National Institute for Health and Care Excellence

Final

Osteoarthritis in over 16s: diagnosis and management

[P] Evidence reviews for outcomes of joint replacement surgery dependent on body mass index

NICE guideline NG226

Evidence reviews underpinning recommendations 1.6.3 to 1.6.4 in the NICE guideline

October 2022

Final

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ISBN: 978-1-4731-4740-9

Contents

1 Joint replacement surgery outcome by BMI

1.1 Review question

Do people with osteoarthritis who are at less than or more than healthy weight have similar outcomes after joint replacement surgery then people of healthy weight?

1.1.1 Introduction

Overweight and obese people with osteoarthritis are often told to lose weight before they will be considered for joint replacement. However, losing weight often requires exercise and people report having difficulty exercising when they have joint pain. Delays caused by attempts to lose weight or being unable to lose weight to reach a pre-defined BMI risks further functional deterioration and worsening of co-existent medical problems, which in itself may worsen outcomes of surgery. Being overweight or obese is determined by a person's BMI but it is not clear that a person with a high BMI will not gain as much or more benefit from joint replacement as a person with healthy weight. It is important to identify whether pre-operative weight does influence the outcome of joint replacement surgery to prevent interventions being undertaken that are harmful but also to reduce unnecessary delays to progression to surgery when this is indicated.

This review aims to determine whether people who are underweight (BMI<18.0), overweight (BMI 25-30) or obese (BMI >30) with osteoarthritis have different outcomes following joint replacement surgery then people who are of normal weight (BMI 18.0-24.9).

1.1.2 Summary of the protocol

Table 1: PICO characteristics of review question

Population	Inclusion:
	• Adults (age ≥16 years) with osteoarthritis affecting any joint who have had joint replacement surgery
	• Stratified by osteoarthritis joint site:
	  ○ Knee
	  ○ Hip
	  ○ Shoulder
	If there is a mixed joint site population we would use an 80% cut-off point.
	
	Exclusion:
	• Children (age <16 years)
	• People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, diseases of childhood that may predispose to osteoarthritis, medical conditions presenting with joint inflammation and malignancy).

Prognostic variables under consideration	• Body mass index before surgery
	  ○ Underweight – BMI <18.0 kg/m^2
	  ○ Healthy weight – BMI 18.5 kg/m^2 to 24.9 kg/m^2
	  ○ Overweight – BMI 25 kg/m^2 to 29.9 kg/m^2
	  ○ Obesity I – BMI 30 kg/m^2 to 34.9 kg/m^2
	  ○ Obesity II – BMI 35 kg/m^2 to 39.9 kg/m^2
	  ○ Obesity III – BMI 40 kg/m^2 or more

Confounding factors	Key confounding factors that may be independently associated with prognostic variables: • Age • Sex All of the key confounders must be adjusted for in a multivariate analysis. Other confounders: • Smoking status • Ethnicity • Presence of comorbidities (ASA, Elixhauser, Charlson, any other validated scales) These confounders will be assessed on a case-by-case basis.
Outcomes	Stratify by ≤/>3 months (longest time-point in each): Critical outcomes: • Mortality [time-to-event or dichotomous outcomes, time-to-event prioritised] • Health-related quality of life [validated patient-reported outcomes, continuous data prioritised] 1. EQ-5D 2. SF-36 3. Any other validated measures • Post-operative patient-reported outcome measure [continuous outcomes] (change scores) (at 6 months or 1 year) ○ Knee osteoarthritis 1. Oxford Knee score 2. KOOS (aggregate score) 3. WOMAC (aggregate score) ○ Hip osteoarthritis 1. Oxford Hip score 2. HOOS (aggregate score) 3. WOMAC (aggregate score) 4. Harris Hip Score ○ Shoulder osteoarthritis 1. Oxford Shoulder Score (OSS) 2. Constant Score 3. Shoulder Pain and Disability Index (SPADI) 4. The Disabilities of the Arm, Shoulder and Hand Score (DASH) • Reoperation or revision to the prosthesis [time to event outcome] Important outcomes: • Total adverse events up to 90 days [dichotomous data] • Surgical site infection (wound infection) [dichotomous data] • Venous thromboembolism [dichotomous data]
Study design	Non-randomised evidence, including: 1. Secondary analyses of RCTs (stratified by weight categories) 2. Prospective and retrospective cohort studies Studies will only be included if all of the key confounders have been accounted for in a multivariate analysis.

For full details see the review protocol in Appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Prognostic evidence

1.1.4.1 Included studies

Five prospective cohort studies[35, 46, 77, 78, 98] and ten retrospective cohort studies[14, 52, 63, 64, 83, 99, 119, 135, 165, 175] were included in the review; these are summarised in below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

Comparisons to all relevant BMI categories were present for people with knee[14, 35, 46, 52, 64, 98, 99, 175] and hip[63, 83, 98, 119, 135, 175] osteoarthritis. Some studies reported outcomes for people with hip and knee osteoarthritis together[77, 78, 165], the outcomes from these studies were reported separately. No relevant clinical studies investigating the effects of different BMI categories before shoulder arthroplasty were identified.

See also the study selection flow chart in Appendix A, study evidence tables in Appendix D, forest plots in Appendix E and GRADE tables in Appendix F.

1.1.4.1.1 Confounding factors

All studies reported outcomes adjusted for the key confounders (age and sex). No studies reported adjusted outcomes for all other confounders. However, some studies accounted for one or more other confounders:

- Smoking status[52, 135, 175]
- Ethnicity[35]
- Comorbidities[14, 63, 64, 83]
- Ethnicity and comorbidities[98]

1.1.4.1.2 Indirectness

The majority of studies included were deemed to have indirect evidence. The reasons for this included:

- Population indirectness – Reporting people requiring joint replacement surgery but not specifying if the population had osteoarthritis (or the proportion of the population that had osteoarthritis)[46, 52, 63, 77]
- Prognostic variable indirectness – Reporting BMI categories that were not those stated in the protocol[14, 35, 77, 78, 99, 175]
- Outcome indirectness:
  - Reporting only some subscales of a scale rather than the aggregate scale (for example: reporting WOMAC pain and physical function subscales, but not WOMAC stiffness subscale and not reporting the aggregate score)[35, 98]
  - Reporting follow up times less than the specified time in the protocol[35]
  - Reporting infection which may include non-wound site infection[63]

1.1.4.1.3 Meta analysis

No studies reported comparable populations and outcomes that could be meta-analysed. Therefore, all outcomes will be considered individually.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the prognostic evidence

Table 2: Summary of studies included in the evidence review

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
Baker 2012[14]	People who underwent knee arthroplasty with relevant information registered in the National Joint Registry (United Kingdom) between May 1, 2008, to September 1, 2010 n=13,673	Multiple linear regressions to adjust the changes.	Group 1 (BMI 15-24.9 kg/m^2) = 1292 (this group will be considered as indirect evidence for normal weight) Group 2 (BMI 25-39.9 kg/m^2) = 11363 Group 3 (BMI 40 to 60 kg/m^2) = 1018	Factors included in the adjusted analysis: age, sex, ASA grade, number of comorbidities and general health rating using multiple linear regressions to adjust the changes.	Health-related Quality of Life – EQ-5D (Index score will be used in the analysis) at >3 months (mean 7 months) Post-operative Patient Reported Outcome Measures - Oxford Knee Score at 1 year (mean 7 months)	Risk of bias: Very high Prognostic variable indirectness (One or more BMI categories include people outside of the categories agreed in the protocol)
Collins 2017[35]	People with primary knee osteoarthritis who underwent total knee arthroplasty (United States of America) n=633	Mixed-effects logistic regression models to make a multivariate model.	Healthy weight* (BMI <25 kg/m^2) = 120 (this group will be considered as indirect evidence for normal weight) Overweight (BMI 25-29.9 kg/m^2) = 203 Obesity I (BMI 30-34.9 kg/m^2) = 174 Obesity II (BMI 35-39.9 kg/m^2) = 79 Obesity III (BMI ≥40 kg/m^2) = 57	Factors included in the adjusted analysis: age, sex, race, diabetes, musculoskeletal functional limitations index, pain medication use and study site.	Post-operative Patient Reported Outcome Measures – WOMAC pain and WOMAC function at 6 months	Risk of bias: High Prognostic variable indirectness (One or more BMI categories include people outside of the categories agreed in the protocol) and outcome indirectness (downgraded twice: WOMAC subscales reported rather than aggregate scores and follow up time less than the

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
						minimum time stated in the protocol)
Evans 2021[46]	People who had a knee replacement operation included in the national joint registry (United Kingdom) from 1 April 2003 to 31 December 2016. n=490351	Multivariate analysis using Cox regression models.	Underweight (BMI <18.5 kg/m^2) = 1338 (0.27%) Healthy weight (BMI 18.5-24.99 kg/m^2) = 49860 (10.10%) Overweight (BMI 25-29.99 kg/m^2) = 168947 (34.22%) Obesity I (BMI 30-34.99 kg/m^2) = 159056 (32.22%) Obesity II (BMI 35-39.99 kg/m^2) = 80166 (16.24%) Obesity III (BMI ≥40 kg/m^2) = 34343 (6.96%)	Factors included in the adjusted analysis: age, sex, ASA grade, indication for operation and year of primary total knee replacement.	Mortality at ≤3 months (within 90 days) Reoperation or revision to the prosthesis at >3 months – Revision (within 11 years)	Risk of bias: Very high Population indirectness (does not state if people had knee osteoarthritis)
George 2018[52]	People who had a knee replacement and was registered into the American College of Surgeons NSQIP database between January 2011 and December 2015 (United States of America) n=150934	Multivariate logistic regression analysis.	Healthy weight (BMI ≥18.5-<25 kg/m^2) = 14989 Overweight (BMI ≥25-<30 kg/m^2) = 41155 Obesity I and II (BMI ≥30-<40 kg/m^2) = 71709 (this group is not included in the analysis as it cannot be placed into either category) Obesity III (BMI ≥40 kg/m^2) = 23081	Factors included in the adjusted analysis: age, gender, American Society of Anaesthesiologists, functional status, (independent vs partially/totally dependent), smoking, BMI, anaesthesia (general vs others), congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, disseminated cancer,	Mortality at 30 days (≤3 months) Reoperation at 30 days (≤3 months) Deep vein thrombosis at 30 days* - Both values will be reported as they could both be relevant, but will not be meta-analysed unless studies only report these individual categories (≤3 months)	Risk of bias: Very high Population indirectness (does not state if people had knee osteoarthritis)

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
				dialysis, corticosteroid use, recent weight loss.	Pulmonary embolism at 30 days* (≤3 months) Superficial infection at 30 days+ - Both values will be reported as they could both be relevant, but will not be meta-analysed unless studies only report these individual categories (≤3 months) Periprosthetic joint infection at 30 days+ (≤3 months)	
Gurunathan 2018[63] In this report this is labelled: Gurunathan 2018A	People who had an elective primary unilateral hip replacement performed between 22 February 2006 and 15 December 2010 (Australia) n=964	Multivariate analysis using logistic regression.	Underweight (BMI <18.5 kg/m^2) = 11 (1.1%) – the study did not have a sufficient number of participants to be included in the analysis, so were excluded. Healthy weight (BMI 18.5-24.99 kg/m^2) = 191 (19.8%) Overweight (BMI 25-29.99 kg/m^2) = 378 (39.2%) Obesity I (BMI 30-34.99 kg/m^2) = 219 (22.7%) Obesity II (BMI 35-39.99 kg/m^2) = 110 (11.4%)	Factors included in the adjusted analysis: age, gender, comorbidity (ASA classification), underlying pathology, procedure performed, private health insurance status and type of anaesthesia.	Total adverse events up to 90 days – Overall complications (30 days) Surgical site infection (wound infection) at ≤3 months – Infectious complications (30 days) Venous thromboembolic events at ≤3 months – Thromboembolic complications (30 days)	Risk of bias: Very high Population indirectness (does not state if people had knee osteoarthritis) and outcome indirectness (surgical site infection outcome could include other infections)

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
			Obesity III (BMI ≥40 kg/m^2) = 55 (5.7%)			
Gurunathan 2018[64] In this report this is labelled: Gurunathan 2018B	People who had an elective primary total knee replacement performed between January 1, 2006 and December 31, 2010 (Australia) n=1665	Multivariate analysis using logistic regression.	Underweight (BMI <18.5 kg/m^2) = 2 (0.1%) – the study did not have a sufficient number of participants to be included in the analysis, so were excluded. Healthy weight (BMI 18.5-24.99 kg/m^2) = 141 (8.5%) Overweight (BMI 25-29.99 kg/m^2) = 481 (28.9%) Obesity I (BMI 30-34.99 kg/m^2) = 508 (30.5%) Obesity II (BMI 35-39.99 kg/m^2) = 320 (19.2%) Obesity III (BMI ≥40 kg/m^2) = 213 (12.8%)	Factors included in the adjusted analysis: age, gender, comorbidity (ASA classification), underlying pathology and type of anaesthesia.	Total adverse events up to 90 days – Overall complications (30 days)	Risk of bias: High
Jamsen 2012[77]	People having primary hip and knee replacement procedures between September 1, 2002, and January 31, 2008 (Finland) n(knee replacements) = 3915 n(hip replacements) = 3266	Multivariate analysis using logistic regression.	Healthy weight* (BMI <25 kg/m^2) = 1105 (this group will be considered as indirect evidence for normal weight) Overweight (BMI 25-29.99 kg/m^2) = 2461 Obesity I (BMI 30-34.99 kg/m^2) = 1635 Obesity II (BMI 35-39.99 kg/m^2) = 2927 Obesity III (BMI ≥40 kg/m^2) = 140	Factors included in the adjusted analysis: age, sex, American Society of Anaesthesiologists (ASA) risk score, arthroplasty site (hip or knee), BMI and diabetic status.	Surgical site infection (wound infection) at >3 months – perioperative joint infection during the first postoperative year (>3 months)	Risk of bias: Very high Population indirectness (does not state if people had knee osteoarthritis) and prognostic variable indirectness (One or more BMI categories include people outside of the

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
	n(total)=7181					categories agreed in the protocol)
Jamsen 2013[78]	People having primary hip and knee replacements from September 1, 2002 through January 31, 2009 (Finland) n(Knee replacements) = 1242 n(hip replacement) = 756 n(total) = 1998	Multivariate analysis using Cox regression analysis.	Healthy weight* (BMI 20-24 kg/m^2) = 373 (the study reported a <20 kg/m^2 group – for this analysis only the 20-24 kg/m^2 group will be considered. However, this group will be considered as indirect evidence for normal weight) Overweight (BMI 25-30 kg/m^2) = 786 Obesity I* (BMI >30 kg/m^2) = 482 (this group will be considered as indirect evidence for Obesity I as it could include people in higher BMI categories)	Factors included in the adjusted analysis: age, sex, operated joint, laterality and anaesthesiological risk score.	Mortality at >3 months – follow up for at most 5 years	Risk of bias: Very high Prognostic variable indirectness (One or more BMI categories include people outside of the categories agreed in the protocol)
Judge 2014[83]	People within the four databases: EUROHIP in 2002, EPOS between 1999 and 2002, EOC between 2005-2008, St. Helier Hospital outcome programme between 1995-2007. n=4413	Multivariate analysis using Cox regression analysis.	Underweight (BMI <18.5 kg/m^2) = 24 Healthy weight (BMI 18.5-25 kg/m^2) = 864 Overweight (BMI 25-30 kg/m^2) = 1139 Obesity I (BMI 30-35 kg/m^2) = 502 Obesity II (BMI 35-40 kg/m^2) = 150 Obesity III (BMI >40 kg/m^2) = 47	Factors included in the adjusted analysis: age, sex, SF-36 mental health, comorbidities, fixed flexion, analgesic use, college education, OA in other joints, expectation of less pain, radiographic K&L grade, ASA grade, years of hip pain.	Post-operative patient-reported outcome measures at 1 year (1 year)	Risk of bias: Very high

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
Li 2017[98]	People who underwent primary unilateral total knee or hip replacement between May 2011 and March 2013 (United States of America) n(total hip replacement) = 2040 n(total knee replacement) = 2964 n(total) = 5004	Multivariate analysis using linear mixed models	Total hip replacement = 2040: Under or healthy weight* (BMI <25 kg/m^2) = 530 (this group includes people who were underweight or of healthy weight, this will be included as healthy weight but downgraded for indirectness) Overweight (BMI 25-29.99 kg/m^2) = 763 Obesity I (BMI 30-34.99 kg/m^2) = 453 Obesity II (BMI 35-39.99 kg/m^2) = 204 Obesity III (BMI ≥40 kg/m^2) = 90 Total knee replacement = 2964: Under or healthy weight* (BMI <25 kg/m^2) = 396 (this group includes people who were underweight or of healthy weight, this will be included as healthy weight but downgraded for indirectness) Overweight (BMI 25-29.99 kg/m^2) = 978 Obesity I (BMI 30-34.99 kg/m^2) = 861	Factors included in the adjusted analysis: differences in baseline function and pain score, sex, age, race, household income, education, living alone, type of insurance, medical comorbidities, low back pain, number of other painful joints, and surgical volume of the hospital	Health-related quality of life at >3 months (6 months) Post-operative patient-reported outcome measures at 6 months (6 months)	Risk of bias: High Prognostic variable indirectness (one or more BMI categories include people outside of the categories agreed in the protocol) and outcome indirectness (subscales reported rather than aggregate scores)

