progressively declined with tighter HbA1c control 4. DM with pre-op uncontrolled HbA1c or HbA1c <10% also required prolonged LOS but the mean length of stay was similar between groups. 5. No diff in incidence of system-specific complications between DM regardless of HbA1c control compared with -DM 6. Significant correlation between (n) of complications per pt and HbA1c (n = 0.339 × HbA1c – 1.46; r = 0.32, P < 0.01). *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, discharge to long-term care facility, and patient-reported outcomes all are not reported.

5248 Kremers 2017 (73)	retrospective cohort	Mean 6.1 years after TJA	7176 primary THA and 8909 primary TKA procedures Dx of DM in 2911 (18%) surgeries with a higher prevalence in TKA (21%) than in THA (15%) procedures (Table 1). A total of 1458 patients received antidiabetic drugs during hospitalization. Glucose testing was performed at least once preoperatively in 3636 (23%) procedures and postoperatively in 3969 procedures, resulting in 7055 (44%) procedures with at least 1 blood glucose measurement ±1 week surgery. Of those, 1964 (28%) were classified as having perioperative hyperglycemia with at least 1 blood glucose value >180 mg/dL.	All blood glucose values around the time of surgery (within 1 week) were retrieved. Subsequent revision surgeries and the reasons for revision were ascertained through the institutional joint registry. Multivariate Cox models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for aseptic loosening associated with diabetes mellitus and hyperglycemia adjusting for age, gender, body mass index, and surgery type.	1. Overall risk of revision was significantly elevated among diabetic pts (HR, 1.27; 95% CI, 1.02-1.58), but there was no excess risk of revision for aseptic loosening (HR, 0.87; 95% CI, 0.55-1.38) (Table 2). 2. Association with the diabetic drugs followed the same pattern. 3. Adjusting for age, gender, surgery type, and BMI, higher pre-op glucose values on the day before surgery were significantly associated with both the overall excess risk of revisions (HR, 2.80; 95% CI, 1.00-7.85) and revisions for aseptic loosening (HR, 4.95; 95% CI, 1.26-19.54). 4. These analyses were based on 40 revisions, of which 11 were aseptic in the cohort of 1056 surgeries with preOp glucose values on the day before surgery. 5. No association with the postop glucose values. 6. Data were limited to examine associations with the HbA1c levels *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5246 Rajamaki 2015 (75)	Prospective concerning perioperative hyperglycemia	18 months (11–28) after TJA	200 patients scheduled for primary hip or knee replacement for osteoarthritis in a single orthopedic hospital Compared to other patients undergoing primary hip or knee	Pain in the operated joint was surveyed 1–2 years after the operation, using a postal questionnaire.	1.Prev dxed DM was a significant risk factor for having persistent pain, but not for having a painful joint 2. Other glucose metabolism disorders and MetS were not associated with a painful joint or persistent pain. 3. higher proportion of severely obese pts had a painful joint than pts with BMI < 30.

			replacement for osteoarthritis in the same hospital during the study period (n = 2,565) in terms of sex (the proportion of females in the study population was 65% as compared to 63% in the other patients; p = 0.6) and in terms of joint operated (the proportion of knee replacements in the study population was 61% as compared to 57% in the other patients; p = 0.3), but the mean age was lower in the study population (66 (SD 9) years vs. 68 (SD 11) years; p = 0.002).		4. The results concerning the effects of DM and severe obesity did not change when ASA score and BMI were added to the adjusted models: OR for persistent pain in pts with prev dxed DM was 20 (CI: 3–132) and OR for a painful joint in severely obese pts was 4 (CI: 1.3–14). 5. Influence of obesity on the prevalence of a painful joint was similar in knee and hip pts. 14 of 39 non-obese knee pts, 11 of 26 obese knee pts, and 11 of 14 severely obese knee pts had a painful joint (p = 0.02), and the corresponding proportions of hip pts were 4/32, 6/15, and 3/7, respectively (p = 0.05). 6. Higher proportion of hip pts with MetS had a painful joint (12/36) than hip pts without MetS (1/18) (p = 0.04). Prev dxed DM was associated with persistent pain in hip pts (2/10 vs. 0/43; p = 0.03) but not in knee pts (3/8 vs. 13/71; p = 0.3). 7.In a post-hoc analysis the statistical power in these analyses (with the probability of type 1-error set to 5%) turned out to be low for both hip and knee replacements: 47% and 83% for the effect of obesity on a painful joint (severely obese vs. non-obese), and 71% and 30% for the effect of DM on persistent pain, respectively. In pts with DM, preOp HbA1c was not associated with a painful joint (7/14 and 13/19 in pts with HbA1c < 6.5% and ≥ 6.5%, respectively; p = 0.3) or persistent pain (3/14 and 3/19; p = 1.0). 8.To study the influence of recovery time on the prevalence of pain, pts categorized into 3 groups based on the length of the follow-up time: < 15 months (55 pts), 15–21 months (51 pts), and > 21 months (28 pts). 9. No statistically significant differences were found in these groups regarding DM, MetS, and different groups of BMI (data not shown). 10. Similar proportions of pts in the different follow-up time groups had a painful joint (20/55, 21/51, and 8/27, respectively; p = 0.6). 11. 10 of the 54 pts with the shortest follow-up time and 8 of the 51 pts with a follow-up time of 15–21 months reported having

					persistent pain, but none of the 27 pts with follow-up time of over 21 months reported having persistent pain (p = 0.04). 12. Poor pain relief was common in pts with prev dxed DM—of whom 3/16 had no improvement (or had more pain) at rest (6/92 among the others; p = 0.1) and 5/17 had no improvement (or had more pain) in motion (7/93 among the others; p = 0.02). MetS and obesity were not associated with poor pain relief (data not shown). *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
4740 Shohat 2019 (63)	Prospective Cohort; Multi-institutional	90 days after TJA (THA + TKA)	Fructosamine<293: N=1059 Fructosamine>=293: N=60 Number of patients who underwent TJA (specify TKA or THA or both) =**1119** FOR EACH COHORT % Female = 60.7% in the 1st group and 58.3% in the 2nd group. Mean Age= 65.3yrs in both Groups Mean BMI (range): 1st Group 31.2; 2nd Group 31.9.	- Patients (DM and non-DM) were assessed using fructosamine and HbA1c levels within 30 days of surgery. - Complications were assessed for 12 weeks from surgery and included prosthetic joint infection (PJI), wound complication, re-admission, re-operation, and death. - Mean HbA1c level was 5.8% (4.0% to 10.8%) and the mean fructosamine level was 239.0 µmol/l (105 to 403).	1.The adverse outcomes seen in the elevated fructosamine group remained significant for PJI (p < 0.01), re-admission (p = 0.01), and re-operation (p = 0.03) after controlling for potential confounders, including Op time, length of hospital stay, BMI, 2. Elixhauser comorbidity score, and ASA in a multiple regression analysis 3. Mortality rates too low to assess in a regression model. *The outcomes of hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