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
			Obesity II (BMI 35-39.99 kg/m^2) = 457 Obesity III (BMI ≥40 kg/m^2) = 272			
Liao 2017[99]	People who underwent a primary total knee replacement procedure between July 2009 and October 2013 (Taiwan) n=354	Multivariate analysis using repeated-measures ANOVA with adjustment for baseline prognostic confounding factors	Healthy weight* (BMI 18.5-24.0 kg/m^2) = 59 Overweight* (BMI 24.0-29.9 kg/m^2) = 185 Obesity I (BMI 30.0-34.9 kg/m^2) = 82 Obesity II* (BMI ≥35 kg/m^2) = 28	Factors included in the adjusted analysis: age, sex, CIRS score, length of stay, pre-operative knee flexion and pre-operative WOMAC physical function score.	Post-operative patient-reported outcome measures at 6 months (6 months)	Risk of bias: High Prognostic variable indirectness (one or more BMI categories include people outside of the categories agreed in the protocol) and outcome indirectness (subscales reported rather than aggregate scores)
Mukka 2020[119]	Patients with primary osteoarthritis who were treated surgically with total hip arthroplasty between January 1, 2008, and December 31, 2015 (Sweden) n=64055	Multivariate analysis using linear regression analyses.	Underweight (BMI <18.5 kg/m^2) = 395 Healthy weight (BMI 18.5-24.9 kg/m^2) = 19,892 Overweight (BMI 25.0-29.9 kg/m^2) = 28,221 Obesity I (BMI 30.0-34.9 kg/m^2) = 12,036 Obesity II (BMI 35.0-39.9 kg/m^2) = 2,899 Obesity III (BMI ≥40.0 kg/m^2) = 612	Factors included in the adjusted analysis: age, sex, ASA class, preoperative health-related quality of life and Charnley classification.	Health-related quality of life at >3 months (1 year)* (this study reports EQ-5D-3L and EQ VAS. For this analysis we have extracted the value for EQ-5D-3L).	Risk of bias: Very high
Peters 2020[135]	People who had hip arthroplasty procedures in the	Multivariate analysis using logistic	Underweight (BMI <18.5 kg/m^2) = 649	Factors included in the adjusted analysis: age, gender,	Reoperation or revision to the	Risk of bias: High

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
	Dutch Arthroplasty Registry between 2007 and 2018 (Sweden) n=218214	regression analyses.	Healthy weight (BMI 18.5-25.0 kg/m^2) = 33,998 Overweight (BMI >25.0-30 kg/m^2) = 46,507 Obesity I/II (BMI >30.0-40.0 kg/m^2) = 25,453 (this group will not be included in the analysis as it doesn't clearly fit either category) Obesity III (BMI >40.0 kg/m^2) = 1336	American Society of Anaesthesiologists score, body mass index, Charnley score, smoking and previous operations to the hip.	prosthesis at >3 months (3 years)	
Thornqvist 2014[165]	People who had undergone elective primary hip and knee replacement surgery between 2005 and 2011 (Denmark) n=37744	Multivariate analysis using Cox regression models.	Underweight (BMI <18.5 kg/m^2) = 353 Healthy weight (BMI 18.5-25.0 kg/m^2) = 9589 Overweight (BMI >25.0-30.0 kg/m^2) = 13,787 Obesity I (BMI >30.0-35.0 kg/m^2) = 7450 Obesity II (BMI >35.0-40.0 kg/m^2) = 3295	Factors included in the adjusted analysis: age, gender, hip vs. knee replacement surgery, heart failure, previous myocardial infarction, chronic ischaemic heart disease, atrial fibrillation, peripheral artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, renal disease, diabetes and cemented vs. non-cemented prosthesis.	Mortality at ≤3 months (30 days) and >3 months (1 year)	Risk of bias: Very high
Wallace 2014[175]	People who had a total hip replacement or total knee replacement	Multivariate analysis using logistic regression analyses.	**Hip replacement** Underweight (BMI <18.5 kg/m^2) = 462	Factors included in the adjusted analysis: age, gender, drinking, smoking, socioeconomic	Mortality at >3 months (6 months) Venous thromboembolic	Risk of bias: High Prognostic variable indirectness (one or more BMI categories

Study	Population	Analysis	Prognostic variable(s)	Confounders	Outcomes	Limitations
	between 1995 and 2011 (United Kingdom) N=32485		Healthy weight (BMI 18.5-25.0 kg/m^2) = 9006 Overweight (BMI 25.0-30 kg/m^2) = 12,619 Obesity I (BMI 30.0-35.0 kg/m^2) = 6809 Obesity II (BMI 35.0-40.0 kg/m^2) = 2224 Obesity III (BMI >40.0 kg/m^2) = 697 **Knee replacement** Underweight (BMI <18.5 kg/m^2) = 138 Healthy weight (BMI 18.5-25.0 kg/m^2) = 5396 Overweight (BMI 25.0-30 kg/m^2) = 12,403 Obesity I (BMI 30.0-35.0 kg/m^2) = 9272 Obesity II (BMI 35.0-40.0 kg/m^2) = 3829 Obesity III (BMI >40.0 kg/m^2) = 1447	status, year of surgery, previous occurrence of outcome, prior use of statins, antihypertensives, aspirin, antidepressants, anticoagulants, antibiotics, previous diagnosis of diabetes, hypertension, chronic obstructive pulmonary disease, atrial fibrillation, ischaemic heart disease.	events at >3 months (6 months) Surgical site infection (wound infection) at >3 months (6 months)	include people outside of the categories agreed in the protocol)

See Appendix D for full evidence tables

1.1.6 Summary of the prognostic evidence

1.1.6.1 Knee osteoarthritis

Table 3: Clinical evidence summary: joint replacement for people who are underweight compared to people who are of healthy weight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	51198 (1) 90 days	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted HR: 1.64 (0.87 to 3.09)
Mortality at >3 months[b]	5534 (1) 6 months	MODERATE[c] Due to risk of bias	Adjusted OR: 4.61 (1.64 to 12.96)
Reoperation or revision of prosthesis at >3 months[a]	51198 (1) 11 years	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted HR: 0.88 (0.55 to 1.41)
Surgical site infection (wound infection) at >3 months[b]	5493 (1) 6 months	LOW[c,e] Due to risk of bias, imprecision	Adjusted OR: 0.97 (0.36 to 2.61)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) Downgraded by 1 increment for population indirectness (does not specify the proportion of people with osteoarthritis)
(e) 95% CI around the effect size crosses null line.

Table 4: Clinical evidence summary: joint replacement for people who are overweight compared to people who are of healthy weight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	218807 (1) 90 days	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted HR: 0.75 (0.65 to 0.89)
Mortality at ≤3 months[b]	56144 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.97 (0.53 to 1.78)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[c]	323 (1) 3 months	VERY LOW[f,i] Due to risk of bias, indirectness	Adjusted MD: -4.9 (-9.42 to -0.38)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[c]	323 (1) 3 months	VERY LOW[f,h,i] Due to risk of bias, indirectness, imprecision	Adjusted MD: -3.5 (-7.53 to 0.53)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	154 (1) 6 months	VERY LOW[f,h,j] Due to risk of bias, indirectness, imprecision	Adjusted MD: -3.2 (-5 to -1.4)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[d]	1260 (1) 6 months	VERY LOW[f,h,i] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.4 (-3.24 to 0.44)
Reoperation or revision to the prosthesis at ≤3 months[b]	56144 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.94 (0.79 to 1.12)
Total adverse events up to 90 days[e]	622 (1) 30 days	LOW[f,h] Due to risk of bias, imprecision	Adjusted OR: 1.11 (0.68 to 1.81)
Surgical site infection (superficial infection) at ≤3 months[b]	56144 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.85 (0.64 to 1.13)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Surgical site infection (periprosthetic joint infection) at ≤3 months[b]	56144 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.90 (0.61 to 1.33)
Venous thromboembolic events (deep vein thrombosis) at ≤3 months[b]	56144 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR 1.10 (0.90 to 1.34)
Venous thromboembolic events (pulmonary embolism) at ≤3 months[b]	56144 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.49 (1.12 to 1.98)
Mortality at >3 months[b]	17799 (1) 6 months	LOW[f,h] Due to risk of bias, imprecision	Adjusted OR: 1.12 (0.74 to 1.69)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[d]	1293 (1) 6 months	VERY LOW[f,h,i] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.8 (-1.94 to 0.34)
Reoperation or revision to the prosthesis at >3 months[a]	218807 (1) 11 years	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted HR: 1.05 (0.97 to 1.14)
Venous thromboembolic events at >3 months[b]	17688 (1) 6 months	MODERATE[f] Due to risk of bias	Adjusted OR: 1.59 (1.26 to 2.01)
Surgical site infection (wound infection) at >3 months[b]	17688 (1) 6 months	MODERATE[f] Due to risk of bias	Adjusted OR: 1.23 (1.01 to 1.50)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(e) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidity

(f) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(g) Downgraded by 1 increment for population indirectness (does not specify the proportion of people with osteoarthritis)
(h) 95% CI around the effect size crosses null line.
(i) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(j) Downgraded by 1 increment due to outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 5: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are of healthy weight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	208916 (1) 90 days	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted HR: 0.69 (0.58 to 0.82)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[b]	294 (1) 3 months	VERY LOW[f,h] Due to risk of bias, indirectness	Adjusted MD: -8.8 (-13.51 to -4.09)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[b]	294 (1) 3 months	VERY LOW[f,h] Due to risk of bias, indirectness	Adjusted MD: -8.7 (-12.85 to -4.55)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	149 (1) 6 months	VERY LOW[f,j] Due to risk of bias, indirectness	Adjusted MD: -5.7 (-7.61 to -3.79)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[c]	957 (1) 6 months	VERY LOW[f,h,i] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.4 (-3.38 to 0.57)
Total adverse events up to 90 days[d]	649 (1) 30 days	LOW[f,i] Due to risk of bias, imprecision	Adjusted OR: 0.85 (0.52 to 1.39)
Mortality at >3 months[d]	14668 (1)	LOW[f,i] Due to risk of bias, imprecision	Adjusted OR: 1.12 (0.78 to 1.88)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	6 months		
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[c]	983 (1) 6 months	VERY LOW[f,h,i] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.7 (-1.97 to 0.57)
Reoperation or revision to the prosthesis at >3 months[a]	208916 (1) 11 years	VERY LOW[f,g,i] Due to risk of bias, indirectness, imprecision	Adjusted HR: 1.08 (0.99 to 1.18)
Venous thromboembolic events at >3 months[d]	14583 (1) 6 months	MODERATE[f] Due to risk of bias	Adjusted OR: 1.59 (1.26 to 2.01)
Surgical site infection (wound infection) at >3 months[d]	14583 (1) 6 months	MODERATE[f] Due to risk of bias	Adjusted OR: 1.23 (1.01 to 1.50)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidity
(e) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(f) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(g) Downgraded by 1 increment for population indirectness (does not specify the proportion of people with osteoarthritis)
(h) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(i) 95% CI around the effect size crosses null line.
(j) Downgraded by 1 increment for outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 6: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are overweight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[a]	377 (1) 3 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: -3.9 (-8.05 to 0.25)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	377 (1) 3 months	VERY LOW[d,e] Due to risk of bias, indirectness	Adjusted MD: -5.2 (-8.86 to -1.54)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[b]	185 (1) 6 months	VERY LOW[d,g] Due to risk of bias, indirectness	Adjusted MD: -4.9 (-6.51 to -3.29)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[c]	1187 (1) 6 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0 (-1.84 to 1.84)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[c]	1216 (1) 6 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.1 (-1.04 to 1.24)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(e) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(f) 95% CI around the effect size crosses null line.
(g) Downgraded by 1 increment due to outcome indirectness (WOMAC/KOOS subscales reported instead of aggregate value)

Table 7: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are of healthy weight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	130026 (1) 90 days	VERY LOW[e,f,g] Due to risk of bias, indirectness, imprecision	Adjusted HR: 0.88 (0.72 to 1.08)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[b]	199 (1) 3 months	VERY LOW[e,h] Due to risk of bias, indirectness	Adjusted MD: -12.5 (-18.11 to -6.89)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[b]	199 (1) 3 months	VERY LOW[e,h] Due to risk of bias, indirectness	Adjusted MD: -10.1 (-15.08 to -5.12)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	141 (1) 6 months	LOW[e,j] Due to risk of bias, indirectness	Adjusted MD: -8.3 (-10.32 to -6.28)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[c]	709 (1) 6 months	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted MD: -2.3 (-4.73 to 0.13)
Total adverse events up to 90 days[d]	461 (1) 30 days	LOW[e,g] Due to risk of bias, imprecision	Adjusted OR: 0.69 (0.42 to 1.13)
Mortality at >3 months[d]	10672 (1) 6 months	VERY LOW[e,g,i] Due to risk of bias, imprecision	Adjusted OR: 0.95 (0.50 to 1.81)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[c]	734 (1) 6 months	LOW[e,h] Due to risk of bias, indirectness	Adjusted MD: -3.2 (-4.77 to -1.63)
Reoperation or revision to the prosthesis at >3 months[a]	130026 (1)	LOW[e,f] Due to risk of bias, indirectness	Adjusted HR: 1.21 (1.10 to 1.33)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	11 years		
Venous thromboembolic events at >3 months[d]	10619 (1) 6 months	LOW[e,i] Due to risk of bias, indirectness	Adjusted OR: 1.93 (1.45 to 2.57)
Surgical site infection (wound infection) at >3 months[d]	10619 (1) 6 months	LOW[e,i] Due to risk of bias, indirectness	Adjusted OR: 1.39 (1.11 to 1.74)

(k) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex.
(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity.
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity.
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidity.
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status.
(e) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias.
(f) Downgraded by 1 increment for population indirectness (does not specify the proportion of people with osteoarthritis)
(g) 95% CI around the effect size crosses null line.
(h) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time).
(i) Downgraded by 1 increment due to prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol).
(j) Downgraded by 1 increment due to outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time).

Table 8: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are overweight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[a]	282 (1)	VERY LOW[d,e] Due to risk of bias, indirectness	Adjusted MD: -7.6 (-12.75 to -2.45)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	3 months		
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	282 (1) 3 months	VERY LOW[d,e] Due to risk of bias, indirectness	Adjusted MD: -6.6 (-11.17 to -2.03)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[b]	87 (1) 6 months	LOW[d,f] Due to risk of bias, indirectness	Adjusted MD: -7.5 (-9.24 to -5.76)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[c]	939 (1) 6 months	VERY LOW[d,e,g] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.8 (-3.22 to 1.42)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[c]	967 (1) 6 months	LOW[d,e] Due to risk of bias, indirectness	Adjusted MD: -2.4 (-3.87 to -0.93)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(e) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(f) Downgraded by 1 increment due to outcome indirectness (WOMAC/KOOS subscales reported instead of aggregate value)
(g) 95% CI around the effect size crosses null line.

Table 9: Clinical evidence summary: joint replacement for people who have obesity II compared to people who have obesity I with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[a]	253 (1) 3 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: -3.7 (-9.01 to 1.61)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	253 (1) 3 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.4 (-6.08 to 3.28)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[b]	172 (1) 6 months	LOW[d,g] Due to risk of bias, indirectness	Adjusted MD: -2.6 (-4.28 to -0.92)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[c]	636 (1) 6 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.9 (-3.33 to 1.53)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[c]	657 (1) 6 months	VERY LOW[d,e] Due to risk of bias, indirectness	Adjusted MD: -2.5 (-4.07 to -0.93)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(e) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(f) 95% CI around the effect size crosses null line.
(g) Downgraded by 1 increment due to outcome indirectness (WOMAC/KOOS subscales reported instead of aggregate value)

Table 10: Clinical evidence summary: joint replacement for people who have obesity III compared to people who are of healthy weight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	84203 (1) 90 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted HR: 1.17 (0.90 to 1.52)
Mortality at ≤3 months[b]	38070 (1) 30 days	VERY LOW[f,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.25 (0.67 to 2.33)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[c]	177 (1) 3 months	VERY LOW[f,i] Due to risk of bias, indirectness	Adjusted MD: -14.1 (-20.39 to -7.81)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[c]	177 (1) 3 months	VERY LOW[f,i] Due to risk of bias, indirectness	Adjusted MD: -9.9 (-15.48 to -4.32)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	87 (1) 6 months	LOW[f,k] Due to risk of bias, indirectness	Adjusted MD: -10.4 (-13.1 to -7.7)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[d]	601 (1) 6 months	VERY LOW[f,h,i] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.9 (-4.08 to 2.28)
Reoperation or revision to the prosthesis at ≤3 months[b]	38070 (1) 30 days	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted OR: 1.49 (1.24 to 1.79)
Total adverse events up to 90 days[e]	354 (1) 30 days	MODERATE[f] Due to risk of bias	Adjusted OR: 1.02 (1.00 to 1.04)
Surgical site infection (superficial infection) at ≤3 months[b]	38070 (1) 30 days	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted OR: 2.02 (1.53 to 2.67)
Surgical site infection (periprosthetic joint infection) at ≤3 months[b]	38070 (1)	VERY LOW[f,g]	Adjusted OR: 2.14 (1.48 to 3.09)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	30 days	Due to risk of bias, indirectness	
Venous thromboembolic events (deep vein thrombosis) at ≤3 months[b]	38070 (1) 30 days	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted OR 0.80 (0.64 to 1.00)
Venous thromboembolic events (pulmonary embolism) at ≤3 months[b]	38070 (1) 30 days	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted OR: 1.92 (1.42 to 2.60)
Health-related quality of life (EQ-5D, -0.11-1, higher is better, change score) at >3 months[e]	2310 (1) 7 months	VERY LOW[f,h,i] Due to risk of bias, indirectness imprecision	Adjusted MD: 0.01 (-0.01 to 0.04)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[d]	620 (1) 6 months	LOW[f,l] Due to risk of bias, indirectness	Adjusted MD: -4.4 (-6.48 to -2.32)
Post-operative Patient Reported Outcome Measures (OKS, 0-48, higher is better, change score) at 1 year[e]	2310 (1) 7 months	VERY LOW[f,h,j] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.5 (-0.28 to 1.28)
Reoperation or revision to the prosthesis at >3 months[a]	84203 (1) 11 years	VERY LOW[f,g] Due to risk of bias, indirectness	Adjusted HR: 1.13 (1.02 to 1.25)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(e) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidity
(f) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(g) Downgraded by 1 increment for population indirectness (does not specify the proportion of people with osteoarthritis)
(h) 95% CI around the effect size crosses null line.
(i) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(j) Downgraded by 1 increment due to prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)
(k) Downgraded by 1 increment due to outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 11: Clinical evidence summary: joint replacement for people who have obesity III compared to people who are overweight with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[a]	260 (1) 3 months	VERY LOW[c,d] Due to risk of bias, indirectness	Adjusted MD: -9.2 (-15.09 to -3.31)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	260 (1) 3 months	VERY LOW[c,d] Due to risk of bias, indirectness	Adjusted MD: -6.4 (-11.63 to -1.17)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[f]	123 (1) 6 months	LOW[c,g] Due to risk of bias, indirectness	Adjusted MD: -9.6 (-12.1 to -7.1)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[b]	831 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.5 (-2.6 to 3.6)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[b]	853 (1) 6 months	LOW[c,d] Due to risk of bias, indirectness	Adjusted MD: -3.6 (-5.6 to -1.6)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(e) 95% CI around the effect size crosses null line.
(f) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(g) Downgraded by 1 increment for outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 12: Clinical evidence summary: joint replacement for people who have obesity III compared to people who have obesity I with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[a]	231 (1) 3 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -5.3 (-11.33 to 0.73)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	231 (1) 3 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.2 (-6.52 to 4.12)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[f]	118 (1) 6 months	LOW[c,g] Due to risk of bias, indirectness	Adjusted MD: -4.7 (-7.15 to -2.25)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[b]	528 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.5 (-2.68 to 3.68)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[b]	543 (1) 6 months	LOW[c,d] Due to risk of bias, indirectness	Adjusted MD: -3.7 (-5.78 to -1.62)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity.
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity.
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias.
(d) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(e) 95% CI around the effect size crosses null line.
(f) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex.
(g) Downgraded by 1 increment for outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 13: Clinical evidence summary: joint replacement for people who have obesity III compared to people who have obesity II with knee osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months[a]	136 (1) 3 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.6 (-8.36 to 5.16)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[a]	136 (1) 3 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.2 (-5.79 to 6.19)
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months[f]	110 (1) 6 months	VERY LOW[c,e,g] Due to risk of bias, indirectness, imprecision	Adjusted MD: -2.1 (-4.64 to 0.44)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[b]	280 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: 1.4 (-2.08 to 4.88)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[b]	294 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.2 (-3.48 to 1.08)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity.
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidity.
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias.
(d) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time).
(e) 95% CI around the effect size crosses null line.
(f) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex.
(g) Downgraded by 1 increment for outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

1.1.6.2 Hip osteoarthritis

Table 14: Clinical evidence summary: joint replacement for people who are underweight compared to people who are of healthy weight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at >3 months[a]	9468 (1) 6 months	MODERATE[d] Due to risk of bias	Adjusted OR: 2.17 (1.67 to 2.82)
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months[b]	20187 (1) 1 year	LOW[d] Due to risk of bias	Adjusted MD: -0.04 (-0.07 to -0.01)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[c]	888 (1) 1 year	LOW[d,e] Due to risk of bias, imprecision	Adjusted MD: -0.51 (-4.95 to 3.93)
Venous thromboembolic events at >3 months[a]	9319 (1) 6 months	LOW[d,e] Due to risk of bias, imprecision	Adjusted OR: 0.75 (0.35 to 1.61)
Surgical site infection (wound infection) at >3 months[a]	9319 (1) 6 months	LOW[c,e] Due to risk of bias, imprecision	Adjusted OR: 1.03 (0.48 to 2.21)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(e) 95% CI around the effect size crosses null line.

Table 15: Clinical evidence summary: joint replacement for people who are underweight compared to people who are overweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Reoperation or revision to the prosthesis at >3 months[a]	47156 (1) 3 years	LOW[c,d] Due to risk of bias, imprecision	Adjusted OR: 1.73 (0.94 to 3.18)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	1163 (1) 1 year	VERY LOW[c,d] Due to risk of bias, imprecision	Adjusted MD: 0.19 (-4.24 to 4.62)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) 95% CI around the effect size crosses null line.

Table 16: Clinical evidence summary: joint replacement for people who are overweight compared to people who are of healthy weight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1298 (1) 6 months	VERY LOW[e,f] Due to risk of bias, indirectness	Adjusted MD: 0.5 (-1.58 to 2.58)
Total adverse events at up to 90 days[b]	569 (1) 30 days	VERY LOW[e,g] Due to risk of bias, indirectness	Adjusted OR: 0.62 (0.43 to 0.89)
Surgical site infection (wound infection) at ≤3 months[b]	569 (1) 30 days	VERY LOW[e,g,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.22 (0.62 to 2.40)
Venous thromboembolic events at ≤3 months[b]	569	VERY LOW[e,g,h]	Adjusted OR: 0.38 (0.11 to 1.31)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	(1) 30 days	Due to risk of bias, indirectness, imprecision	
Mortality at >3 months[c]	21625 (1) 6 months	MODERATE[e] Due to risk of bias	Adjusted OR: 0.61 (0.46 to 0.81)
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months[d]	48113 (1) 1 year	MODERATE[e] Due to risk of bias	Adjusted MD: -0.02 (-0.02 to -0.01)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1374 (1) 6 months	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.1 (-0.98 to 1.18)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	2003 (1) 1 year	LOW[e,h] Due to risk of bias, imprecision	Adjusted MD: -0.7 (-2.95 to 1.55)
Venous thromboembolic events at >3 months[c]	21399 (1) 6 months	MODERATE[e] Due to risk of bias	Adjusted OR: 1.39 (1.16 to 1.67)
Reoperation or revision to the prosthesis at >3 months[c]	80505 (1) 3 years	MODERATE[e] Due to risk of bias	Adjusted OR: 0.76 (0.65 to 0.89)
Surgical site infection (wound infection) at >3 months[c]	21399 (1) 6 months	MODERATE[e] Due to risk of bias	Adjusted OR: 1.34 (1.09 to 1.65)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(e) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias

(f) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

(g) Downgraded by 1 increment due to population indirectness (proportion of people with osteoarthritis unclear)

(h) 95% CI around the effect size crosses null line.

Table 17: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are of healthy weight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1188 (1) 6 months	VERY LOW[e,f,g] Due to risk of bias, indirectness, imprecision	Adjusted MD: 1.4 (-3.48 to 0.68)
Total adverse events at up to 90 days[b]	410 (1) 30 days	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.70 (0.46 to 1.07)
Surgical site infection (wound infection) at ≤3 months[b]	410 (1) 30 days	VERY LOW[e,f,i] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.45 (0.69 to 3.05)
Venous thromboembolic events at ≤3 months[b]	410 (1) 30 days	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.08 (0.36 to 3.24)
Mortality at >3 months[c]	15815 (1) 6 months	MODERATE[e] Due to risk of bias	Adjusted OR: 0.62 (0.43 to 0.89)
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months[d]	31918 (1) 1 year	LOW[e] Due to risk of bias	Adjusted MD: -0.06 (-0.07 to -0.05)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1323 (1)	VERY LOW[e,f] Due to risk of bias, indirectness	Adjusted MD: -1.2 (-2.28 to -0.12)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	6 months		
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	1366 (1) 1 year	VERY LOW[e,g] Due to risk of bias, imprecision	Adjusted MD: -2.19 (-4.54 to 0.16)
Venous thromboembolic events at >3 months[c]	15640 (1) 6 months	MODERATE[e] Due to risk of bias	Adjusted OR: 1.64 (1.34 to 2.01)
Surgical site infection (wound infection) at >3 months[c]	15640 (1) 6 months	MODERATE[e] Due to risk of bias	Adjusted OR: 1.52 (1.21 to 1.91)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(e) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(f) 95% CI around the effect size crosses null line.
(g) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(h) Downgraded by 1 increment due to population indirectness (proportion of people with osteoarthritis unclear)
(i) Downgraded by 2 increments due to population indirectness (proportion of people with osteoarthritis unclear) and outcome indirectness (may include infection not limited to the surgical site)

Table 18: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are underweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[a]	526 (1)	VERY LOW[b,c] Due to risk of bias, imprecision	Adjusted MD: -1.68 (-6.17 to 2.81)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	1 year		

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) 95% CI around the effect size crosses null line.

Table 19: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are overweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1744 (1) 6 months	VERY LOW[c,d] Due to risk of bias	Adjusted MD: -1.9 (-3.59 to -0.21)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1905 (1) 6 months	VERY LOW[c,d] Due to risk of bias	Adjusted MD: -1.3 (-2.15 to -0.45)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	1641 (1) 1 year	VERY LOW[c,e] Due to risk of bias, imprecision	Adjusted MD: -1.49 (-3.84 to 0.86)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(e) 95% CI around the effect size crosses null line.

Table 20: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are of healthy weight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	797 (1) 6 months	VERY LOW[e,f,g] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.6 (-2.93 to 1.73)
Total adverse events at up to 90 days[b]	301 (1) 30 days	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.60 (0.36 to 1.00)
Surgical site infection (wound infection) at ≤3 months[b]	301 (1) 30 days	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.65 (0.69 to 3.95)
Venous thromboembolic events at ≤3 months[b]	301 (1) 30 days	VERY LOW[e,f,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.53 (0.10 to 2.81)
Mortality at >3 months[c]	11927 (1) 6 months	VERY LOW[e,f,i] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.65 (0.36 to 1.17)
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months[d]	22791 (1) 1 year	LOW[e] Due to risk of bias	Adjusted MD: -0.11 (-0.13 to -0.09)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	852 (1) 6 months	VERY LOW[e,g] Due to risk of bias, indirectness	Adjusted MD: -1.8 (-3 to -0.6)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	1014 (1) 1 year	LOW[e] Due to risk of bias	Adjusted MD: -2.93 (-5.63 to -0.23)
Venous thromboembolic events at >3 months[c]	11780 (1)	LOW[e,i] Due to risk of bias, indirectness	Adjusted OR: 1.51 (1.16 to 1.97)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	6 months		
Surgical site infection (wound infection) at >3 months[c]	11780 (1) 6 months	LOW[e,i] Due to risk of bias, indirectness	Adjusted OR: 2.18 (1.67 to 2.85)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(d) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(e) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(f) 95% CI around the effect size crosses null line.
(g) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(h) Downgraded by 1 increment due to population indirectness (proportion of people with osteoarthritis unclear)
(i) Downgraded by 2 increments due to prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)

Table 21: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are underweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[a]	526 (1) 1 year	VERY LOW[b,c] Due to risk of bias, imprecision	Adjusted MD: -2.42 (-7.1 to 2.26)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) 95% CI around the effect size crosses null line.

Table 22: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are overweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1353 (1) 6 months	VERY LOW[c,d] Due to risk of bias, indirectness	Adjusted MD: -1.1 (-3.1 to 0.9)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1435 (1) 6 months	VERY LOW[c,d] Due to risk of bias, indirectness	Adjusted MD: -1.9 (-2.9 to -0.9)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	1289 (1) 1 year	VERY LOW[c,e] Due to risk of bias, imprecision	Adjusted MD: -2.23 (-4.93 to 0.47)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(e) 95% CI around the effect size crosses null line.

Table 23: Clinical evidence summary: joint replacement for people who have obesity II compared to people who have obesity I with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1243 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.8 (-1.2 to 2.8)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1384 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.6 (-1.6 to 0.4)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	652 (1) 1 year	VERY LOW[c,e] Due to risk of bias, imprecision	Adjusted MD: -0.74 (-3.52 to 2.04)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(e) 95% CI around the effect size crosses null line.

Table 24: Clinical evidence summary: joint replacement for people who have obesity III compared to people who are of healthy weight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	622 (1) 6 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: -1.5 (-4.11 to 1.11)
Total adverse events at up to 90 days[b]	246 (1) 30 days	VERY LOW[d,e,g] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.31 (0.64 to 2.68)
Surgical site infection (wound infection) at ≤3 months[b]	246 (1) 30 days	VERY LOW[d,e,h] Due to risk of bias, indirectness, imprecision	Adjusted OR: 2.47 (0.91 to 6.70)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Venous thromboembolic events at ≤3 months[b]	246 (1) 30 days	VERY LOW[d,e,g] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.49 (0.05 to 4.80)
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months[c]	20504 (1) 1 year	VERY LOW[d,f] Due to risk of bias, indirectness	Adjusted MD: -0.15 (-0.17 to -0.13)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	668 (1) 6 months	MODERATE[d] Due to risk of bias	Adjusted MD: -1.5 (-2.84 to -0.16)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	911 (1) 1 year	VERY LOW[d,e] Due to risk of bias, imprecision	Adjusted MD: -2.02 (-5.85 to 1.81)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(e) 95% CI around the effect size crosses null line.
(f) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)
(g) Downgraded by 1 increment due to population indirectness (proportion of people with osteoarthritis unclear)
(h) Downgraded by 2 increments due to population indirectness (proportion of people with osteoarthritis unclear) and outcome indirectness (may include infection not limited to the surgical site)

Table 25: Clinical evidence summary: joint replacement for people who have obesity III compared to people who are underweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[a]	71 (1) 1 year	VERY LOW[b,c] Due to risk of bias, imprecision	Adjusted MD: -1.51 (-6.92 to 3.9)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) 95% CI around the effect size crosses null line.

Table 26: Clinical evidence summary: joint replacement for people who have obesity III compared to people who are overweight with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1223 (1) 6 months	VERY LOW[d,e,f] Due to risk of bias, indirectness, imprecision	Adjusted MD: -2 (-4.32 to 0.32)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1250 (1) 6 months	VERY LOW[d,f] Due to risk of bias	Adjusted MD: -1.6 (-2.76 to -0.44)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	1186 (1) 1 year	VERY LOW[d,e] Due to risk of bias, imprecision	Adjusted MD: -1.32 (-5.15 to 2.51)
Reoperation or revision to the prosthesis at >3 months[c]	478343 (1) 3 years	MODERATE[d] Due to risk of bias	Adjusted OR: 1.91 (1.27 to 2.87)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities

(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, smoking status
(d) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(e) 95% CI around the effect size crosses null line.
(f) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 27: Clinical evidence summary: joint replacement for people who have obesity III compared to people who have obesity I with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	1068 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.1 (-2.42 to 2.22)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	1199 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.3 (-1.46 to 0.86)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	549 (1) 1 year	VERY LOW[c,d] Due to risk of bias, imprecision	Adjusted MD: 0.17 (-3.72 to 4.06)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) 95% CI around the effect size crosses null line.
(e) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

Table 28: Clinical evidence summary: joint replacement for people who have obesity III compared to people who have obesity II with hip osteoarthritis

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months[a]	677 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: -0.9 (-3.45 to 1.65)
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months[a]	729 (1) 6 months	VERY LOW[c,d,e] Due to risk of bias, indirectness, imprecision	Adjusted MD: 0.3 (-0.98 to 1.58)
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year[b]	197 (1) 1 year	VERY LOW[c,d] Due to risk of bias, imprecision	Adjusted MD: 0.91 (-3.2 to 5.02)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, ethnicity, comorbidities
(b) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex, comorbidities
(c) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(d) 95% CI around the effect size crosses null line.
(e) Downgraded by 2 increments for prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol) and outcome indirectness (WOMAC/KOOS/SF-36 subscales reported instead of aggregate value and/or outcome reported at less than the specified follow up time)

1.1.6.3 Mixed osteoarthritis (hip and knee osteoarthritis)

Table 29: Clinical evidence summary: joint replacement for people who are underweight compared to people who are overweight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	14140 (1)	LOW[b] Due to risk of bias	Adjusted HR: 7.0 (2.8 to 17.5)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
	30 days		
Mortality at >3 months[a]	14140 (1) 1 year	LOW[b] Due to risk of bias	Adjusted HR: 5.20 (3.50 to 7.73)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias

Table 30: Clinical evidence summary: joint replacement for people who are overweight compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	23376 (1) 30 days	LOW[b] Due to risk of bias	Adjusted HR: 2.00 (1.20 to 3.33)
Mortality at >3 months[a]	1268 (1) 5 years	VERY LOW[b,c] Due to risk of bias, indirectness	Adjusted HR: 1.43 (1.06 to 1.93)
Mortality at >3 months[a]	23376 (1) 1 year	LOW[b] Due to risk of bias	Adjusted HR: 1.60 (1.30 to 1.97)
Surgical site infection (wound infection) at >3 months[a]	3566 (1) 1 year	VERY LOW[b,d,e] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.01 (0.32 to 3.19)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) Downgraded by 1 increment due to prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)

(d) Downgraded by 2 increments due to population indirectness (proportion of people with osteoarthritis unclear) and prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)
(e) 95% CI around the effect size crosses null line.