5228 Tarabichi 2017 (76)	Prospective cohort. Multi-institutional	0-90 days after TJA	1645 diabetic patients undergoing 1004 TKAs and 641 THAs with an average HbA1c level of 6.6% (range, 4.6-13.2)	The primary outcome of interest was PJI at 1 year. Patients who may have developed PJI were identified using the ICD-9 and ICD-10 diagnosis codes. The medical records of patients with PJI were then verified ensuring that they met the Musculoskeletal Infection Society criteria for the diagnosis of PJI [17] . Other complications were categorized as orthopedic and medical. Orthopedic complications included wound complications at 90 days and mechanical complications at 1 year. Nonorthopedic complications were all assessed at 90 days and included sepsis, venous thromboembolism, genitourinary complications, and cardiovascular complications.	1.PJI was the only complication associated with higher HbA1c levels 2. The threshold for HbA1c predictive of PJI to be 7.7% (95% confidence interval [CI], 6.25-8.05; Youden index, 0.38, cut point, 0.019). 3. 18 (10.1%) dxed with mechanical complications at 1 year. 4. Although younger age (OR, 0.95; CI, 0.91- 1.00; P 1⁄4 .03) and female gender (OR, 0.29; CI, 0.09-0.90; P 1⁄4 .03) were statistically significantly associated with mechanical complications, 5. HbA1c only showed a trend toward significance (OR, 1.3; CI, 0.97-1.88; P 1⁄4 .07). 6. No 90-day complications were seemed to be associated with HbA1c levels. 7. Higher HbA1c levels slightly correlated with wound complications (OR, 1.2; CI, 0.9-1.2; P 1⁄4 .14). 8. Elixhauser comorbidity score had large effect on wound complications 9. Overall 82 pts (5.0%) had e complications at 90 days, no association be- tween the cumulative 90-day complications and the HbA1c levels (OR, 0.9; CI, 0.7-1.2; P 1⁄4 .6). 10. LOS associated variables: Op time (P < .0001), age (P < .0001), HbA1c (P 1⁄4 .03), Elixhauser score (P 1⁄4 .06), and gender (0.09) in descending order of significance. *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5079	Prospectively cohort	5 years after TKR	1553 TKR patients were included in the analysis	Multilevel modelling was used to analyze long-term QoL patterns of patients	1. DM report lower QoL (on average by 0.028, p < 0.001) and did not improve to the same level as pts without the disease

Tew 2019 (77)			n = 319 with DM	undergoing TKR between 2006 and 2011. Patient-reported QoL at baseline and up to 5 years post-surgery were included.	2. Females significantly lower QoL (by 0.030, p < 0.001) compared to males. 3. Impact of DM on QoL much more pronounced in females than males. 4. Females with and without DM have the same level of improvement up to 1 year post-surgery, however, their QoL trajectories diverge in subsequent years, resulting in a significant difference in QoL between those with and without DM. 5. Contrarily, among males, those with DM achieve less improvement at 1-year post-surgery than those without DM but this difference reduces in subsequent years. 6. Subgrouping by HbA1c and med. types did not reveal any statistically significant differences in QoL trends among pts with DM. *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5110 Webb 2017 (74)	retrospective cohort; American College of Surgeons National Surgical Quality Improvement Program database	0-30 days after TKA	A total of 114,102 patients who underwent TKA were selected (IDDM = 4881 [4.3%]; NIDDM = 15,367 [13.5%]; and no DM = 93,854 [82.2%]).	Patients who underwent TKA between 2005 and 2014 were identified and characterized as having insulin-dependent DM (IDDM), non–insulin-dependent DM (NIDDM), or not having DM. Multivariate Poisson regression was used to control for demographic and comorbid factors and to assess the relative risks of multiple adverse events	1.Compared to -DM, NIDDM had increased RR for MI (RR ¼ 1.67; 99.7% CI ¼ 1.01-2.77; P ¼ .002) and extended LOS (RR ¼ 1.42; CI ¼ 1.28-1.57; P < .001). 2.Compared with -DM, IDDM increased RR for sepsis or septic shock (RR ¼ 2.42; CI ¼ 1.38-4.23; P < .001), MI (RR ¼ 2.71; CI ¼ 1.38-5.33; P < .001), renal failure (RR ¼ 4.66; CI ¼ 1.78-12.22; P < .001), ventilator time >48 hours (RR ¼ 2.88; CI ¼ 1.07-7.74; P ¼ .001), unplanned intubation (RR ¼ 2.45; CI ¼ 1.21-5.01; P < .001), renal insufficiency (RR ¼ 3.03; CI ¼ 1.48-6.19; P < .001), return to the operating room (RR ¼ 1.51; CI ¼ 1.09- 2.09; P < .001), wound dehiscence (RR ¼ 2.04; CI ¼ 1.04-3.98; P ¼ .001), readmission (RR ¼ 1.65; CI ¼ 1.35-2.01; P < .001), pneumonia (RR ¼ 2.47; CI ¼ 1.48-4.12; P < .001), urinary

				in the initial 30 postoperative days.	tract infection (RR 1⁄4 1.53; CI 1⁄4 1.05-2.20; P < .001), and extended LOS (RR 1⁄4 1.99; CI 1⁄4 1.72-2.31; P < .001). 3. Of note, not only were many more adverse events associated with IDDM than with NIDDM when compared with pts without DM, the RRs of MI and extended LOS were greater for pts with IDDM than for pts with NIDDM (MI: RR 1⁄4 2.71 vs 1.67, respectively; and extended LOS: RR 1⁄4 1.99 vs 1.42, respectively). *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

PICO 11: In our defined population with nicotine dependence, what is the relative impact of delaying arthroplasty for nicotine cessation versus proceeding to arthroplasty on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of evidence:

A systematic review of the literature identified twenty-five studies that answered our PICO question. Only one study (78) directly answered our PICO question and was used as direct evidence. The remaining twenty-four studies looked at the influence of smoking on outcome after total joint arthroplasty (TJA) and were used as indirect evidence. The overall certainty of evidence was low due to indirectness and imprecision.

There was one randomized trial (Moller 2002 (78)) with moderate quality of evidence (imprecision). It reported statistically significant differences in favor of non-smoking in regard to the risk of overall complications, wound infections, non-orthopaedic unit days, ICU days, and overall length of stay; all showed strong effects using number needed to treat analysis.