Table 31: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Surgical site infection (wound infection) at >3 months[a]	3566 (1) 1 year	VERY LOW[b,c,d] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.76 (0.56 to 5.53)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) Downgraded by 2 increments due to population indirectness (proportion of people with osteoarthritis unclear) and prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)
(d) 95% CI around the effect size crosses null line.

Table 32: Clinical evidence summary: joint replacement for people who have obesity I compared to people who are overweight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	21237 (1) 30 days	VERY LOW[b,c,d] Due to risk of bias, indirectness, imprecision	Adjusted HR: 1.50 (0.87 to 2.59)
Mortality at >3 months[a]	1268 (1) 5 years	VERY LOW[c,d] Due to risk of bias, imprecision	Adjusted HR: 0.89 (0.65 to 1.22)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at >3 months[a]	21237 (1) 1 year	VERY LOW[c,d] Due to risk of bias, imprecision	Adjusted HR: 1.10 (0.87 to 1.39)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) Downgraded by 1 increment due to prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)
(d) 95% CI around the effect size crosses null line.

Table 33: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Surgical site infection (wound infection) at >3 months[a]	1664 (1) 1 year	VERY LOW[b,c,d] Due to risk of bias, indirectness, imprecision	Adjusted OR: 0.83 (0.17 to 4.05)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) Downgraded by 2 increments due to population indirectness (proportion of people with osteoarthritis unclear) and prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)
(d) 95% CI around the effect size crosses null line.

Table 34: Clinical evidence summary: joint replacement for people who have obesity II compared to people who are overweight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Mortality at ≤3 months[a]	17082 (1) 30 days	VERY LOW[b,c] Due to risk of bias, indirectness, imprecision	Adjusted HR: 1.90 (0.90 to 4.01)
Mortality at >3 months[a]	17082 (1) 1 year	VERY LOW[b] Due to risk of bias	Adjusted HR: 1.40 (1.01 to 1.94)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) 95% CI around the effect size crosses null line.

Table 35: Clinical evidence summary: joint replacement for people who have obesity III compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Surgical site infection (wound infection) at >3 months[a]	1298 (1) 1 year	VERY LOW[b,c] Due to risk of bias, indirectness, imprecision	Adjusted OR: 1.40 (1.01 to 1.94)

(a) Methods: multivariable analysis, including key covariates used in analysis to assess if it is an independent risk factor. Key covariates included: age, sex
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of evidence was at very high risk of bias
(c) Downgraded by 2 increments due to population indirectness (proportion of people with osteoarthritis unclear) and prognostic variable indirectness (at least one comparison uses a different cut off value for BMI then specified in the protocol)

See Appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G.

1.1.8 Summary of included economic evidence

There was no economic evidence found.

1.1.9 Economic model

This area was not prioritised for new cost-effectiveness analysis.

1.1.10 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Resource	Unit costs	Source
Weighted average cost using HRG codes HD23D to HD23J (Inflammatory, spine, joint or connective tissue disorders)	£763	NHS Reference Costs 2019/20 [125]

1.1.11 Economic evidence statements

- No relevant economic evaluations were identified.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The critical outcomes were mortality, health-related quality of life, post-operative patient-reported outcome measures (measured at 6 months or 1 year) and reoperation or revision to the prosthesis. These were considered critical due to their relevance to people with osteoarthritis. Mortality and reoperation or revision to the prosthesis are significant adverse events. Health-related quality of life gives a broader perspective on the person's wellbeing, allowing for examination of the biopsychosocial impact of interventions. Post-operative patient reported outcome measures are commonly used to examine the response to surgery and so was an important factor to compare between groups.

Total adverse events (measured at up to 90 days), surgical site infection (wound infection) and venous thromboembolism were considered as important outcomes. Total adverse events (measured at up to 90 days), surgical site infection (wound infection) and venous thromboembolism were considered as important outcomes. These were rated as important rather than critical as these events could explain the critical outcomes listed above, and are thus contributory factors rather than critical outcome in their own right.

Evidence was available for each outcome. However, all of the evidence provided was for people with knee and hip osteoarthritis, with no studies discussing people with shoulder osteoarthritis.

1.1.12.2 The quality of the evidence

Evidence was reported for people with knee and hip osteoarthritis with no evidence being available for people with shoulder osteoarthritis. Comparisons to all relevant BMI categories were present. Some studies reported outcomes for people with hip and knee osteoarthritis together, for which these outcomes were considered separately. All studies included a multivariate analysis adjusting for the key confounders of age and sex. No relevant studies investigated the effects of different BMI categories before shoulder arthroplasty.

The quality of outcomes ranged between moderate to very low. Outcomes were commonly downgraded for risk of bias and indirectness, with some outcomes being downgraded for imprecision. Outcomes were commonly downgraded for risk of bias due to study confounding, as while studies adjusted for the key confounders, no study adjusted for all of the other confounders listed in the protocol (including smoking status, ethnicity and comorbidities). Otherwise, where further risk of bias was identified, outcomes were more commonly downgraded for study participation or study attrition bias.

The majority of included studies were deemed to have indirect evidence. The reasons for this included population indirectness (where studies did not report if people had osteoarthritis in

the study, and so other populations could have been included), prognostic variable indirectness (where different BMI categories to those stated in the protocol were used) and outcome indirectness (for various reasons, including reporting only subscales of score rather than an aggregate score, reporting follow up times for less than the specified time and infections that may include non-wound site infections). The committee acknowledged that where studies did not report if people had osteoarthritis (and therefore other population could have been included) the majority of participants likely had osteoarthritis and therefore, the evidence is likely to still be broadly applicable for interpretation.

As studies were not comparable (by not adjusting for the same confounding variables, including different definitions of outcomes and different populations) no outcomes were meta-analysed and instead the outcomes from each study were reported separately.

Knee osteoarthritis

Outcomes were reported in eight studies comparing all of the relevant BMI categories.

- Mortality at ≤3 months – Outcomes compared people who were underweight, overweight, had obesity I, II and III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Mortality at >3 months – Outcomes compared people who were underweight, overweight, had obesity I and II to people who were of healthy weight and ranged from moderate to low quality due to risk of bias, indirectness and imprecision.
- Health-related quality of life at >3 months – Outcomes compared people who were of healthy weight, overweight, had obesity I, II and III to each other and ranged from moderate to very low quality due to risk of bias, indirectness and imprecision.
- Post-operative patient-reported outcome measures (KOOS, WOMAC) at 6 months – Outcomes compared people who were of healthy weight, overweight, had obesity I, II and III to each other and were of very low quality due to risk of bias, indirectness and imprecision.
- Post-operative patient-reported outcome measures (Oxford Knee Score) at 1 years – The outcome compared people who had obesity III and people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Reoperation or revision of prosthesis at ≤3 months – Outcomes compared people who were overweight and had obesity III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Reoperation or revision of prosthesis at >3 months – Outcomes compared people who were underweight, overweight, had obesity I and II to people who were of healthy weight and ranged from moderate to low quality due to risk of bias, indirectness and imprecision.
- Total adverse events up to 90 days – Outcomes compared people who were overweight, had obesity I, II and III to people who were of healthy weight and ranged from moderate to low quality due to risk of bias and imprecision.
- Surgical site infection (wound infection) at ≤3 months – Outcomes compared people who were underweight, overweight and had obesity III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Surgical site infection (wound infection) at >3 months – Outcomes compared people who were underweight, overweight, had obesity I and II to people who were of healthy weight and ranged from moderate to low quality due to risk of bias, indirectness and imprecision
- Venous thromboembolic events at ≤3 months – Outcomes compared people who were overweight and had obesity III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Venous thromboembolic events at >3 months – Outcomes compared people who were underweight, overweight, had obesity I and II to people who were of healthy weight and ranged from moderate to low quality due to risk of bias, indirectness and imprecision

Hip osteoarthritis

Outcomes were reported in six studies comparing all of the relevant BMI categories

- Mortality at >3 months – Outcomes compared people who were underweight, overweight and had obesity I and II to people who were of healthy weight and ranged from moderate to very low quality due to risk of bias, indirectness and imprecision
- Health-related quality of life at >3 months – Outcomes compared people who were underweight, of healthy weight, overweight, had obesity I, II and III to each other and ranged from moderate to very low quality due to risk of bias, indirectness and imprecision
- Post-operative patient-reported outcome measures at 6 months (KOOS) – Outcomes compared people who were underweight, of healthy weight, overweight, obesity I, II and III to each other and was of very low quality due to risk of bias, indirectness and imprecision
- Post-operative patient-reported outcome measures (Oxford Hip Score) at 12 months – Outcomes compared people who were underweight, of healthy weight, overweight, obesity I, II and III to each other and ranged from low to very low quality due to risk of bias, indirectness and imprecision
- Reoperation or revision to the prosthesis at >3 months – Outcomes compared people who were underweight, of healthy weight and had obesity III to people who were overweight and ranged from moderate to low quality due to risk of bias and imprecision
- Total adverse events at up to 90 days – Outcomes compared people who were overweight, had obesity I, II and III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Surgical site infection (wound infection) at ≤3 months – Outcomes compared people who were overweight, had obesity I, II and III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Surgical site infection (wound infection) at >3 months – Outcomes compared people who were underweight, overweight and had obesity I and II to people who were of healthy weight and ranged from moderate to very low quality due to risk of bias, indirectness and imprecision.
- Venous thromboembolic events at ≤3 months – Outcomes compared people who were overweight and had obesity I, II and III to people who were of healthy weight and was of very low quality due to risk of bias, indirectness and imprecision.
- Venous thromboembolic events at >3 months – Outcomes compared people who were underweight, overweight and had obesity I and II to people who were of healthy weight and ranged from moderate to very low quality due to risk of bias, indirectness and imprecision.

Mixed (knee and hip) osteoarthritis

Outcomes were reported in three studies comparing all of the relevant BMI categories

- Mortality at ≤3 months – Outcomes compared people who were underweight, who were of healthy weight and had obesity I and II to people who were overweight and ranged from low to very low quality due to risk of bias, indirectness and imprecision.
- Mortality at >3 months – Outcomes compared people who were overweight to people who were of healthy weight, and people who were underweight, of healthy weight and had obesity I and II to people who were overweight and ranged from low to very low quality due to risk of bias, indirectness and imprecision.
- Surgical site infection (wound infection) at >3 months – Outcomes compared people who overweight and had obesity II and III to people who were of healthy weight and were of very low quality due to risk of bias, indirectness and imprecision.

1.1.12.3 Benefits and harms

Key uncertainties

The committee noted the limitations of using BMI categories for this review. BMI was used as in some scenarios it will correctly identify people with similar health risks because of their weight in relation to their height. However, it was noted that this may not be a suitable measure for some people (for example: athletes with significant muscle mass who may be physically well but fall into higher BMI classifications). It was acknowledged that defining healthy weight in this manner has limitations and that a holistic view of the person's health should be taken, and appropriate goals set for the individual depending on what is healthy for them rather than relying purely on numerical values. Other measures for considering people who may be at risk for worse outcomes may be more appropriate, such as waist circumference (please see CG189 Obesity: identification, assessment and management for additional information). The committee encouraged that further work in this area should consider these classification systems, but they can still be used in current practice and should not be used as barriers for people who are being referred for joint replacement surgery. The committee considered the evidence for people who were underweight to be an area of uncertainty. In all studies, people who were underweight were often less significantly represented compared to the rest of the population, which influenced the precision of the outcomes and could have exaggerated outcome effect sizes. The committee reflected that people who were underweight could be people with significant comorbidities, who may have worse outcomes for mortality than other groups. These people often had worse outcomes for mortality than the other groups. The committee acknowledged that this may be confounded by other factors, such as the presence of comorbidities and frailty. Further uncertainty was introduced by some studies where the underweight and healthy weight BMI categories were combined in the analysis. In this review, outcomes from those studies were considered as indirect outcomes and participants were included in the healthy weight group due to the likelihood of people having a BMI classification in that range was higher. However, in doing so this introduced uncertainty in the conclusions made regarding people who are underweight. Taking into account all of this information, the committee concluded that this would not be a reason to avoid joint replacement surgery for people who were underweight.

Knee osteoarthritis – underweight

Outcomes were reported in two studies comparing people who were underweight to people who were of healthy weight. The evidence showed that there were higher mortality rates in people who were underweight. However, it also showed lower rates of reoperation and revision of the prosthesis and surgical site infection (wound infection).

The committee acknowledged the limited evidence for people who were underweight. The number of participants who were underweight were significantly lower than the number of people who were of healthy weight, meaning that small changes in outcomes could have much larger effects on the relative effect. There were also studies that included people who were underweight into the healthy weight group, where it was not possible to analyse the groups separately, introducing additional uncertainty.

Knee osteoarthritis – overweight

Outcomes were reported in eight studies comparing all relevant BMI categories. The evidence showed that there were higher mortality rates in people who had obesity III when compared to people of a healthy weight, but otherwise similar or lower rates for other BMI categories at less than or equal to 3 months. However, there were higher rates in all groups when compared to people in the healthy weight BMI category at more than 3 months. All groups had large improvements in health-related quality of life and patient-reported outcome measures (such as WOMAC pain and function and KOOS pain) and when compared to each other had likely non-significant differences between the groups. Reoperation rates were higher for people with obesity III, but lower than for overweight people when compared to

people of healthy weight at less than and equal to 3 months. However, reoperation rates were higher in all groups when compared to people of a healthy weight at more than 3 months. For all adverse events (including total adverse events, infections and thromboembolic events), the event rate was generally higher for people of higher BMI categories.

The committee discussed the significance of these changes. They noted that there was significant imprecision in some outcomes, which made the significance of the outcomes debatable. In addition, the committee noted that confounding variables could have affected the outcomes making it difficult to interpret the results (for example: people of higher weight may be more likely to have venous thromboembolic events regardless of if they had surgery when compared to people of healthy weight). However, they noted that the benefits from joint replacement surgery were seen for all groups, including for quality of life. In addition, while adverse events may be higher, mortality rates did not appear to be significantly higher for most groups (with the events being lower than people in the healthy weight group for the overweight, obesity I and II groups, and imprecision being seen in the other groups) and quality of life was higher.

Hip osteoarthritis – underweight

Outcomes were reported in four studies comparing people who were underweight with people from all relevant BMI categories. When compared to people of healthy weight, the evidence showed that people who were underweight had higher mortality rates than people who were of healthy weight. Improvements were seen in health-related quality of life and post-operative patient-reported outcome measures overall, with likely non-significant differences between different categories. People who were underweight were found to have a lower risk of venous thromboembolic events and had no particular difference from people of healthy weight in the rates of surgical site infection (wound infection).

When compared to people who were overweight, the same trend was seen in post-operative patient-reported outcome measures. However, people who were underweight were found to have an increased risk of reoperation or revision to the prosthesis then people who were overweight. Studies for all other comparisons only reported post-operative patient-reported outcome measures, which followed the same pattern as for the preceding comparisons.

As for people with knee osteoarthritis, the committee acknowledged the limited evidence for people who were underweight. The number of participants who were underweight were significantly lower than the number of people who were of healthy weight, meaning that small changes in outcomes could have much larger effects on the relative effect. There were also studies that included people who were underweight into the healthy weight group, where it was not possible to analyse the groups separately, introducing additional uncertainty.

Hip osteoarthritis – overweight

Outcomes were reported in six studies comparing all relevant BMI categories. The evidence showed that mortality rates were lower for people in higher BMI categories. All groups had large improvements in health-related quality of life and patient-reported outcome measures (such as the Oxford Hip Score and HOOS pain) and when compared to each other had likely not significant differences between the groups. Revision rates were generally higher in all weight categories when compared to the healthy weight group. Mostly, for the study reported outcome ‘total adverse events’, there were lower rates of total adverse events in all groups when compared to the healthy weight group. However, higher rates of surgical site infections were seen in all groups when compared to the healthy weight group. However, there were mostly lower rates of venous thromboembolic events at less than and equal to 3 months, but more at greater than 3 months when compared to people of healthy weight.

As with people with knee osteoarthritis, the committee discussed the significance of these changes. They noted that there was significant imprecision in some outcomes, which made

the significance of the outcomes debatable. In addition, the committee noted that confounding variables could have affected the outcomes making it difficult to interpret the results (for example: people of higher weight may be more likely to have venous thromboembolic events regardless of if they had surgery when compared to people of healthy weight). However, they noted that the benefits from joint replacement surgery were seen for all groups, including for quality of life. In addition, while adverse events may be higher, mortality rates did not appear to be significantly higher for most groups (with the events being lower than people in the healthy weight group for the overweight, obesity I and II groups, and imprecision being seen in the other groups) and quality of life was higher.

Mixed (knee and hip) osteoarthritis – underweight

Outcomes were reported in one study comparing people who were underweight to people who were overweight. This study reported mortality at less than and equal to 3 months and greater than 3 months. In both outcomes people who were underweight had a higher risk of mortality then people who were overweight. As for the other categories, the committee acknowledged the limited evidence for people who were underweight and the additional sources of uncertainty.