Six observational studies were appropriate for Revman abstraction (Agrawal 2021 (79), Khan 2009 (80), Singh 2015 (81), Duchman 2015 (82), Malik 2004 (83), Moller 2003 (84)). With low quality of evidence, four papers collectively demonstrated statistically significant differences in favor of non-smoking for both deep and superficial infections, three for one-year revision rates, two for all complications and hospital length of stay, and one each for infection within 30 days, ICU admissions, and 30-day mortality. One paper demonstrated a confounding lower length of stay for smokers.

Of those not appropriate for Revman abstraction, there was one prospective case control study (Ehnert 2019 (85)), three retrospective case control studies (Baier 2019 (86), Matharu 2019 (87), Yao 2017 (88), Nwachukwu 2015 (89)), eleven various single center and registry retrospective cohort studies (Halawi, 2019 (90), Matharu 2019, Bernstein 2018 (91), Gonzalez 2018 (92), Lim, 2017 (93), Bohl 2016 (94), Minhas 2016 (95), Kopp 2015 (96), Kremer 2015 (97), Maoz, 2015 (98), Sadr Azodi 2006 (99)), one cross sectional cohort study (Winemaker, 2015 (100)), and two observational cohort studies (Jorgensen 2013 (101), Lavernia 1999 (102)). The majority of the papers favored non-smoking with a low level of evidence.

Overall impression: One study directly compared patients randomized to smoking intervention vs. no intervention prior to arthroplasty. However, overall numbers were small, with only 52 and 56 patients analyzed for outcomes. Other included studies simply demonstrated an association between smoking and outcomes. This is why we rate down for indirectness and imprecision.

Quality of the evidence: Low

Table 1: Smoking cessation vs Usual Care for TJA. 5384 Moller 2002 (78).

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smoking cessation	Control	Relative (95% CI)	Absolute (95% CI)	
Overall complications, up to 65 days (discharge)											
1	randomized trial	not serious	not serious	not serious	serious[a]	none	10/56 (17.9%)	27/52 (51.9%)	**RR 0.34** (0.19 to 0.64)	**343 fewer per 1,000** (from 421 fewer to 187 fewer)	⊕⊕⊕◯ Moderate
Wound-related infection, up to 65 days											
1	randomized trial	not serious	not serious	not serious	serious[a]	none	2/56 (3.6%)	12/52 (23.1%)	**RR 0.15** (0.04 to 0.66)	**196 fewer per 1,000** (from 222 fewer to 78 fewer)	⊕⊕⊕◯ Moderate
UTI, up to 65 days											
1	randomised trial	not serious	not serious	not serious	serious[b]	none	5/56 (8.9%)	6/52 (11.5%)	**RR 0.77** (0.25 to 2.38)	**27 fewer per 1,000** (from 87 fewer to 159 more)	⊕⊕⊕◯ Moderate
Secondary surgery - total replacement, up to 65 days											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smoking cessation	Control	Relative (95% CI)	Absolute (95% CI)	
1	randomised trial	not serious	not serious	not serious	serious[b]	none	2/56 (3.6%)	8/52 (15.4%)	**RR 0.23** (0.05 to 1.04)	**118 fewer per 1,000** (from 146 fewer to 6 more)	⊕⊕⊕◯ Moderate

Secondary surgery - vascular, up to 65 days

1	randomised trial	not serious	not serious	not serious	serious[b]	none	1/56 (1.8%)	1/52 (1.9%)	**RR 0.93** (0.06 to 14.47)	**1 fewer per 1,000** (from 18 fewer to 259 more)	⊕⊕⊕◯ Moderate

Secondary surgery - wound-related, up to 65 days

1	randomised trial	not serious	not serious	not serious	serious[b]	none	1/56 (1.8%)	7/52 (13.5%)	**RR 0.13** (0.02 to 1.04)	**117 fewer per 1,000** (from 132 fewer to 5 more)	⊕⊕⊕◯ Moderate

Total days in non-orthopedic department, up to 65 days

1	randomised trial	not serious	not serious	not serious	serious[a]	none	2/56 (3.6%)	49/52 (94.2%)	**RR 0.04** (0.01 to 0.15)	**905 fewer per 1,000** (from 933 fewer to 801 fewer)	⊕⊕⊕◯ Moderate

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smoking cessation	Control	Relative (95% CI)	Absolute (95% CI)	
Days in ICU, up to 65 days											
1	randomised trial	not serious	not serious	not serious	serious[a]	none	2/56 (3.6%)	32/52 (61.5%)	**RR 0.06** (0.01 to 0.23)	**578 fewer per 1,000** (from 609 fewer to 474 fewer)	⨁⨁⨁◯ Moderate
Days in medical or surgical departments, up to 65 days											
1	randomised trial	not serious	not serious	not serious	serious[a]	none	0/56 (0.0%)	17/52 (32.7%)	**RR 0.03** (0.00 to 0.43)	**317 fewer per 1,000** (from 186 fewer to --)	⨁⨁⨁◯ Moderate

CI: confidence interval; **RR:** risk ratio

Explanations

a. Single study

b. Single study, 95% CI includes the possibility of no difference

Table 2: **Non-smokers compared to smokers. 4870 Agrawal 2021 (79), 5121 Khan 2009 (80), 5197 Singh 2015 (81), 5391 Duchman 2015 (82), 5327 Malik 2004 (83), 5389 Moller 2003 (84).**

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Non-smokers	Smokers	Relative (95% CI)	Absolute (95% CI)	
Infection at 30 days											
1	observational studies	not serious	not serious	serious	not serious	none	279/28134 (1.0%)	176/9378 (1.9%)	**RR 0.53 (0.44 to 0.64)**	**9 fewer per 1,000 (from 11 fewer to 7 fewer)**	⊕⊕◯◯ Low
Deep infection											
4	observational studies	not serious	not serious	serious	not serious	none	278/78986 (0.4%)	126/17189 (0.7%)	**RR 0.46 (0.36 to 0.58)**	**4 fewer per 1,000 (from 5 fewer to 3 fewer)**	⊕⊕◯◯ Low
Superficial infection											
4	observational studies	not serious	not serious	serious	not serious	none	647/79568 (0.8%)	224/17457 (1.3%)	**RR 0.70 (0.59 to 0.83)**	**4 fewer per 1,000 (from 5 fewer to 2 fewer)**	⊕⊕◯◯ Low
Peri-prosthetic fracture											
1	observational studies	not serious	not serious	serious	serious[a]	none	134/7361 (1.8%)	10/565 (1.8%)	**RR 1.03 (0.54 to 1.94)**	**1 more per 1,000 (from 8**	⊕◯◯◯ Very low

										fewer to 17 more)	

Aseptic loosening

1	observational studies	not serious	not serious	serious	serious[a]	none	49/137 (35.8%)	10/25 (40.0%)	**RR 1.02 (0.66 to 1.41)**	**8 more per 1,000 (from 136 fewer to 164 more)**	⊕◯◯◯ Very low

All complications

2	observational studies	not serious	not serious	serious	not serious	none	3568/64550 (5.5%)	560/8294 (6.8%)	**RR 0.87 (0.79 to 0.94)**	**9 fewer per 1,000 (from 14 fewer to 4 fewer)**	⊕⊕◯◯ Low

Urinary tract infection

1	observational studies	not serious	not serious	serious	serious[a]	none	31/579 (5.4%)	17/232 (7.3%)	**RR 0.74 (0.41 to 1.29)**	**19 fewer per 1,000 (from 43 fewer to 21 more)**	⊕◯◯◯ Very low

ICU admission

1	observational studies	not serious	not serious	serious	not serious	none	4/579 (0.7%)	9/232 (3.9%)	**RR 0.18 (0.05 to 0.58)**	**32 fewer per 1,000 (from 37 fewer to 16 fewer)**	⊕⊕◯◯ Low

Revision surgery (within 1 year)

3	observational studies	not serious	not serious	serious	not serious	none	137/8857 (1.5%)	33/1065 (3.1%)	**RR 0.52 (0.35 to 0.79)**	**15 fewer per 1,000 (from 20 fewer to 7 fewer)**	⊕⊕◯◯ Low

Extended length of stay

1	observational studies	not serious	not serious	serious	not serious	none	2956/18756 (15.8%)	1620/9378 (17.3%)	**RR 0.92 (0.86 to 0.97)**	**14 fewer per 1,000 (from 24 fewer to 5 fewer)**	⊕⊕◯◯ Low

Hospital length of stay

2	observational studies	not serious	not serious	serious	not serious	none	1161	500	-	MD **0.76 higher (0.28 higher to 1.24 higher)**	⊕⊕◯◯ Low

Mortality at 6 months

1	observational studies	not serious	not serious	serious	serious[a]	none	10/821 (1.2%)	1/236 (0.4%)	**RR 2.78 (0.64 to 11.74)**	**8 more per 1,000 (from 2 fewer to 46 more)**	⊕◯◯◯ Very low

Mortality at 30 days

1	observational studies	not serious	not serious	serious			12/6158 (0.2%)	128/8062 (1.6%)	**RR 0.04 (0.03 to 0.06)**	**15 fewer per 1,000 (from 15 fewer to 15 fewer)**	-

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Wide CI crosses significant and non-significant effect thresholds

Table 3: Smoking compared to no smoking, 90 days for TJR outcomes. 7265 Statz 2021.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smoking	No smoking, 90 days	Relative (95% CI)	Absolute (95% CI)	
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	50/3177 (1.6%)	600/44747 (1.3%)	**RR 1.17** (0.88 to 1.56)	**2 more per 1,000** (from 2 fewer to 8 more)	⊕◯◯◯ Very low
1	observational studies	not serious	not serious	serious[a]	not serious	none	184/3177 (5.8%)	1970/44747 (4.4%)	**RR 1.32** (1.14 to 1.52)	**14 more per 1,000** (from 6 more to 23 more)	⊕⊕◯◯ Low
1	observational studies	not serious	not serious	serious[a]	serious[b]	none	335/3177 (10.5%)	4382/44747 (9.8%)	**RR 1.08** (0.97 to 1.20)	**8 more per 1,000** (from 3 fewer to 20 more)	⊕◯◯◯ Very low
1	observational studies	not serious	not serious	serious[a]	serious[b]		12/3177 (0.4%)	190/44747 (0.4%)	**RR 0.89** (0.50 to 1.59)	**0 fewer per 1,000** (from 2 fewer to 3 more)	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. No smoke cessation. Compared to non-smokers.

b. Wide CI crosses no-effect and significant effect thresholds

Table 4: Current smoking compared to ex smoking for TJR outcomes. 7420 Simon 2022.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Current smoking	Ex smoking	Relative (95% CI)	Absolute (95% CI)		
SSI, 6 months												
1	observational studies	not serious	not serious	not serious	serious[a]	none	4/585 (0.7%)	15/4675 (0.3%)	**RR 2.13** (0.71 to 6.40)	**4 more per 1,000** (from 1 fewer to 17 more)	⊕◯◯◯ Very low	

CI: confidence interval; **RR:** risk ratio

Explanations

a. Wide CI crosses no-effect and significant effect thresholds

Table 3: Additional Data from Observational Studies and Randomized Controlled Trials Not Suitable for RevMan for PICOs 11

Ref ID, Author, year	Study type (e.g., RCT)	Mean Follow-Up (Range)	Population Description	Treatment given to relevant population	Results (if not reported indicate so)

5732, Baier 2019 (86)	Retrospective case-control	1 year follow-up on all patients (range not reported)	Patients who underwent primary TKA at single center over 4-year period 2439 primary TKA 68% Female Mean age 69 6.5% over BMI 40	Compared characteristics of patients who experience SSI vs. not within 12 months of surgery	237 patients reported regular smoking (9.7%). 17/237 (7%) had an SSI (RR=2.36, p=0.002) Multivariate analysis independent risk for SSI HR 2.22 (1.27-3.90) p=0.005 *No other data on the smoking cohort *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6757, Ehnert et al., 2019 (85)	Observational cohort Prospective Consecutive series	6 months (not directly reported but all patients included completed a 6-month questionnaire for complications.) (range not reported)	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery 0, no intervention performed Number of patients who underwent TJA (specify TKA or THA or both) 817 patients who underwent TJA included 510 primary TJA and 278 revisions) Overall % Female 359 female 43.7%	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention No smoking intervention performed Preop and 6-month postop interviews to identify complications	1. Mortality at 6 months: 1/510 (.2%) of primary TJA vs 0/278 revisions at 6 months, no comparisons in smokers 2. Complications at 6 months: Compared to non-smokers (17.8 ± 1.9%), the complication rate increased with increasing cigarette consumption (1–20 pack-years (PY): 19.2 ± 2.4% and >20 PY: 30.4 ± 3.6%; p = 0.002). 3. OR for complications increased with increasing Pack years (PY). For primary TJA: (i) >0 PY: OR = 1.601, (ii) >10 4. PY: OR = 1.624, and (iii) >20 PY: OR = 1.875; p = 0.034. 5. For revision TJA: (i) >0 PY: OR = 1.453, (ii) >10 PY: OR = 1.527, and (iii) >20 PY: OR = 2.062; p = 0.015. 6. Infection at 6 months: 14/510 (2.78%) primary TJA developed infection vs 18/278 6.47% revision TJA 7. Deep vein thrombosis at 6 months: 4/510 (0.79% primary TJA developed VTE vs 2/278 (0.72%) revision TJA 8. Length of hospital stay: Delaying to achieve nicotine cessation % v. Immediate TJA % (Mean or Median, IQR, CI or range, p value). Mean LOS was longer in heavy smokers (>20 pack years) (18.4 ± 1.0 day) than non-smokers (15.3 ± 0.5 day; p = 0.009) or moderate smokers (15.9 ± 0.6 day).