Mixed (knee and hip) osteoarthritis – overweight

Outcomes were reported in three studies comparing all relevant BMI categories. However, evidence was only available discussing mortality and surgical site infections. The evidence showed that mortality rates were higher in all groups when compared to people who were overweight, but highest for people who had obesity III. There were mostly higher surgical site infections in all groups compared to people who were of healthy weight, but these were highest for people who had obesity III.

The committee concluded that there was more limited information for this population. However, the findings were complementary with those for people with knee osteoarthritis or hip osteoarthritis.

Weighing up the clinical benefits and harms

Taking into account the evidence and findings for people with hip and knee osteoarthritis, the committee acknowledged that people from each BMI category were likely to benefit from joint replacement surgery. While there are some people who may be at higher risk (for example: people with comorbidities), in general the possible benefits for surgery in improving quality of life and as a way of supporting people to participate in other interventions that can improve their osteoarthritis symptoms, such as exercise, outweighed the possible harms. Therefore, the committee agreed recommendation A1. However, they also agreed that adverse events should be considered and discussed with each person to ensure that they are aware of the risks of the procedure (see recommendation A2).

1.1.12.4 Cost effectiveness and resource use

There were no published economic evaluations included. The committee's decision to highlight the benefit of joint replacement surgery in people with osteoarthritis who are overweight or obese was based on the clinical data, which showed slightly more adverse events for people who are overweight or underweight but substantial improvements in quality of life across all groups.

The previous guideline recommended that patient factors such as BMI should not be barriers for surgery. However, this recommendation is not consistently applied in current practice. This recommendation may therefore increase referral for surgery and therefore lead to an increase in costs to the NHS as well as a substantial improvement to quality of life of patients. Although there were no studies identified during the economic review outside the US that looked the impact of joint surgery across different BMI ranges, a study by Dakin

2012 in a UK osteoarthritis cohort undergoing total knee replacement reported that surgery was cost effective versus no surgery with an incremental QALY gain of 1.33 and a cost per QALY gained of £5,623.[39] This study would suggest that joint replacement surgery is a highly cost-effective intervention for the NHS overall, though the population is not fully representative of this review question.

1.1.12.5 Other factors the committee took into account

The committee acknowledged that people who are overweight or have obesity should be supported by healthcare professionals to reduce their weight where possible. Additional information about supporting people with this can be found in CG189 Obesity: identification, assessment and management for additional information.

The committee noted that the research identified does not appear to represent the diverse community of people who can have osteoarthritis. Osteoarthritis is more common in people in lower socio-economic groups. Obesity is also more common in people in lower socio-economic groups and access to surgery on the basis of BMI has been raised by stakeholder groups as an important equality issue. They agreed that any further research should be representative of the population, including people from different family backgrounds, and socioeconomic backgrounds, disabled people, and people of different ages and genders. Future work should be done to consider the different experiences of people from diverse communities to ensure that the approach taken can be made equitable for everyone.

While this review looked at BMI the committee also agreed that that everyone should be treated equally. They also recommended that people should not be excluded from referral for joint replacement based on their age, sex, smoking habits, or comorbidities. They noted that there are few contraindications to surgery and the surgeon would be best placed to assess and discuss an individual's suitability for joint replacement on a case-by-case basis.

The committee discussed other factors that may affect consideration of surgery. This included: age, sex or gender, smoking and comorbidities.

- Age: People of a younger age may be less likely to receive a referral for joint replacement due to concerns that they will require reoperation in the future. People of older age may be less likely to receive a referral for joint replacement due to concerns that the risks of the procedure may outweigh the benefits received.
- Sex or gender: Healthcare professionals may be less likely to refer women for surgery for various reasons (which could include perceptions of joint replacement procedure indications, risks and benefits or preference for surgery, gender bias, barriers in patient-physician interaction)[18].
- Smoking: People who smoke may be less likely to receive a referral for joint replacement as they may have an increased risk of adverse events after surgery.
- Comorbidities: People who have comorbidities may be less likely to receive a referral for joint replacement as they may have an increased risk of adverse events after surgery.

The committee agreed that people should not be excluded from referral for joint replacement because of these factors and that the choice about whether someone should have surgery should be discussed between the person and their surgeon where, if these factors are relevant they may be considered then.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.6.3 and 1.6.4. Other evidence supporting these recommendations can be found in evidence review P.

1.1.14 References

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Appendices

Appendix A – Review protocols

Review protocol for do people with osteoarthritis who are at less than or more than ideal weight have better outcomes after joint replacement surgery then people of healthy weight?

ID	Field	Content
0.	PROSPERO registration number	CRD42021266765
1.	Review title	Do people with osteoarthritis who are at less than or more than healthy weight have similar outcomes after joint replacement surgery to people of healthy weight?
2.	Review question	8.2 Do people with osteoarthritis who are at less than or more than healthyweight have better outcomes after joint replacement surgery than people of healthy weight?
I3.	Objective	To determine whether people who are underweight (BMI<18.0), overweight (BMI 25-30) or obese (BMI >30) with osteoarthritis have different outcomes following joint replacement surgery then people who are of normal weight (BMI 18.0-24.9).
4.	Searches	The following databases (from inception) will be searched: • Embase • MEDLINE Searches will be restricted by: • English language • Human studies • Letters and comments are excluded Other searches:

		• Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meetingand further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Osteoarthritis (of any joint) in adults
6.	Population	Inclusion: • Adults (age ≥16 years) with osteoarthritis affecting any joint who have had joint replacement surgery • Stratified by osteoarthritis joint site: ○ Knee ○ Hip ○ Shoulder If there is a mixed joint site population we would use an 80% cut-off point. Exclusion: • Children (age <16 years) • People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, diseases of childhood that may predispose to osteoarthritis, medical conditions presenting with joint inflammation and malignancy).

7.	Exposure	Risk factor: • Body mass index before surgery ○ Underweight – BMI <18.0 kg/m^2 ○ Healthy weight – BMI 18.5 kg/m^2 to 24.9 kg/m^2 ○ Overweight – BMI 25 kg/m^2 to 29.9 kg/m^2 ○ Obesity I – BMI 30 kg/m^2 to 34.9 kg/m^2 ○ Obesity II – BMI 35 kg/m^2 to 39.9 kg/m^2 ○ Obesity III – BMI 40 kg/m^2 or more
8.	Confounding factors	Key confounding factors that may be independently associated with prognostic variables: • Age • Sex All of the key confounders must be adjusted for in a multivariate analysis. Other confounders: • Smoking status • Ethnicity • Presence of comorbidities (ASA, Elixhauser, Charlson, any other validated scales) These confounders will be assessed on a case-by-case basis. •
9.	Types of study to be included	Non-randomised evidence, including: 1. Secondary analyses of RCTs (stratified by weight categories) 2. Prospective and retrospective cohort studies Studies will only be included if all of the key confounders have been accounted for in a multivariate analysis.

10.	Other exclusion criteria	• Non-English language studies • Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available. • People having hip resurfacing operations • People having large head metal-on-metal hip replacements • Studies not accounting for all key confounders (prognostic factors) in a multivariable analysis. • Studies using a univariate analysis or matched groups.
11.	Context	People with osteoarthritis who are requiring joint replacement surgery. In particular this review is looking at people who are overweight or obese before surgery to see what their outcomes are after joint replacement surgery when there has been no formal methods taken to cause them to lose weight. The previous (2014) guideline indicated that decisions should be based on discussion rather than scoring tools. There were no recommendations regarding patient factors except that it should be done before there is prolonged and established functional limitation and severe pain. Weight loss was thought a key factor in HCP decisions for referral and therefore should be focused on, however amount of weight loss is hard to quantify and so healthy weight (BMI) was thought important.
12.	Primary outcomes (critical outcomes)	Stratify by ≤/>3 months (longest time-point in each): • Mortality [time-to-event or dichotomous outcomes, time-to-event prioritised] • Health-related quality of life [validated patient-reported outcomes, continuous data prioritised] 1. EQ-5D 2. SF-36 3. Any other validated measures • Post-operative patient-reported outcome measure [continuous outcomes] (change scores) (at 6 months or 1 year) ○ Knee osteoarthritis 1. Oxford Knee score 2. KOOS (aggregate score) 3. WOMAC (aggregate score)

		○ Hip osteoarthritis 1.Oxford Hip score 2.HOOS (aggregate score) 3.WOMAC (aggregate score) 4.Harris Hip Score ○ Shoulder osteoarthritis 1.Oxford Shoulder Score (OSS) 2.Constant Score 3.Shoulder Pain and Disability Index (SPADI) 4.The Disabilities of the Arm, Shoulder and Hand Score (DASH) • Reoperation or revision to the prosthesis [time to event outcome] The COMET database was searched and several core outcome sets were identified for specific sites of osteoarthritis (including hand, knee and hip). The committee took these into account when defining outcomes: https://onlinelibrary.wiley.com/doi/full/10.1002/acr.22868 https://www.ncbi.nlm.nih.gov/pubmed/26136489 https://www.ncbi.nlm.nih.gov/pubmed/30647185 The committee did not include stiffness or global scores as Delphi discussions by the OMERACT group have found these to not be as important to people with osteoarthritis or clinicians. The outcomes included were universal for all groups allowing for broader comparisons.
13.	Secondary outcomes (important outcomes)	• Totaladverse events up to 90 days [dichotomous data] • Surgical site infection (wound infection) • VTE
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources

		will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Non randomised study, including cohort studies: Cochrane ROBINS-I
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5) if it is appropriate to do so (methodologies and cut-off points will need to be similar in the studies). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. • Data from the meta-analysis will be presented and quality assessed in adapted GRADE tables taking into account individual study quality and the meta-analysis

		results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. Heterogeneity between studies in the effect measures will be assessed using the I^2 statistic and visual inspection. We will consider an I^2 value great than 50% as indicative of substantial heterogeneity. If significant heterogeneity is identified during meta-analysis then subgroup analysis, using subgroups predefined by the GC, will take place. If this does not explain the heterogeneity, the results will be presented using a random-effects model.	
17.	Analysis of sub-groups	None	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☒	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	

20.	Country	England		
21.	Anticipated or actual start date	23/08/2019		
22.	Anticipated completion date	25/08/2021		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☐	☐
		Piloting of the study selection process	☐	☐
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail [Guideline email]@nice.org.uk [Developer to check with Guideline Coordinator for email address] 5e Organisational affiliation of the review		

		National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
25.	Review team members	From the National Guideline Centre: Carlos Sharpin [Guideline lead] Julie Neilson [Senior systematic reviewer] George Wood [Systematic reviewer] David Wonderling [Senior health economist] Joseph Runicles [Information specialist] Amber Hernaman [Project manager]
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10127

29.	Other registration details		
30.	Reference/URL for published protocol		
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Adults; Age; BMI; Joint replacement surgery; Osteoarthritis; Preoperative	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information	N/A	
36.	Details of final publication	www.nice.org.uk	

Table 36: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken for all years using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2005 or later, that were included in the previous guidelines, will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[123] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2005 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2005 will be rated as ‘Not applicable’.
- Studies published before 2005 (including any such studies included in the previous guidelines) will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B – Literature search strategies

- Do people with osteoarthritis who are at less than or more than healthy weight have similar outcomes after joint replacement surgery to people of healthy weight?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[123]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed by combining an Osteoarthritis population with prognostic/risk factor terms and search filters

Table 37: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 17 November 2021	Observational studies Prognostic studies Exclusions (animals studies, letters, comments)
Embase (OVID)	1974 – 17 November 2021	Observational studies Prognostic studies Exclusions (animals studies, letters, comments)

Medline (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/

19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	predict.ti.
28.	(validat* or rule*).ti,ab.
29.	(predict* and (outcome* or risk* or model*)).ti,ab.
30.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
31.	decision*.ti,ab. and Logistic models/
32.	(decision* and (model* or clinical*)).ti,ab.
33.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
34.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
35.	ROC curve/
36.	or/27-35
37.	Epidemiologic studies/
38.	Observational study/
39.	exp Cohort studies/
40.	(cohort adj (study or studies or analys* or data)).ti,ab.
41.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
42.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
43.	Controlled Before-After Studies/
44.	Historically Controlled Study/
45.	Interrupted Time Series Analysis/
46.	(before adj2 after adj2 (study or studies or data)).ti,ab.
47.	exp case control studies/
48.	case control*.ti,ab.
49.	Cross-sectional studies/
50.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
51.	or/37-50
52.	((hip* or knee* or shoulder* or joint*) adj (replace* or arthroplast* or prosthe* or endoprosthe* or implant* or artifical)).ti,ab.
53.	exp *arthroplasty, replacement, hip/ or exp *arthroplasty, replacement, knee/ or exp *arthroplasty, replacement, shoulder/
54.	52 or 53
55.	26 and 54
56.	55 and (36 or 51)
57.	exp overweight/ or *body weight/

58.	(obese or obesity or obeseness or overweight or over weight).ti,ab.
59.	Thinness/
60.	(slim or slender or leanness or lean or thin or thinness or underweight or under weight).ti,ab.
61.	body mass index/
62.	BMI.ti,ab.
63.	(body adj (fat or composition or mass)).ti,ab.
64.	((body or normal or healthy or ideal) adj weight).ti,ab.
65.	or/57-64
66.	56 and 65

Embase (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	(conference abstract or conference paper).pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/7-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/
20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice or rodent*).ti.
23.	or/15-22
24.	6 not 23
25.	limit 24 to English language
26.	predict.ti.
27.	(validat* or rule*).ti,ab.
28.	(predict* and (outcome* or risk* or model*)).ti,ab.
29.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
30.	decision*.ti,ab. and Statistical model/
31.	(decision* and (model* or clinical*)).ti,ab.

32.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
33.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
34.	Receiver operating characteristic/
35.	or/26-34
36.	Clinical study/
37.	Observational study/
38.	family study/
39.	longitudinal study/
40.	retrospective study/
41.	prospective study/
42.	cohort analysis/
43.	follow-up/
44.	cohort*.ti,ab.
45.	43 and 44
46.	(cohort adj (study or studies or analys* or data)).ti,ab.
47.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
48.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
49.	(before adj2 after adj2 (study or studies or data)).ti,ab.
50.	exp case control study/
51.	case control*.ti,ab.
52.	cross-sectional study/
53.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	or/36-42,45-53
55.	((hip* or knee* or shoulder* or joint*) adj (replace* or arthroplast* or prosthe* or endoprosthe* or implant* or artifical)).ti,ab.
56.	exp *hip arthroplasty/ or exp *knee arthroplasty/ or exp *shoulder arthroplasty/
57.	55 or 56
58.	25 and 57
59.	58 and (35 or 54)
60.	*obesity/
61.	*body weight/
62.	(obese or obesity or obeseness or overweight or over weight).ti,ab.
63.	underweight/
64.	(slim or slender or leanness or lean or thin or thinness or underweight or under weight).ti,ab.
65.	*body mass/
66.	BMI.ti,ab.
67.	(body adj (fat or composition or mass)).ti,ab.
68.	((body or normal or healthy or ideal) adj weight).ti,ab.
69.	or/60-68
70.	59 and 69

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a Gout population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updates after March 2018). NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics studies and quality of life studies. Searches for quality of life studies were run for general information.

Table 38: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1 January 2014 – 17 November 2021	Health economics studies Quality of life studies Exclusions (animals studies, letters, comments)
Embase	1 January 2014 – 17 November 2021	Health economics studies Quality of life studies Exclusions (animals studies, letters, comments)
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	None

Medline (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/

19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	quality-adjusted life years/
45.	sickness impact profile/
46.	(quality adj2 (wellbeing or well being)).ti,ab.
47.	sickness impact profile.ti,ab.
48.	disability adjusted life.ti,ab.
49.	(qal* or qtime* or qwb* or daly*).ti,ab.
50.	(euroqol* or eq5d* or eq 5*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.

58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/44-61
63.	26 and (43 or 62)

Embase (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	6 not 22
24.	Limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.