			Primary TJA 34.6% female Revision TJA 34.9 % female Mean Age ± SD Primary TJA 62.7 ± 14.8 (61.5-64.0) Revision TJA 60.0 ± 16.3 (58.1-61.9) Mean BMI (SD) Primary TJA: 28.3 ± 5.2 Revision TJA: 28.5 ± 6.1		*Included are those outcomes relevant to smoking. The authors reported on outcomes of revision and primary TJA however they do not make statistical comparisons. Included above are those specifically related to smokers and non-smokers. *The outcomes of hospital readmissions, emergency department visits, reoperations, revisions, admission to higher level of care, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6880, Halawi, 2019 (90)	Single-center cohort	30-year period (range not reported)	Retrospective non-interventional cohort of patients undergoing primary or revision TKA or THA at a single tertiary center. Number of patients who delayed TJA to achieve nicotine cessation prior to surgery: 0 Number of smokers who underwent TKA or THA (no breakdown provided): 951/ 20126	No intervention. Average nicotine use not reported.	Patient-reported outcomes Smokers vs. Non-Smokers (MV linear regression adj. for baseline differences) WOMAC 6mo post-op: -35.8 vs -43.8 (p=0.002) WOMAC 12mo post-op: -38.5 vs -47.2 (p=0.002) SF-12 PCS 6mo post-op 13.0 vs 16.8 p=0.008 SF-12 PCS 12mo post-op 15 vs 18.3 p=0.03 SF-12 MCS 6mo post-op 4.3 vs 1.0 p=0.017 SF-12 MCS 12mo post-op 0.5 vs 0.4 p=0.946 *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep

			Number of never-smokers who underwent TKA/THA: 7678/20126 *No breakdown between smokers and non-smokers* 55% Female Mean Age 66.3 Mean BMI NR		vein thrombosis, admission to higher level of care, length of hospital stay, and discharge to long-term care facility all are not reported.
5390, Matharu 2019 (87)	Retrospective cohort	6-month follow-up on all patients (range not reported)	Patients undergoing primary THA and TKA in UK administrative database over 22-year period 11% smoker, 57% non-smoker, 11% smoker, 33% ex-smoker 60,812 THA Mean age (63 vs. 70 vs 70) Normal BMI (34 vs. 30 vs. 23) Female (59% vs. 67% vs. 51%) 56,212 TKA Mean age (64 vs 70 vs 70)	Evaluated 6-month complications, 1-year mortality, 6-months PROMs (OKS/OHS) between smoker, ex-smoker, non-smoker groups	**THA** 1. Smokers increased risk of death at 1 year (2.5% vs. 1.5% vs. 2%, HR 0.37 (0.29-0.49), no p-value) compared to non- and ex-smoker respectively 2. Revision surgery at 20 years HR 1.1 (0.88-1.5) 3. Infection at 6 months (1.9% vs. 1.7% vs. 1.6%, no p-value) 4. DVT at 6 months (1.6% vs. 1.7% vs. 1.5%, no p-value), PE (0.7% vs. 0.8% vs. 0.8%, no p-value) 5. PROMs Oxford Hip Score (41 vs 43 vs. 42, no p-value) **TKA** 1. Smokers increased risk of death at 1 year (1.1% vs. 0.9% vs. 1.1%, HR = 0.52, CI 0.34–0.81), no p-value) compared to non- and ex-smoker respectively 2. Complications at 6 months (11% vs. 10% vs. 12%, no p-value) 3. 6-month readmissions (13% vs. 13% vs. 15%, no p-value) 4. Revision surgery at 20 years HR 1.2 (0.90-1.6) 5. Infection at 6 months (2.9% vs. 2.8% vs. 3.0%, no p-value) 6. DVT at 6 months (1.5% vs. 1.6% vs. 1.5%, no p-value), PE (0.6% vs. 0.8% vs. 0.9%, no p-value) 7. PROMs Oxford Hip Score (35 vs 38 vs. 37, no p-value)

			Normal BMI (20 vs 17 vs 13) Female (49% vs. 66% vs. 43%)		*The outcomes of complications, hospital readmissions, emergency department visits, reoperations, admission to higher level of care, length of hospital stay, and discharge to long-term care facility were all not reported.
5440, Bernstein 2018 (91)	Retrospective cohort	90-day follow-up (range not reported)	Patients undergoing primary THA and TKA at single center 351 preimplementation (216 TKA, 135 THA) 314 postimplementation (173 TKA, 141 THA) Mean age (65.8 vs. 64.2) Mean BMI (29.4 vs. 29.5) Female (61% vs. 58%)	Compared outcomes before and after implementation of a pre-optimization pathway. Of 228 patients with at least 1 risk factor, 27 patients were current tobacco users who received "informational materials on smoking cessation, and a referral to their primary care physician for medical assistance." Of 228 patients with at least 1 risk factor, 46 individuals were "not optimized, and 182 individuals were "optimized." Number of tobacco users optimized NR.	1. 90-day hospital readmissions: 4 (8.7%) not optimized, 15 (8.2%) optimized, p=0.92 2. Length of hospital stay (mean±SD): 2.1±0.9 not optimized, 2.1±1.3 optimized; p=0.36 3. Discharge to skilled nursing facility: 8 (17.4%) not optimized, 18 (9.9%) optimized; p=0.15 4. Discharge to inpatient rehabilitation facility: 2 (4.3%) not optimized, 5 (2.7%) optimized; p=0.57 5. 12: PROM: NR *The outcomes of mortality, complications, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, and patient-reported outcomes all are not reported.
5837, Gonzalez et al., 2018 (92)	Retrospective cohort (Retrospective review of Prospective instituti	Median 67 months Interquartile range 33-113 months	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery No intervention performed 3 groups Never smokers (5,722), former smokers	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention	1. Mortality at median 67 months: Delaying to achieve nicotine cessation % v. Immediate TJA % No intervention. Overall death rate: 15.4% mortality rate at median 67 months interquartile range 33-106.3, 833 deaths (14.6%) in never smokers, 232 (17.6%) in former smokers, and 257 deaths (16.7%) in current smokers. 123 deaths occurred within 1 year (1.4%). (p values NR) 2. Revisions median 67 months (final follow up): Delaying to achieve nicotine cessation % v. Immediate TJA % (p value) No intervention. Revision for infection 3.4% (289 TJA, 97 knees, 192 hips) revision rate overall, 42 (0.7%) in never smoker

	onal registry 3 cohorts Never smokers Ever smokers Current Smokers		(1,315), active smokers (1,522) Number of patients who underwent TJA (specify TKA or THA or both) 8,559 primary hip and knee replacements 3,361 TKA 5,198 THA % Female 60.5% Ever smoker %female 42.4% Never smoker %female 69.5% Mean Age Never smoker mean age ± SD 71.2 ± 10.7 yrs Ever smoker mean age ± SD 66.1 ± 11.9 yrs Mean BMI (range) Never smoker BMI Mean ± SD 27.9± 5.4 kg/m^2	No intervention performed in study Primary outcome: periprosthetic joint infection after primary total hip or knee replacement	group, 19 (1.4%) in former smoker group, 15 (1.0%) in current smoker group. (p values NR) 3. Infection at 12 months: Delaying to achieve nicotine cessation % v. Immediate TJA % (p value) No intervention performed. Reported on periprosthetic joint infection rate at 1 year: Never smoker 0.47%, former smoker 1.01%, active smoker 1.09%. (p values NR) 4. Risk of infection Ever smoker vs never smoker crude HR 2.35 (95% CI 1.39-3.98), adjusted HR 1.8 (95% CI 1.04-3.2). At final follow up crude HR 1.37 (95% CI 0.78-2.39), adjusted HR 1.12 (95% CI 0.61-2.04; p values NR) 5. During entire study period, 108 PJI's occurred at median 11.4 months follow-up (IQR 1.6-37.8 months). 56 PJI occurred within 1 year postop 26 (0.5%) Never smoker, 30 (1.1% ever smoker), 16 1.1% current smoker, 14 (1.1% former smoker) (p values NR) 6. No significant difference in rate of infection after 1 year 32 PJI in never smokers, 20 in Ever smokers, 10 in former smokers, 10 in current smokers (HR listed above for within 1 year and after 1 year) *The outcomes of complications, hospital readmissions, emergency department visits, reoperations, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

			Ever smoker mean BMI ± SD 27.5 ± 5.2 kg/m^2		
6762, Yue, 2017 (93)	Retrospective registry cohort	10-year period (range not reported)	Patients referred to tertiary center for TKA revision Number of patients who delayed TJA to achieve nicotine cessation prior to surgery: 0 Number of smokers who underwent revision TKAs: 41 *No breakdown between smokers and non-smokers* 55% Female Mean Age 60.7 Mean BMI (SD) 32 (7.5)	No intervention. Average nicotine use not reported.	1. Revisions at 90 months: smokers 37/41, non-smokers 274/357 (p=0.031)- this is the people with early revision (<7.5 years) 2. Infection at 90 months: smokers 10/11; non-smokers 53/68 (p=0.294)- this is infection as a cause of early revision (<7.5 years) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5741, Bohl et al., 2016 (94)	Retrospective cohort	30 days (range not reported)	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery 0, no intervention Number of patients who underwent TJA	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine	1. Mortality at 30 days: Delaying to achieve nicotine cessation % v. Immediate TJA % (p value) Not reported, no intervention. 2. Development of sepsis associated with higher risk of mortality 3.7% vs 0.1% RR 28.4, 95% CI 16.7-48.2, p<0.001) 3. Complications at 30 days: Delaying to achieve nicotine cessation % v. Immediate TJA % (p value) Not reported. 402 patients developed sepsis incidence of 0.34% (95% CI 0.1%-0.37%). Active smoker independent risk factor for developing sepsis 0.43 % vs 0.33 % incidence RR 1.4 95% CI 1.0-1.9, p=0.036, Active smoking identified as independent risk factor

			(specify TKA or THA or both) 45,612 THA, 72,323 TKA FOR EACH COHORT % Female 46,814, 39.7 % Mean Age Not reported (Only age groups reported 4 groups) Mean BMI (range) Not reported (Only 3 BMI groups reported)	use (and/or Packs per day) pre- and post-intervention Not reported. No intervention performed in this study Reported only on active smokers 12,054, 10.2%	for developing pneumonia within 30 days, 0.4% incidence, RR 1.4 95% CI 1.0-1.9, p=0.026 *The outcomes of hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6082, Minhas 2016 (95)	Retrospective cohort (NSQIP registry)	30 days (range not reported)	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery 0, no intervention Analysis of multiple orthopaedic procedures ACDF, Posterior lumbar fusion, THA, TKA, and Total shoulder (44,120 patients) Number of patients who underwent TJA	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention No intervention performed in this study	Current smoking found to be independent risk factor for readmission on multivariate analysis. (OR 1.92 95% CI 1.37-2.69 p<0.001) 1. Overall 30-day readmission rate after THA 3.6% 2. Overall 30-day readmission rate after TKA 3.8% 3. Surgical site complication identified as reason for readmission within 30 days, reported as percentage of those that required readmission THA 106 (31.8%) TKA 189 (34.2%) 4. VTE identified as reason for readmission within 30 days, reported as percentage of those that required readmission 5. THA Readmissions for VTE within 30 days (31, 9.3%) 6. TKA readmission for VTE within 30 days (67, 12.1%)

			(specify TKA or THA or both) 14,295 THA 22,452 TKA FOR EACH COHORT % Female Not reported Mean Age Not reported Mean BMI (range) Not reported		*The outcomes of mortality, emergency department visits, reoperations, revisions, infections, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5671, Kopp 2015 (96)	Retrospective case-control	One-year follow-up on all patients (range not reported)	Patients undergoing primary or revision THA or TKA at single institution 202 with SSI (48 THA, 40 rTHA, 89 TKA, 25rTKA) Matched cohort of 404 non-SSI (96 THA, 80 rTHA, 178 TKA, 50 rTKA) Mean age (65.5 SSI vs. 69 non-SSI) Mean BMI (34.2 vs. 30.3) Gender NR	Evaluated all SSIs over 11-year period and identified risk factors. No data on nicotine other than current smoking status.	1. Risk of any SSI in current smoking patients increased (13% vs. 3%, OR 5.54 (2.59-11.84, p<0.001), multivariate OR 5.10 (2.30-11.33, p<0.001) 2. Risk of deep SSI in current smoking patients increased (14% vs. 3%, multivariate OR 5.86 (2.07-16.83, p<0.001)) 3. Risk of superficial SSI in current smoking increased (9% vs. 3%, multivariate OR 4.29 (1.09-16.92, p=0.038)) *No other data reported *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