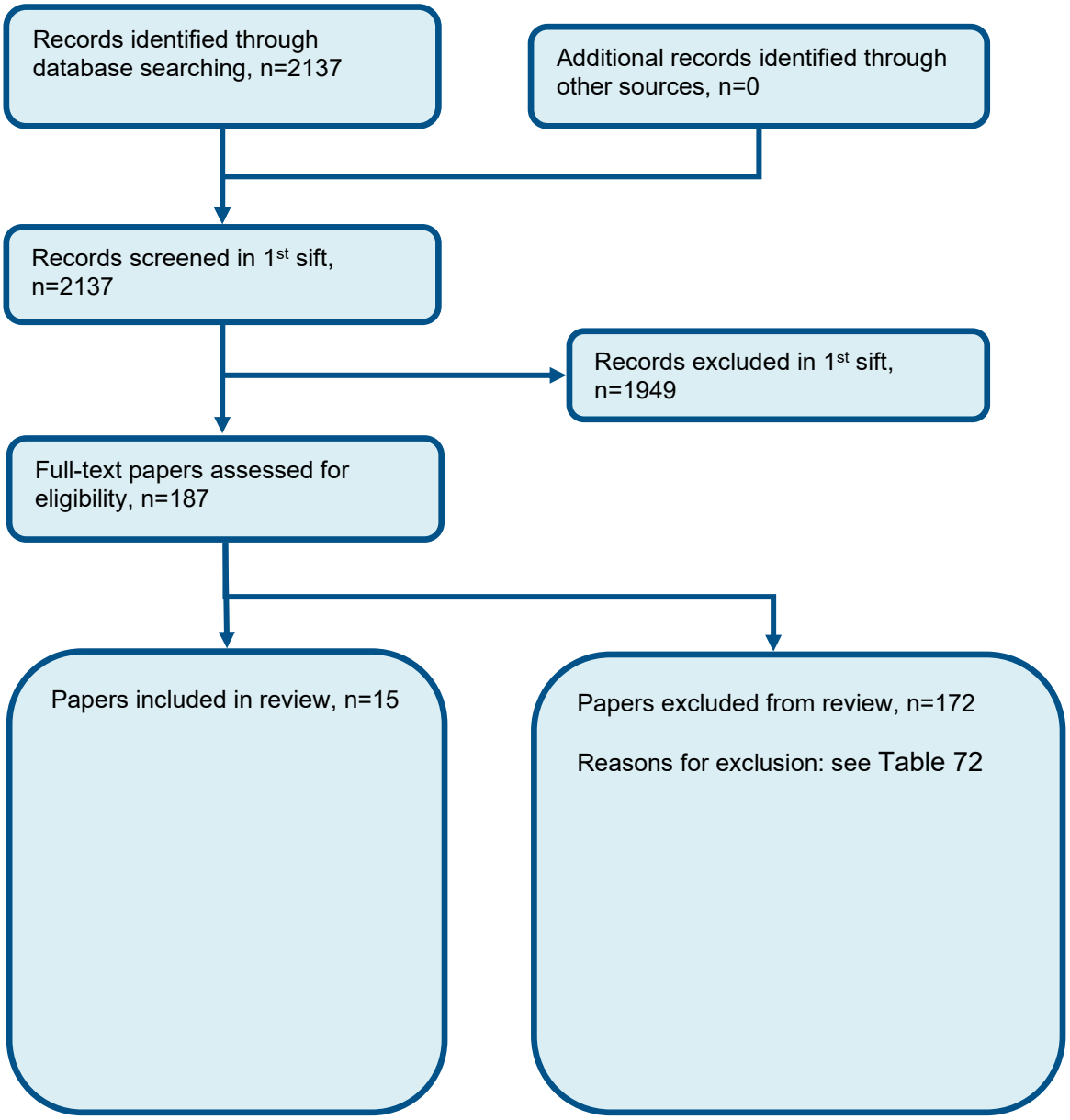
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	quality adjusted life year/
40.	"quality of life index"/
41.	short form 12/ or short form 20/ or short form 36/ or short form 8/
42.	sickness impact profile/
43.	(quality adj2 (wellbeing or well being)).ti,ab.
44.	sickness impact profile.ti,ab.
45.	disability adjusted life.ti,ab.
46.	(qal* or qtime* or qwb* or daly*).ti,ab.
47.	(euroqol* or eq5d* or eq 5*).ti,ab.
48.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
49.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
50.	(hui or hui1 or hui2 or hui3).ti,ab.
51.	(health* year* equivalent* or hye or hyes).ti,ab.
52.	discrete choice*.ti,ab.
53.	rosser.ti,ab.
54.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
55.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
56.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
57.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
58.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
59.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
60.	or/39-59
61.	24 and (38 or 60)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Osteoarthritis EXPLODE ALL TREES
#2.	((osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*))
#3.	((degenerative adj2 arthritis))
#4.	(coxarthrosis)
#5.	(gonarthrosis)
#6.	#1 OR #2 OR #3 OR #4 OR #5
#7.	(#6) IN NHSEED
#8.	(#6) IN HTA

Appendix C –Prognostic evidence study selection

Figure 1: Flow chart of clinical study selection for the review of outcomes of joint replacement surgery dependent on body mass index



Appendix D – Prognostic evidence

Reference	Baker, 2012 #3481
Study type and analysis	Retrospective cohort study using prospectively collected data from the National Joint Registry and the NHS Information Centre. Adjusting data for differences in age, sex, ASA grade, number of comorbidities and general health rating using multiple linear regressions to adjust the changes. United Kingdom

Number of participants and characteristics	N=40925 patients were registered with both the National Joint Registry and the Patient Reported Outcome Measures project as of September 2010. 8043 were excluded for missing either the preoperative or the postoperative PROMs questionnaire: 2676 people who had missing dates of completion for the PROMS questionnaires; 5195 patients who had completed the preoperative questionnaire more than ninety days prior to surgery or who had completed the postoperative questionnaire <180 days or >365 days after surgery; 1618 people who had undergone a unicondylar, patellofemoral or revision knee arthroplasty; and 595 people who had a primary indication that was not osteoarthritis. From the remaining 22798 people, 9125 people were excluded as they had missing BMI data or data outside of the range of 15-60kg/m^2. In total, 13,673 people fulfilled these criteria and were included in the analysis.
	
	Inclusion criteria:
	People who underwent knee arthroplasty with relevant information registered in the National Joint Registry between May 1, 2008, to September 1, 2010.
	
	Exclusion criteria:
	Missing data
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	• Age (SD): 69.7 (8.8) years
	• Male:Female = 6117:7556 (45%:55%)
	• ASA grade
	  ○ 1 = 1424 (10%)
	  ○ 2 = 10,077 (74%)

Reference	Baker, 2012 #3481
	○ 3 and 4 = 2172 (16%) • Preoperative general health rating ○ Excellent = 483 (4%) ○ Very good = 3433 (25%) ○ Good = 6112 (45%) ○ Fair = 2899 (21%) ○ Poor = 385 (3%) ○ Missing data = 361 (3%) • Number of comorbidities ○ Zero = 4933 (36%) ○ One = 5480 (40%) ○ Two or more = 3260 (24%) • Preoperative Oxford Knee Score (95% CI): 18.9 (18.8-19.0) • Preoperative EQ-5D index (95% CI): 0.389 (0.384-0.394) • Preoperative EQ-5D VAS (95% CI): 69.0 (68.7-69.3) **Population source:** Patients from the National Joint Registry
Prognostic variables	Group 1 (BMI 15-24.9 kg/m^2) = 1292 (this group will be considered as indirect evidence for normal weight) Group 2 (BMI 25-39.9 kg/m^2) = 11363 Group 3 (BMI 40 to 60 kg/m^2) = 1018
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, ASA grade, number of comorbidities and general health rating using multiple linear regressions to adjust the changes.
Outcomes and effect sizes	Health-related Quality of Life – EQ-5D (Index score will be used in the analysis) at >3 months (mean 7 months) Post-operative Patient Reported Outcome Measures - Oxford Knee Score at 1 year (mean 7 months) **Obesity III (BMI ≥40 kg/m^2) compared to healthy weight* (BMI 18.5 kg/m^2 to 24.9 kg/m^2)** **Health-related quality of life – EQ-5D index change (95% CI) at >3 months** • **Obesity III (n=1018) = 0.323 (0.301-0.344)**

Reference	Baker, 2012 #3481
	• **Healthy weight (n=1292) = 0.309 (0.291-0.327)** **Post-operative Patient Reported Outcome Measures – Oxford Knee Score change (95% CI) at 1 year** • **Obesity III (n=1018) = 15.9 (15.3-16.5)** • **Healthy weight (n=1292) = 15.4 (14.9-16.0)**
Comments	**<u>Health-related quality of life – EQ-5D index change at >3 months</u>** Risk of bias: 1. Study participation — HIGH 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH **<u>Post-operative Patient Reported Outcome Measures – Oxford Knee Score change at 1 year</u>** Risk of bias: 1. Study participation — HIGH 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH Indirectness: Prognostic variable indirectness – Healthy weight group includes a mixture of people who were underweight and of healthy weight. The majority of the BMI categories appeared to be in the healthy weight category and so it has been included in this group, but will be downgraded for indirectness.

Reference	Collins 2017[35]
Study type and analysis	Prospective cohort study. Mixed-effects logistic regression models to make a multivariate model. Adjusting data for differences in age, sex, race, diabetes, musculoskeletal functional limitations index, pain medication use and study site. United States of America, secondary care (across 4 medical centres)

Number of participants and characteristics	N=691 enrolled, 633 had baseline BMI data and completed at least 1 follow-up questionnaire. 58 were excluded: 16 on the basis of missing BMI data, 39 for missing all follow-up questionnaires, and 3 for missing both BMI data and all follow-up questionnaires (the excluded participants reported, on average, worse preoperative WOMAC scores for pain and function compared to those in the analytic cohort).
	
	Inclusion criteria:
	English-speaking adults who lived in the community, were at least 40 years of age, and were undergoing total knee arthroplasty for a primary diagnosis of osteoarthritis.
	
	Exclusion criteria:
	Diagnoses other than osteoarthritis (e.g., inflammatory arthritis), dementia, unicompartmental knee arthroplasty, and bilateral total knee arthroplasty.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Overall:
	• Age (SD): 65.9 (8.5) years
	• Male:Female = 258:375 (40.8%:59.2%)
	• Race
	  ○ Non-white = 43 (7.0%)
	  ○ White = 573 (93.0%)
	• WOMAC
	  ○ Function = 42.5 (17.0)
	  ○ Pain = 40.8 (17.9)
	• Musculoskeletal functional limitations index = 3.3 (2.1)
	• Diabetes = 77 (12.6%)

Reference	Collins 2017[35]

	• Study center
	  ○ MD = 88 (13.9%)
	  ○ CO = 103 (16.3%)
	  ○ NY = 54 (8.5%)
	  ○ MA = 388 (61.3%)
	• Pain medication use for knee
	  ○ No = 141 (22.4%)
	  ○ Yes, occasionally = 215 (34.2%)
	  ○ Yes, almost every day = 273 (43.4%)
	• Preoperative Oxford Knee Score (95% CI): 18.9 (18.8-19.0)
	• Preoperative EQ-5D index (95% CI): 0.389 (0.384-0.394)
	• Preoperative EQ-5D VAS (95% CI): 69.0 (68.7-69.3)
	
	Population source: Participants enrolled in 1 of 3 studies assessing outcomes of total knee arthroplasty: the AViKA cohort study, the AViKA Care Navigator randomized controlled trial and STARs.

Prognostic variables	Healthy weight* (BMI <25 kg/m^2) = 120 (this group will be considered as indirect evidence for normal weight) Overweight (BMI 25-29.9 kg/m^2) = 203 Obesity I (BMI 30-34.9 kg/m^2) = 174 Obesity II (BMI 35-39.9 kg/m^2) = 79 Obesity III (BMI ≥40 kg/m^2) = 57
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, race, diabetes, musculoskeletal functional limitations index, pain medication use and study site.
Outcomes and effect sizes	Post-operative Patient Reported Outcome Measures – WOMAC pain and WOMAC function* at 6 months Data is reported at 3-6 months and 6-24 months, but as they report change scores that were not measured against baseline, these values will not be included in this analysis. The value between baseline-3 months will be used but downgraded for indirectness for not reaching the minimum time stated in the protocol. **Obesity III (BMI ≥40 kg/m^2) compared to obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2) and healthy weight* (BMI 18.5 kg/m^2 to 24.9 kg/m^2)**

Reference	Collins 2017[35]
	Post-operative Patient Reported Outcome Measures – WOMAC pain mean change (95% CI) • **Healthy weight* (BMI <25 kg/m^2) (n=120) = -18.1 (-21.7 to -14.5)** • **Overweight (BMI 25-29.9 kg/m^2) (n=203) = -23.0 (-25.8 to -20.1)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=174) = -26.9 (-30.0 to -23.9)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=79) = -30.6 (-35.0 to -26.2)** • **Obesity III (BMI ≥40 kg/m^2) (n=57) = -32.2 (-37.5 to -27.0)** **Post-operative Patient Reported Outcome Measures – WOMAC function mean change (95% CI)** • **Healthy weight* (BMI <25 kg/m^2) (n=120) = -19.5 (-22.7 to -16.3)** • **Overweight (BMI 25-29.9 kg/m^2) (n=203) = -23.0 (-25.5 to -20.5)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=174) = -28.2 (-30.9 to -25.5)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=79) = -29.6 (-33.5 to -25.7)** • **Obesity III (BMI ≥40 kg/m^2) (n=57) = -29.4 (-34.1 to -24.7)**
Comments	**Post-operative Patient Reported Outcome Measures – WOMAC pain mean change** Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH **Post-operative Patient Reported Outcome Measures – WOMAC function mean change** Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW

Reference	Collins 2017[35]	
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	HIGH
	Indirectness: Prognostic variable indirectness – Healthy weight group may include a mixture of people who were underweight and of healthy weight. This group will be included, but will be downgraded for indirectness. Outcome indirectness – Downgraded twice. WOMAC outcomes report two subscales rather than the aggregate score stated in the protocol. Also outcomes are reported at less than the minimum time stated in the protocol. Therefore, these will be included but will be downgraded for indirectness.	

Reference	Evans 2021[46]
Study type and analysis	Retrospective observational cohort study. Multivariate analysis using Cox regression models. Adjusting data for differences in age, sex, ASA grade, indication for operation and year of primary total knee replacement. England
Number of participants and characteristics	N=975739 records of knee replacement operations performed between 1 April 2003 and 31 December 2016 in the National Joint registry. 97548 were excluded due to unicondylar or patellofemoral replacements. 72535 records before BMI was collected (1/12/05). 303839 missing BMI. 1802 incoherent BMI data (under 10 or greater than 60). Age less than or equal to 0 or missing (2). Sex missing (1). Unknown NHS number (95). Missing implant details (3322). Trauma as indication (2723). Unknown indication (162). 493710 primary total knee replacements with complete BMI and patient characteristics (used for revision data). 3359 bilateral cases removed for mortality analysis, leading to 490351 participants with primary total knee replacements and complete BMI and patients' characteristics dataset used to investigate revision and mortality. **Inclusion criteria:** People who had a knee replacement operation included in the national joint registry. **Exclusion criteria:**

Reference	Evans 2021[46]

	Unicondylar or patellofemoral replacements; missing data; trauma as indication; unknown indication; missing implant details, unknown NHS number.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Overall:
	• Male:Female = 210549:283161 (42.6%:57.4%)
	• ASA grade
	  ○ P1 = 48134 (9.75%)
	  ○ P2 = 362745 (73.5%)
	  ○ P3 = 81342 (16.5%)
	  ○ P4-5 = 1489 (0.3%)
	• Fixation type
	  ○ Cemented = 473303 (95.9%)
	  ○ Uncemented = 17380 (3.52%)
	  ○ Hybrid = 3027 (0.61%)
	• Age in years
	  ○ <50 = 9883 (2%)
	  ○ 50-54 = 20024 (4.06%)
	  ○ 55-59 = 40688 (8.24%)
	  ○ 60-64 = 72014 (14.6%)
	  ○ 65-69 = 96459 (19.5%)
	  ○ 70-74 = 98844 (20%)
	  ○ 75-79 = 85619 (17.3%)
	  ○ 80-84 = 50293 (10.2%)
	  ○ At least 85 = 19886 (4.03%)
	
	Population source: Participants from the National Joint Registry

Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 1338 (0.27%) Healthy weight (BMI 18.5-24.99 kg/m^2) = 49860 (10.10%) Overweight (BMI 25-29.99 kg/m^2) = 168947 (34.22%)

Reference	Evans 2021[46]
	Obesity I (BMI 30-34.99 kg/m^2) = 159056 (32.22%) Obesity II (BMI 35-39.99 kg/m^2) = 80166 (16.24%) Obesity III (BMI ≥40 kg/m^2) = 34343 (6.96%) *Numbers reported in patient characteristics table. These do not add up to the total number of people in the flow diagram above (instead the number of joint replacements from the revision data, this may double count some patients).
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, ASA grade, indication for operation and year of primary total knee replacement.
Outcomes and effect sizes	Mortality at ≤3 months (within 90 days) Reoperation or revision to the prosthesis at >3 months – Revision (within 11 years) **Obesity III (BMI ≥40 kg/m^2) compared to obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), healthy weight (BMI 18.5 kg/m^2 to 24.9 kg/m^2) and underweight (BMI <18.5 kg/m^2)** **Mortality at ≤3 months – HR (95% CI)** • **Underweight (BMI <18.5 kg/m^2) (n=1338) = 1.64 (0.87, 3.09)** • **Healthy weight (BMI 18.5-25 kg/m^2) (n=49860) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=168947) = 0.76 (0.65, 0.90)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=159056) = 0.69 (0.58, 0.82)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=80166) = 0.88 (0.72, 1.09)** • **Obesity III (BMI ≥40 kg/m^2) (n=34343) = 1.17 (0.90, 1.54)** **Reoperation or revision to the prosthesis at >3 months – HR (95% CI)** • **Underweight (BMI <18.5 kg/m^2) (n=1338) = 0.88 (0.55, 1.41)** • **Healthy weight (BMI 18.5-25 kg/m^2) (n=49860) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=168947) = 1.05 (0.97, 1.14)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=159056) = 1.08 (0.99, 1.18)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=80166) = 1.21 (1.10, 1.32)** • **Obesity III (BMI ≥40 kg/m^2) (n=34343) = 1.13 (1.02, 1.26)**
Comments	**Mortality at ≤3 months** Risk of bias:

Reference	Evans 2021[46]	
	1. Study participation	HIGH
	2. Study attrition	HIGH
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Reoperation or revision to the prosthesis at >3 months	
	Risk of bias:	
	1. Study participation	HIGH
	2. Study attrition	HIGH
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Indirectness:	
	Population indirectness – Does not state if people had knee replacement for osteoarthritis, and so may include people who had other conditions. This will be included, but downgraded for indirectness.	