6765, Kremer, 2015 (97)	Retrospective single-center registry analysis	1 year (range not reported)	Retrospective non-interventional registry analysis of patients undergoing primary or revision TKA or THA. Non-smokers in this population include ex-smokers. Multivariable adjusted estimates by cox regression: adjusting for age, gender, BMI, calendar year, surgery type, number of prior surgery on same joint, diabetes status, ASA score and procedure duration. Number of patients who delayed TJA to achieve nicotine cessation prior to surgery: 0 Number of smokers who underwent TKA or THA (no breakdown provided): 951/ 20126 Number of never-smokers who underwent TKA/THA: 7678/20126	No intervention. Average nicotine use not reported.	Multivariate linear regression 1. Mortality of current vs never smokers: aHR 2.2 (1.8 – 2.6) 2. Any complication of current vs never smokers: aHR 1.0 (0.9 – 1.1) 3. Reoperations of current vs never smokers aHR 1.1 (0.9 – 1.4) 4. Revisions of smokers vs.never smokers: aHR 1.2 (0.9 – 1.6) 5. Infection of smokers vs. never-smokers: aHR 1.7 (1.1 – 2.6) *Raw numbers not reported. No group of deferred surgery in order to quit surgery. "Current smoking was associated with a significantly higher risk of surgical site infections (HR: 1.7, 95% CI: 1.1–2.6), but not the overall risk of complications, reoperations or revisions. Alcohol use was associated with a significantly lower risk of reoperations and revision surgeries (HR: 0.7, 95% CI: 0.5–0.8)." *The outcomes of hospital readmissions, emergency department visits, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

			Female Sex (smokers vs non-smokers) 47% vs 52% Mean Age (smokers vs non) 55.4 vs 61.2 Mean BMI smokers vs non: 30.6 vs 31		
6169, Maoz et al., 2015 (98)	Retrospective cohort. Single institution registry	Mean 2 years (range 1-4 years)	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery 0, no intervention Number of patients who underwent TJA (specify TKA or THA or both): 3672 THA, 406 revision THA FOR EACH COHORT % Female 1,987 female (48.7%) Mean Age 1,987 Women mean age ± SD of 63.0 (± 13.3) years and 1685 men with a mean age of 60.0 (± 12.6) years. Mean BMI (range)	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention No intervention performed. Primary outcome was periprosthetic joint infection within 1 year of surgery.	Overall incidence of PJI 1.3% within 1 year of primary THA Smoking not an independent risk factor of infection. 447 active smokers, Univariate analysis RR 1.14 95% CI 0.47-2.76 p=0.78 However additive effect of tobacco use plus additional independent risk factor BMI ≥ 40 + tobacco use OR 7.5 (95% CI 1.69-33.4, p=0.03) Revision surgery + tobacco use OR 7.2 (95% CI 2.4-22.2, p=0.004) S. aureus colonization + revision surgery + tobacco use OR 12.2 (95% CI 1.44-103.9, p=0.09) S. aureus colonization + BMI ≥ 30 + tobacco use OR 12.76 (95% CI 2.47-66.16, p=0.017) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, deep vein thrombosis, admission to higher level of care, length of hospital stay, discharge to long-term care facility, and patient-reported outcomes all are not reported.

			Not reported, categorized <30, 30-<40, ≥ 40		
6112, Wine maker, 2015 (100)	Cross section al cohort 1 year at single intuition	Not reported, inpatient only	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery 0, No intervention performed. Number of patients who underwent TJA (specify TKA or THA or both): 1459 patients 559 THA 900 TKA FOR EACH COHORT % Female 841 (57.6%) Median Age 67 (Interquartile range 52-82)	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention No intervention. Purpose of study to identify risk factors for longer length of stay. Divided group into ≤3 days, 4 days, ≥5 days and identified risk factors for prolonged stay	Delaying to achieve nicotine cessation % v. Immediate TJA % (p value) No associated risk of admission to higher level of care in smokers vs. nonsmokers (15.3% v. 10.3%, p = 0.05). Length of stay: current smoker predicted post op shorter LOS < 3 days (4 d: OR 0.425, 95% CI 0.274–0.659 p<0.001; ≥ 5 d: OR 0.489, 95% CI 0.314–0.762, p=0.002) *The outcomes of mortality, complications, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, discharge to long-term care facility, and patient-reported outcomes all are not reported.

			Median BMI (interquartile range) 30.4 (22.4-38.4)		
6195, Jorgensen et al, 2013 (101)	Observational cohort	90 days (range not reported)	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery 0, no intervention Number of patients who underwent TJA (specify TKA or THA or both) 3041 hip and knee replacements (break down hips and knees not reported) 458 15.1% active smokers FOR EACH COHORT % Female 45.8% female in smoking group vs 60.3 % female in nonsmoking group (p<0.001) Mean Age Smokers 64.3 yrs ± SD 10.8 yrs	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention No intervention Primary outcome is complications in setting of fast track recovery program in smokers and ETOH users compared to nonusers.	1. Overall 90-day mortality rate 0.49% 15 patients overall; 2 smokers 0.43% 90 day mortality rate in smokers 2. ≤30 days Readmission rate 8.2% (50/608) in those who smoked or drank vs. 6.2% (151/2433) in those who did neither (P = 0.976). *Smoking was not related to readmissions ≤30 days in univariate analysis (P = 0.233). 3. Increased risk of readmission ≤ 30 days in smokers after adjusting for baseline characteristics [OR: 1.60 (1.05–2.44), P = 0.028] 4. 90-day readmission rate 8.6% (52/608) of smokers/alcohol users vs. 8.0% (195/2433) in those who did neither [OR: 1.07 (0.78–1.48), P = 0.664]. *Smoking did not increase readmissions within 90 days after adjusting for baseline characteristics and alcohol use [OR: 1.17 (0.80–1.73), P = 0.419]. 5. ≤30-day readmission for wound infection smokers/ETOH users 11 (1.81%) vs 36 (1.44%) in non-users 6. ≤90-day readmission for wound infection smokers/ETOH users 2 (0.33%) vs 7 (0.29%) in non-users 7. Deep vein thrombosis at 3 months: 8. ≤30 days smokers/ETOH users 2 (0.33%) vs 9 (0.37%) in nonusers 9. ≤90 days smokers/ETOH users 0 (0%) vs 8 (0.33%) in nonusers 10. Length of hospital stay: No intervention