Reference	George 2018[52]
Study type and analysis	Retrospective cohort study. Multivariate logistic regression analysis. Adjusting data for differences in age, gender, American Society of Anaesthesiologists, functional status, (independent vs partially/totally dependent), smoking, BMI, anaesthesia (general vs others), congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, disseminated cancer, dialysis, corticosteroid use, recent weight loss.

Reference	George 2018[52]
	United States of America

Number of participants and characteristics	N=151684 enrolled from the American College of Surgeons National Surgical Quality Improvement Project (NSQIP) database (queried from January 1 2011 to December 31 2015). 403 procedures were excluded due to missing BMI data. 347 underweight people were excluded (as they deemed there were insufficient participants to use the data).
	
	Inclusion criteria:
	People who had a knee replacement and was registered into the American College of Surgeons NSQIP database between January 2011 and December 2015.
	
	Exclusion criteria:
	No additional information.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Healthy weight:
	• Age (SD): 70.6 (10.7) years
	• Male = 31.28%
	• Race
	  ○ White = 78.22%
	  ○ Black = 4.05%
	  ○ Others = 17.59%
	• ASA class
	  ○ 1 = 4.35%
	  ○ 2 = 60%
	  ○ 3 = 34.33%
	  ○ 4+ = 1.25%
	• Independent function status = 97.58%
	• Smoker = 8.94%
	• General anaesthesia = 48.02%
	• Comorbidities
	  ○ Congestive heart failure = 0.235%

Reference	George 2018[52]
	○ Chronic obstructive pulmonary disease = 3.16% ○ Diabetes = 7.77% ○ Dialysis = 0.21% ○ Disseminated cancer = 0.11% ○ Bleeding disorder = 2.33% ○ Steroid use = 5.31% ○ Weight loss = 0.29% **Overweight:** • Age (SD): 69.0 (9.7) years • Male = 45.11% • Race ○ White = 78.73% ○ Black = 4.95% ○ Others = 16.2% • ASA class ○ 1 = 3.5% ○ 2 = 60.46% ○ 3 = 34.71% ○ 4+ = 1.21% • Independent function status = 98.14% • Smoker = 8.42% • General anaesthesia = 49.28% • Comorbidities ○ Congestive heart failure = 0.25% ○ Chronic obstructive pulmonary disease = 3.06% ○ Diabetes = 11.96% ○ Dialysis = 0.17% ○ Disseminated cancer = 0.1% ○ Bleeding disorder = 2.35% ○ Steroid use = 3.44%

Reference	George 2018[52]
	○ Weight loss = 0.1% **Obesity III:** • Age (SD): 61.9 (8.4) years • Male = 26.72% • Race ○ White = 76.94% ○ Black = 11.83% ○ Others = 11.15% • ASA class ○ 1 = 0.36% ○ 2 = 24.3% ○ 3 = 72.07% ○ 4+ = 3.19% • Independent function status = 97.35% • Smoker = 9.13% • General anaesthesia = 57.19% • Comorbidities ○ Congestive heart failure = 0.38% ○ Chronic obstructive pulmonary disease = 4.91% ○ Diabetes = 28.63% ○ Dialysis = 0.13% ○ Disseminated cancer = 0.03% ○ Bleeding disorder = 2.51% ○ Steroid use = 3.38% ○ Weight loss = 0.1% **Population source:** Participants registered into the American College of Surgeons NSQIP database between January 2011 and December 2015
Prognostic variables	Healthy weight (BMI ≥18.5-<25 kg/m^2) = 14989 Overweight (BMI ≥25-<30 kg/m^2) = 41155

Reference	George 2018[52]
	Obesity I and II (BMI ≥30-<40 kg/m^2) = 71709 (this group is not included in the analysis as it cannot be placed into either category) Obesity III (BMI ≥40 kg/m^2) = 23081
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, gender, American Society of Anaesthesiologists, functional status, (independent vs partially/totally dependent), smoking, BMI, anaesthesia (general vs others), congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, disseminated cancer, dialysis, corticosteroid use, recent weight loss.
Outcomes and effect sizes	Mortality at 30 days (≤3 months) Reoperation at 30 days (≤3 months) Deep vein thrombosis at 30 days* - Both values will be reported as they could both be relevant, but will not be meta-analysed unless studies only report these individual categories (≤3 months) Pulmonary embolism at 30 days* (≤3 months) Superficial infection at 30 days+ - Both values will be reported as they could both be relevant, but will not be meta-analysed unless studies only report these individual categories (≤3 months) Periprosthetic joint infection at 30 days+ (≤3 months) **Obesity III (BMI ≥40 kg/m^2) and overweight (BMI 25-29.9 kg/m^2) compared to healthy weight (BMI 18.5 kg/m^2 to 24.9 kg/m^2)** **Mortality at ≤3 months – OR (95% CI)** • **Healthy weight (BMI <25 kg/m^2) (n=14989) = Reference (all comparisons are against normal weight)** • **Overweight (BMI 25-29.9 kg/m^2) (n=41155) = 0.97 (0.53 to 1.75)** • **Obesity III (BMI ≥40 kg/m^2) (n=23081) = 1.25 (0.67 to 2.34)** **Reoperation or revision to the prosthesis at ≤3 months – OR (95% CI)** • **Healthy weight (BMI <25 kg/m^2) (n=14989) = Reference (all comparisons are against normal weight)** • **Overweight (BMI 25-29.9 kg/m^2) (n=41155) = 0.94 (0.79 to 1.13)** • **Obesity III (BMI ≥40 kg/m^2) (n=23081) = 1.49 (1.24 to 1.79)** **Surgical site infection (wound infection) – superficial infection at ≤3 months – OR (95% CI)** • **Healthy weight (BMI <25 kg/m^2) (n=14989) = Reference (all comparisons are against normal weight)** • **Overweight (BMI 25-29.9 kg/m^2) (n=41155) = 0.85 (0.64 to 1.14)**

Reference	George 2018[52]
	• **Obesity III (BMI ≥40 kg/m^2) (n=23081) = 2.02 (1.53 to 2.67)** **Surgical site infection (wound infection) – periprosthetic joint infection at ≤3 months – OR (95% CI)** • **Healthy weight (BMI <25 kg/m^2) (n=14989) = Reference (all comparisons are against normal weight)** • **Overweight (BMI 25-29.9 kg/m^2) (n=41155) = 0.9 (0.61 to 1.32)** • **Obesity III (BMI ≥40 kg/m^2) (n=23081) = 2.14 (1.48 to 3.1)** **Venous thromboembolic events at ≤3 months – deep vein thrombosis – OR (95% CI)** • **Healthy weight (BMI <25 kg/m^2) (n=14989) = Reference (all comparisons are against normal weight)** • **Overweight (BMI 25-29.9 kg/m^2) (n=41155) = 1.1 (0.9 to 1.34)** • **Obesity III (BMI ≥40 kg/m^2) (n=23081) = 0.8 (0.64 to 1.01)** **Venous thromboembolic events at ≤3 months – pulmonary embolism – OR (95% CI)** • **Healthy weight (BMI <25 kg/m^2) (n=14989) = Reference (all comparisons are against normal weight)** • **Overweight (BMI 25-29.9 kg/m^2) (n=41155) = 1.49 (1.12 to 1.99)** • **Obesity III (BMI ≥40 kg/m^2) (n=23081) = 1.92 (1.42 to 2.58)**
Comments	**Mortality at ≤3 months** Risk of bias: 1. Study participation — HIGH 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH **Reoperation or revision to the prosthesis at ≤3 months** Risk of bias: 1. Study participation — HIGH 2. Study attrition — LOW

Reference	George 2018[52]	
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Reoperation or revision to the prosthesis at ≤3 months	
	Risk of bias:	
	1. Study participation	HIGH
	2. Study attrition	LOW
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Surgical site infection (wound infection) at ≤3 months (superficial infection)	
	Risk of bias:	
	1. Study participation	HIGH
	2. Study attrition	LOW
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Surgical site infection (wound infection) at ≤3 months (periprosthetic joint infection)	
	Risk of bias:	

Reference	George 2018[52]	
	1. Study participation	HIGH
	2. Study attrition	LOW
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Venous thromboembolic events at ≤3 months (deep vein thrombosis)	
	Risk of bias:	
	1. Study participation	HIGH
	2. Study attrition	LOW
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Venous thromboembolic events at ≤3 months (pulmonary embolism)	
	Risk of bias:	
	1. Study participation	HIGH
	2. Study attrition	LOW
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH

Reference	George 2018[52]
	Indirectness: Population indirectness – Does not state if people had knee replacement for osteoarthritis, and so may include people who had other conditions. This will be included, but downgraded for indirectness.

Reference	Gurunathan 2018A [63]
Study type and analysis	Retrospective observational cohort study. Multivariate analysis using logistic regression. Adjusting data for differences in age, gender, comorbidity (ASA classification), underlying pathology, procedure performed, private health insurance status and type of anaesthesia. Brisbane, Australia. A tertiary referral hospital (the Prince Charles Hospital).
Number of participants and characteristics	N=966 primary total hip arthroplasty procedures performed, 2 were excluded due to missing BMI information. 964 included. **Inclusion criteria:** People who had an elective primary unilateral hip replacement performed between 22 February 2006 and 15 December 2010, inclusive, from a prospective secure electronic database maintained by the department of orthopedics (osteoarthritis and osteonecrosis accounted for 97.7% of the underlying pathologies. **Exclusion criteria:** No additional information. **Values listed below are presented as mean (SD) or number (%) unless stated otherwise** **Healthy weight:** • Median age (IQR) = 69.0 (18) years • Male = 94 (49.2%) • Diabetes = 25 (13.1%) • Hypertension = 70 (35.6%) • Cardiac issues = 32 (16.8%) • Renal issues = 3 (1.6%) • Steroid use = 2 (1.0%)

Reference	Gurunathan 2018A [63]

	• Pulmonary issues = 28 (14.7%)
	• Neurological issues = 8 (4.2%)
	• History of venous thromboembolic events = 6 (3.1%)
	• Bleeding disorders = 4 (2.1%)
	• Current smoking = 6 (3.1%)
	• ASA grade
	  ○ 1 = 41 (21.7%)
	  ○ 2 = 101 (53.4%)
	  ○ 3 = 43 (22.8%)
	  ○ 4 = 4 (2.1%)
	
	Overweight:
	• Median age (IQR) = 70.0 (15) years
	• Male = 213 (56.3%)
	• Diabetes = 51 (13.5%)
	• Hypertension = 121 (32.0%)
	• Cardiac issues = 76 (20.1%)
	• Renal issues = 16 (4.2%)
	• Steroid use = 5 (1.3%)
	• Pulmonary issues = 47 (12.4%)
	• Neurological issues = 19 (5.0%)
	• History of venous thromboembolic events = 15 (4.0%)
	• Bleeding disorders = 5 (1.3%)
	• Current smoking = 16 (4.2%)
	• ASA grade
	  ○ 1 = 63 (16.8%)
	  ○ 2 = 208 (55.3%)
	  ○ 3 = 100 (26.6%)
	  ○ 4 = 5 (1.3%)

Reference	Gurunathan 2018A [63]

	Obesity I:
	• Median age (IQR) = 68.0 (15) years
	• Male = 118 (53.9%)
	• Diabetes = 24 (11.0%)
	• Hypertension = 78 (35.6%)
	• Cardiac issues = 53 (24.2%)
	• Renal issues = 7 (3.2%)
	• Steroid use = 2 (0.9%)
	• Pulmonary issues = 31 (14.2%)
	• Neurological issues = 9 (4.1%)
	• History of venous thromboembolic events = 4 (1.8%)
	• Bleeding disorders = 9 (4.1%)
	• Current smoking = 4 (1.8%)
	• ASA grade
	  ○ 1 = 20 (9.2%)
	  ○ 2 = 134 (61.5%)
	  ○ 3 = 63 (28.9%)
	  ○ 4 = 1 (0.5%)
	
	Obesity II:
	• Median age (IQR) = 65.0 (16) years
	• Male = 51 (46.4%)
	• Diabetes = 11 (10.0%)
	• Hypertension = 38 (34.5%)
	• Cardiac issues = 22 (20.0%)
	• Renal issues = 1 (0.9%)
	• Steroid use = 0 (0.0%)
	• Pulmonary issues = 15 (13.6%)
	• Neurological issues = 3 (2.7%)
	• History of venous thromboembolic events = 5 (4.5%)

Reference	Gurunathan 2018A [63]

	• Bleeding disorders = 3 (2.7%)
	• Current smoking = 8 (7.3%)
	• ASA grade
	  ○ 1 = 9 (8.2%)
	  ○ 2 = 57 (51.8%)
	  ○ 3 = 42 (38.2%)
	  ○ 4 = 2 (1.8%)
	
	Obesity III:
	• Median age (IQR) = 60.0 (15) years
	• Male = 16 (29.1%)
	• Diabetes = 5 (9.1%)
	• Hypertension = 22 (40.0%)
	• Cardiac issues = 8 (14.5%)
	• Renal issues = 0 (0.0%)
	• Steroid use = 0 (0.0%)
	• Pulmonary issues = 10 (18.2%)
	• Neurological issues = 4 (7.3%)
	• History of venous thromboembolic events = 1 (1.8%)
	• Bleeding disorders = 3 (5.5%)
	• Current smoking = 4 (7.3%)
	• ASA grade
	  ○ 1 = 1 (1.9%)
	  ○ 2 = 22 (40.7%)
	  ○ 3 = 28 (51.9%)
	  ○ 4 = 3 (5.6%)
	
	Population source: People who had hip replacement surgery at the Prince Charles Hospital

Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 11 (1.1%) – the study did not have a sufficient number of participants to be included in the analysis, so were excluded. Healthy weight (BMI 18.5-24.99 kg/m^2) = 191 (19.8%)

Reference	Gurunathan 2018A [63]
	Overweight (BMI 25-29.99 kg/m^2) = 378 (39.2%) Obesity I (BMI 30-34.99 kg/m^2) = 219 (22.7%) Obesity II (BMI 35-39.99 kg/m^2) = 110 (11.4%) Obesity III (BMI ≥40 kg/m^2) = 55 (5.7%)
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, gender, comorbidity (ASA classification), underlying pathology, procedure performed, private health insurance status and type of anaesthesia.
Outcomes and effect sizes	Total adverse events up to 90 days – Overall complications (30 days) Surgical site infection (wound infection) at ≤3 months – Infectious complications (30 days)* Venous thromboembolic events at ≤3 months – Thromboembolic complications (30 days) *This outcome could include other infectious complications (for example: pneumonia) and so will be included but downgraded for indirectness. **Obesity III (BMI ≥40 kg/m^2), obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2) compared to healthy weight (BMI 18.5 kg/m^2 to 24.9 kg/m^2)** **Total adverse events up to 90 days – OR (95% CI)** • **Healthy weight* (BMI 18.5-25 kg/m^2) (n=191) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=378) = 0.62 (0.43, 0.92)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=219) = 0.70 (0.46, 1.08)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=110) = 0.60 (0.36, 0.99)** • **Obesity III (BMI ≥40 kg/m^2) (n=55) = 1.31 (0.64, 2.70)** **Surgical site infection (wound infection) at ≤3 months – OR (95% CI)** • **Healthy weight* (BMI 18.5-25 kg/m^2) (n=191) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=378) = 1.22 (0.62, 2.42)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=219) = 1.45 (0.69, 3.06)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=110) = 1.65 (0.69, 3.94)** • **Obesity III (BMI ≥40 kg/m^2) (n=55) = 2.47 (0.91, 6.71)**

Reference	Gurunathan 2018A [63]
	Venous thromboembolic events at ≤3 months – OR (95% CI) • **Healthy weight* (BMI 18.5-25 kg/m^2) (n=191) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=378) = 0.38 (0.11, 1.29)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=219) = 1.08 (0.36, 3.25)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=110) = 0.53 (0.10, 2.82)** • **Obesity III (BMI ≥40 kg/m^2) (n=55) = 0.49 (0.05, 4.50)**
Comments	**Total adverse events up to 90 days** Risk of bias: 1. Study participation HIGH 2. Study attrition LOW 3. Prognostic factor measurement LOW 4. Outcome Measurement LOW 5. Study confounding HIGH 6. Statistical analysis LOW 7. Other risk of bias LOW OVERALL RISK OF BIAS VERY HIGH **Surgical site infection (wound infection) at ≤3 months** Risk of bias: 1. Study participation HIGH 2. Study attrition LOW 3. Prognostic factor measurement LOW 4. Outcome Measurement LOW 5. Study confounding HIGH 6. Statistical analysis LOW 7. Other risk of bias LOW OVERALL RISK OF BIAS VERY HIGH **Venous thromboembolic events at ≤3 months** Risk of bias:

Reference	Gurunathan 2018A [63]	
	1. Study participation	HIGH
	2. Study attrition	LOW
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Indirectness: Population indirectness – Does not state if people had knee replacement for osteoarthritis (states the majority did for osteoarthritis or osteonecrosis, but no information about just osteoarthritis), and so may include people who had other conditions. This will be included, but downgraded for indirectness. Outcome indirectness – For surgical site infection only. The study reports infectious complications, which may include infections in places other than the surgical site. This will be included but downgraded for indirectness.	