			Non smokers 68.0 ± SD 10.9 yrs, (p<0.001) Mean BMI (range) Smokers mean: 27.9 (SD: 5.3) vs. 28.5 (SD: 5.1), P = 0.008] non-smokers		*Smoking not associated with increased length of stay > 4 days, univariate logistic regression analysis (P = 0.478) or in multivariate analysis (P = 0.171 and 0.127). *The outcomes of complications, emergency department visits, reoperations, revisions, infection, admission to higher level of care, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5710, Sadr Azodi 2006 (99)	Retrospective cohort	60-day follow-up (range not reported)	Patients who underwent primary THA in Sweden included in Construction Worker Registry 3309 primary THA Mean age 65 Mean BMI 26 (range 18-43) 0% female, all patients male	Compared hospital LOS and 60-day complication rates between smokers, nonsmoker, previous smoker and pack-years	1. Median LOS (9 vs. 10 vs. 9 for current, former, non-smoker, no p-value) 2. Median LOS (10 vs. 10 vs. 9 vs. 9 for 40 PY, 20-40 PY, 0-20 PY, none, no p-value) 3. Systemic complication (9% vs. 9% vs. 7%, p=0.013) 4. Systemic complications for Pack Year (14% vs. 11% vs. 8%, vs7%, p=0.004) *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, revisions, infection, deep vein thrombosis, admission to higher level of care, discharge to long-term care facility, and patient-reported outcomes all are not reported.
6750, Lavernia et al., 1999 (102)	Observational cohort, consecutive series	In hospital only (admission duration only)	Number of patients who delayed TJA to achieve nicotine cessation prior to surgery Number of patients who underwent TJA (specify TKA or THA or both) 141 primary 72%	Description of Delaying to achieve good nicotine cessation/Intervention: Provide Details Regarding the Delay to achieve glycemic control, if there is an Intervention provide detail, Amount of delay, Mean Nicotine use (and/or Packs per day) pre-operative, Cohort Mean Nicotine use (and/or Packs per day) pre- and post-intervention	1. Complications: 16% in smokers vs 22% in non-smokers p=0.3 2. Infection at X months: 0 in smokers vs. 5 (2.8%) in nonsmoker, no p value reported 3. Deep vein thrombosis at X months: 0 in smokers vs 1 (0.56%) in non smokers, no p-value reported 4. Length of hospital stay: No significant difference in LOS smokers 5.44 days vs 5.16 days in non-smokers p=0.36 5. Reported on increased admission cost 35,628 ± 16,899 vs. 30,706 ± 9,506 p=0.032, anesthesia time 225.53 ± 84.84 mins vs 191 ± 60 mins p=0.01 and surgical time 156.7± 92 mins vs.

			61 revision 28% 25 smokers 177 nonsmokers (data not stratified by primary or revision surgery) FOR EACH COHORT % Female 126 female 62.4% Mean Age 66.07± 14.01 yrs, range 22-93 Smokers age 58.31 ± 13.69 Nonsmokers age 66.9 ± 13.55 Mean BMI (range)	No intervention in this study	111.8 ±59.5 mins p=0.001 in smokers compared to nonsmokers. *The outcomes of mortality, hospital readmissions, emergency department visits, reoperations, revisions, admission to higher level of care, discharge to long-term care facility, and patient-reported outcomes all are not reported.
5634 Yao 2017 (88)	Case-control	3 years (records identified 2011-2014)	Number of patients with history of nicotine use prior to surgery: 13,340 THA and TKA pts separated into cohorts of no complication vs severe complication/readmission post-discharge ("SAE" per paper) Number of patients who underwent TJA (specify TKA or THA or both): 50,376 THA; 71,293 TKA THA w/o	No delay to glycemic control or nicotine cessation. Nicotine data is presented as "history of smoking" w/o current status or PPD or PY information. There is also no data on patients w/o nicotine exposure with regards to outcomes. THA w/o adverse events (SAE)6486 (14%) Smoking Hx THA w/ SAE290 (18%) Smoking Hx TKA w/o SAE6263 (9.1%) Smoking Hx TKA w/ SAE301 (12%) Smoking Hx	1. Mortality, out of SAEs: THA 1.3%, TKA: 1.5% 2. Complications OR Readmissions, from overall THA/TKA cohorts: THA 3.1%, TKA 3.5% 3. Hospital Readmissions, out of SAEs: THA 88%, TKA: 78% 4. Reoperations ("return to OR"): THA 35%, TKA: 20% 5. Deep vein thrombosis: THA 12.4%, TKA: 24% 6. Length of hospital stay (total length, mean), THA: 2.8 vs 3.3; TKA: 3.0 vs 3.4 (p<0.001) *Smoking history OR (95% CI), p-value: THA 1.38 (1.20-1.58), p<0.001; TKA 1.43 (1.25-1.63), p<0.001 *multivariate analysis controlling for demographics, comorbidities, pre-discharge SAEs

			adverse events (SAE)51% Female Mean Age 62.66.5% BMI >40 THA w/ SAE50% Female Mean Age 64.511% BMI >40 TKA w/o SAE59% Female Mean Age 65.114% BMI >40 TKA w/ SAE52% Female Mean Age 66.416% BMI >40		*Data is presented as either % events or mean values. For post-discharge SAEs and readmission, the data is presented as % of THA cases w/SAE (n=1575) vs TKA cases w/SAE (n=2490). For pre-discharge SAEs the data is further categorized into controls w/o post-discharge events vs cases w/ events, for THA and TKA groups each. *emergency department visits, revisions, infection, admission to higher level of care (e.g., ICU), discharge to long-term care facility, patient-reported outcome scores are not reported
5388 Nwachukwu 2015 (89)	Case-control	Between 1996 and 2006	146 cases (patients that had primary and revision TKA) were matched to 290 controls (patients with primary TKA that was not revised)	Smokers versus non-smokers	Active smoking status was significantly associated with revision (OR 4.46; 95% CI 2.21-9.03) Smoking was associated strongly with risk of aseptic revision (OR 4.41, 95 % CI 1.67, 11.62) but the data did not support a clinically important relationship of smoking with risk for infectious revision (OR 1.22 95 % CI 0.23, 6.64).
7420 Simon 2022	Retrospective study	6 months	11,680 patients who went through THA or TKA. 585 smokers, 4675 non-smokers	Smokers versus non-smokers	Multivariable logistic regression against surgical site infection (SSI) Smoker versus Non-Smoker OR 3.20 (CI: 1.02−10.03), p=0.047

PICO 12 In our defined population who have bone loss with deformity, or severe ligamentous instability, what is the relative impact of delaying arthroplasty for optimization of non-life-threatening conditions versus proceeding to arthroplasty on patient important outcomes including pain, function, infection, hospitalization, and death at one year?

Summary of Evidence:

There were no studies that either directly or indirectly answered our PICO question.

PICO 13. In our defined population who have a neuropathic joint, what is the relative impact of delaying arthroplasty for optimization of non-life-threatening conditions versus preceding to arthroplasty at one year?

Summary of Evidence:

There were no studies that either directly or indirectly answered our PICO question.

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