Reference	Gurunathan 2018B [64]
Study type and analysis	Retrospective observational cohort study. Multivariate analysis using logistic regression. Adjusting data for differences in age, gender, comorbidity (ASA classification), underlying pathology and type of anaesthesia. Brisbane, Australia. A tertiary referral hospital (the Prince Charles Hospital).
Number of participants and characteristics	N=1665 primary total knee arthroplasty procedures performed. **Inclusion criteria:** People who had an elective primary total knee replacement performed between January 1, 2006 and December 31, 2010, inclusive, from a prospective secure electronic database maintained by the department of orthopedics (osteoarthritis was the most common reason occurring in 98.3%). **Exclusion criteria:**

Reference	Gurunathan 2018B [64]

	No additional information.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Healthy weight:
	• Median age (IQR) = 75.0 (14) years
	• Male = 44 (31.2%)
	• Diabetes = 30 (21.3%)
	• Hypertension = 75 (53.2)%)
	• Cardiac issues = 33 (23.4%)
	• Renal issues = 6 (4.3%)
	• Steroid use = 3 (2.1%)
	• Pulmonary issues = 22 (15.6%)
	• Neurological issues = 10 (7.1%)
	• History of venous thromboembolic events = 7 (5.0%)
	• Bleeding disorders = 2 (1.4%)
	• Current smoking = 2 (1.4%)
	• ASA grade
	  ○ 1 = 17 (12.1%)
	  ○ 2 = 84 (59.6%)
	  ○ 3 = 34 (24.1%)
	  ○ 4 = 6 (4.3%)
	• Pathology
	  ○ Osteoarthritis/osteonecrosis = 133 (94.3%)
	  ○ Inflammatory arthritis = 8 (5.7%)
	
	Overweight:
	• Median age (IQR) = 73.0 (11) years
	• Male = 224 (46.6%)
	• Diabetes = 65 (13.5%)
	• Hypertension = 213 (44.3%)

Reference	Gurunathan 2018B [64]

	• Cardiac issues = 115 (23.9%)
	• Renal issues = 20 (4.2%)
	• Steroid use = 8 (1.7%)
	• Pulmonary issues = 86 (17.9%)
	• Neurological issues = 31 (6.4%)
	• History of venous thromboembolic events = 17 (3.5%)
	• Bleeding disorders = 7 (1.5%)
	• Current smoking = 12 (2.5%)
	• ASA grade
	  ○ 1 = 37 (7.7%)
	  ○ 2 = 276 (57.4%)
	  ○ 3 = 147 (30.6%)
	  ○ 4 = 21 (4.4%)
	• Pathology
	  ○ Osteoarthritis/osteonecrosis = 473 (98.3%)
	  ○ Inflammatory arthritis = 8 (1.7%)
	
	Obesity I:
	• Median age (IQR) = 69.0 (11) years
	• Male = 205 (40.4%)
	• Diabetes = 86 (16.9%)
	• Hypertension = 215 (42.3%)
	• Cardiac issues = 139 (27.4%)
	• Renal issues = 11 (2.2%)
	• Steroid use = 4 (0.8%)
	• Pulmonary issues = 92 (18.1%)
	• Neurological issues = 26 (5.1%)
	• History of venous thromboembolic events = 15 (3.0%)
	• Bleeding disorders = 3 (0.6%)
	• Current smoking = 15 (3.0%)

Reference	Gurunathan 2018B [64]

	• ASA grade
	  ○ 1 = 29 (5.7%)
	  ○ 2 = 315 (62.0%)
	  ○ 3 = 13 (26.4%)
	  ○ 4 = 30 (5.9%)
	• Pathology
	  ○ Osteoarthritis/osteonecrosis = 501 (98.6%)
	  ○ Inflammatory arthritis = 7 (1.4%)
	
	Obesity II:
	• Median age (IQR) = 66.0 (11) years
	• Male = 115 (35.9%)
	• Diabetes = 48 (15.0%)
	• Hypertension = 150 (46.9%)
	• Cardiac issues = 79 (24.7%)
	• Renal issues = 2 (0.6%)
	• Steroid use = 2 (0.6%)
	• Pulmonary issues = 61 (19.1%)
	• Neurological issues = 21 (6.6%)
	• History of venous thromboembolic events = 16 (5.0%)
	• Bleeding disorders = 4 (1.3%)
	• Current smoking = 8 (2.5%)
	• ASA grade
	  ○ 1 = 9 (2.8%)
	  ○ 2 = 182 (56.9%)
	  ○ 3 = 110 (34.4%)
	  ○ 4 = 19 (5.9%)
	• Pathology
	  ○ Osteoarthritis/osteonecrosis = 318 (99.4%)
	  ○ Inflammatory arthritis = 2 (0.6%)

Reference	Gurunathan 2018B [64]

	Obesity III:
	• Median age (IQR) = 63.0 (10) years
	• Male = 46 (21.6%)
	• Diabetes = 45 (21.1%)
	• Hypertension = 101 (47.4%)
	• Cardiac issues = 54 (25.4%)
	• Renal issues = 4 (1.9%)
	• Steroid use = 2 (0.9%)
	• Pulmonary issues = 41 (19.2%)
	• Neurological issues = 16 (7.5%)
	• History of venous thromboembolic events = 7 (3.3%)
	• Bleeding disorders = 3 (1.4%)
	• Current smoking = 5 (2.3%)
	• ASA grade
	  ○ 1 = 5 (2.3%)
	  ○ 2 = 92 (43.2%)
	  ○ 3 = 101 (47.4%)
	  ○ 4 = 15 (7.0%)
	• Pathology
	  ○ Osteoarthritis/osteonecrosis = 210 (98.6%)
	  ○ Inflammatory arthritis = 3 (1.4%)
	
	Population source: People who had knee replacement surgery at the Prince Charles Hospital

Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 2 (0.1%) – the study did not have a sufficient number of participants to be included in the analysis, so were excluded. Healthy weight (BMI 18.5-24.99 kg/m^2) = 141 (8.5%) Overweight (BMI 25-29.99 kg/m^2) = 481 (28.9%) Obesity I (BMI 30-34.99 kg/m^2) = 508 (30.5%) Obesity II (BMI 35-39.99 kg/m^2) = 320 (19.2%) Obesity III (BMI ≥40 kg/m^2) = 213 (12.8%)
Confounders	Multivariable analysis

Reference	Gurunathan 2018B [64]
	Factors included in the adjusted analysis: age, gender, comorbidity (ASA classification), underlying pathology and type of anaesthesia.
Outcomes and effect sizes	Total adverse events up to 90 days – Overall complications (30 days) **Obesity III (BMI ≥40 kg/m^2), obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2) compared to healthy weight (BMI 18.5 kg/m^2 to 24.9 kg/m^2)** **Total adverse events up to 90 days – OR (95% CI)** • **Healthy weight* (BMI 18.5-25 kg/m^2) (n=141) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=481) = 1.11 (0.68, 1.81)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=508) = 0.85 (0.52, 1.39)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=320) = 0.69 (0.42, 1.13)** • **Obesity III (BMI ≥40 kg/m^2) (n=213) = 1.02 (1.00, 1.04)**
Comments	**Total adverse events up to 90 days** Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH Indirectness: No indirectness noted

Reference	Jamsen 2012[77]
Study type and analysis	Prospective cohort study.

Reference	Jamsen 2012[77]
	Multivariate analysis using logistic regression. Adjusting data for differences in age, sex, American Society of Anaesthesiologists (ASA) risk score, arthroplasty site (hip or knee), BMI and diabetic status. Finland. Single-centre case series (publicly funded tertiary-care center).

Number of participants and characteristics	N=8775 primary hip and knee replacement procedures between September 1, 2002, and January 31, 2008. All publicly funded joint replacement surgery in the hospital district (which has a population of approximately 470,000) is centralized to this one hospital. People who had undergone open surgery of the involved joint prior to the hip or knee replacement and patients who had undergone both hip and knee replacement during the same anaesthesia session were excluded. 7181 primary hip and knee replacement operations (involving 8083 joints and 6372 patients).
	
	Knee replacements = 3915
	Hip replacement = 3266
	(Unclear if these are due to osteoarthritis)
	
	Inclusion criteria:
	People who had undergone open surgery of the involved joint prior to the hip or knee replacement and patients who had undergone both hip and knee replacement.
	
	Exclusion criteria:
	Patients who had undergone both hip and knee replacement during the same anaesthesia sessions.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Knee replacement:
	• Median age (range) = 72.2 (38.3-97.1) years
	• Female:Male = 2827:1088 (72.2%:27.8%)
	• ASA risk score
	  ○ 1 = 176 (4.5%)
	  ○ 2 = 1846 (47.4%)
	  ○ 3 = 1798 (46.1%)
	  ○ 4 = 78 (2.0%)
	• Body mass index in kg/m^2

Reference	Jamsen 2012[77]
	○ <25 = 405 (12.7%) ○ 25-29 = 1261 (39.6%) ○ 30-34 = 992 (31.1%) ○ 35-39 = 373 (11.7%) ○ ≥40 = 156 (4.9%) • Preoperative glucose level in mmol/L ○ <6.1 = 1819 (60.8%) ○ 6.1-6.8 = 567 (18.9%) ○ ≥6.9 = 608 (20.3%) • Operative data: ○ Unilateral:Bilateral = 3268:647 ○ Cemented:Hybrid:Uncemented = 3671:241:3 ○ Orthopaedic surgeon:Resident = 3212:703 **Hip replacement:** • Median age (range) = 68.7 (26.4-95.0) years • Female:Male = 1761:1505 (53.9%:46.1%) • ASA risk score ○ 1 = 357 (11.0%) ○ 2 = 1694 (52.3%) ○ 3 = 1129 (34.8%) ○ 4 = 62 (1.9%) • Body mass index in kg/m^2 ○ <25 = 700 (25.3%) ○ 25-29 = 1200 (43.4%) ○ 30-34 = 643 (23.2%) ○ 35-39 = 186 (6.7%) ○ ≥40 = 37 (1.3%) • Preoperative glucose level in mmol/L ○ <6.1 = 1556 (63.1%) ○ 6.1-6.8 = 477 (19.3%)

Reference	Jamsen 2012[77]
	○ ≥6.9 = 433 (17.6%) • Operative data: ○ Unilateral:Bilateral = 3011:255 ○ Cemented:Hybrid:Uncemented = 1066:1098:1102 ○ Orthopaedic surgeon:Resident = 2848:418 **Population source:** People who had hip and/or knee replacement surgery at publicly funded tertiary-care center
Prognostic variables	Healthy weight* (BMI <25 kg/m^2) = 1105 (this group will be considered as indirect evidence for normal weight) Overweight (BMI 25-29.99 kg/m^2) = 2461 Obesity I (BMI 30-34.99 kg/m^2) = 1635 Obesity II (BMI 35-39.99 kg/m^2) = 2927 Obesity III (BMI ≥40 kg/m^2) = 140
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, American Society of Anaesthesiologists (ASA) risk score, arthroplasty site (hip or knee), BMI and diabetic status.
Outcomes and effect sizes	Surgical site infection (wound infection) at >3 months – perioperative joint infection during the first postoperative year (>3 months) **Obesity III (BMI ≥40 kg/m^2), obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2) compared to healthy weight (BMI <25 kg/m^2)** **Surgical site infection (wound infection) at >3 months – OR (95% CI)** • **Healthy weight* (BMI 18.5-25 kg/m^2) (n=1105) = 1.00 (reference)** • **Overweight (BMI 25-29.9 kg/m^2) (n=2461) = 1.01 (0.32, 3.21)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=1635) = 1.76 (0.56, 5.56)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=559) = 0.83 (0.17, 4.01)** • **Obesity III (BMI ≥40 kg/m^2) (n=193) = 6.41 (1.67, 24.59)**
Comments	**<u>Surgical site infection (wound infection) at >3 months</u>** Risk of bias: 1. Study participation HIGH 2. Study attrition LOW

Reference	Jamsen 2012[77]	
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	HIGH
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Indirectness: Population indirectness – Does not specify if people had osteoarthritis and so people without osteoarthritis may be included in the data, Prognostic variable indirectness – Includes people with BMI <25 for the healthy weight group, which could include people who were underweight.	

Reference	Jamsen 2013[78]
Study type and analysis	Prospective cohort study. Multivariate analysis using Cox regression analysis. Adjusting data for differences in age, sex, operated joint, laterality and anaesthesiological risk score. Finland. Single institution (publicly funded tertiary-care center).
Number of participants and characteristics	N=2559 primary hip and knee replacements, 306 joints excluded due to subsequent primary joint replacements, excluded for indications other than osteoarthritis (74 acute hip fracture or revision of failed osteosynthesis, 70 inflammatory arthritis, 23 secondary osteoarthritis, 19 osteonecrosis, 10 bone tumour or metastasis, 6 miscellaneous diagnoses); 47 excluded for unicondylar knee replacement, 6 excluded for resurfacing hip replacement. Total included = 756 primary total hip replacements, 1242 primary total knee replacements. Knee replacements = 1242 Hip replacement = 756 **Inclusion criteria:** Primary hip and knee replacements performed at their institution in patients aged 75 years or more at the time of surgery, from September 1, 2002 through January 31, 2009 performed due to primary osteoarthritis.

Reference	Jamsen 2013[78]

	Exclusion criteria:
	People having multiple operations (through simultaneous replacement of both hips or knees were included); operations performed for reasons other than primary osteoarthritis.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Overall:
	• Age group
	  ○ 75-79 years = 1166
	  ○ 80-84 years = 643
	  ○ 85 years or over = 189
	• Female:Male = 1451:547
	• ASA risk score
	  ○ II = 712
	  ○ III = 1208
	  ○ IV or V = 67
	• Charnley Class/Knee Society Class
	  ○ One hip/knee involved = 807
	  ○ Both hips/knees involved = 945
	  ○ Other reasons restrict mobility = 67
	• Use of walking aids = 1323
	• Walking ability
	  ○ Unable to walk = 19
	  ○ Indoors only = 277
	  ○ Less than 1km = 1059
	  ○ Over 1km or unlimited = 470
	• Severe osteoarthritis = 815
	• Anaemia = 240
	• Renal function
	  ○ Normal = 106

Reference	Jamsen 2013[78]
	○ Mild insufficiency = 467 ○ Moderate insufficiency = 304 ○ Severe insufficiency = 9 • Operated joint laterality ○ Unilateral = 1820 ○ Bilateral = 178 • Type of knee replacement ○ Cruciate-retaining = 399 ○ Cruciate-substituting = 766 ○ Constrained = 58 ○ Hinge or tumour prosthesis = 19 • Fixation method ○ Cemented = 1720 ○ Hybrid = 182 ○ Cementless = 96 • Duration of operation ○ No more than 87 minutes = 469 ○ 88-101 min = 432 ○ 102-120 min = 477 ○ >120 min = 435 • Blood loss ○ No more than 200mL = 1056 ○ 201-500mL = 499 ○ 501-800mL = 265 ○ >800 mL = 145 • Blood transfusion = 432 **Population source:** People who had hip and/or knee replacement surgery at a tertiary-care center
Prognostic variables	Healthy weight* (BMI 20-24 kg/m^2) = 373 (the study reported a <20 kg/m^2 group – for this analysis only the 20-24 kg/m^2 group will be considered. However, this group will be considered as indirect evidence for normal weight) Overweight (BMI 25-30 kg/m^2) = 786

Reference	Jamsen 2013[78]
	Obesity I* (BMI >30 kg/m^2) = 482 (this group will be considered as indirect evidence for Obesity I as it could include people in higher BMI categories)
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, operated joint, laterality and anaesthesiological risk score.
Outcomes and effect sizes	Mortality at >3 months – follow up for at most 5 years **Obesity I (BMI 30-34.9 kg/m^2) and healthy weight (BMI <25 kg/m^2) compared to overweight (BMI 25-29.9 kg/m^2)** **Mortality at >3 months – HR (95% CI)** • **Healthy weight* (BMI 20-24 kg/m^2) (n=373) = 1.43 (1.06-1.93)** • **Overweight (BMI 25-30 kg/m^2) (n=786) = 1 (reference)** • **Obesity I* (BMI >30 kg/m^2) (n=482) = 0.89 (0.65-1.23)**
Comments	**<u>Mortality at >3 months</u>** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH Indirectness: Prognostic variable indirectness – Includes people with BMI 20-24 for the healthy weight group, which excludes people between 18-20, and includes people with BMI >30 for obesity I, which could include people in the obesity II and obesity III categories.

Reference	Judge 2014[83]
Study type and analysis	Retrospective cohort study. Multivariate analysis using Cox regression analysis. Adjusting data for differences in age, sex, SF-36 mental health, comorbidities, fixed flexion, analgesic use, college education, OA in other joints, expectation of less pain, radiographic K&L grade, ASA grade, years of hip pain. People from four databases: The European collaborative database of cost and practice patterns of total hip replacement (EUROHIP): across 20 European orthopaedic centres; Exeter Primary Outcomes Study (EPOS) UK setting; Elective Orthopaedic Centre database (EOC) across four acute NHS Trusts in South West London, UK and St. Helier Hospital outcome programme: a district general hospital serving the London Boroughs of Sutton and Merton.

Number of participants and characteristics	N=6377 patients receiving primary total hip replacement for osteoarthritis, of whom 4413 completed both baseline and 12-month follow up Oxford Hip Scores and were included in the analysis.
	
	Inclusion criteria:
	People within the four databases: EUROHIP in 2002, EPOS between 1999 and 2002, EOC between 2005-2008, St. Helier Hospital outcome programme between 1995-2007.
	
	Exclusion criteria:
	No additional information.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Overall:
	• Mean age (SD)
	  ○ EPOS = 72.64 (9.93) years
	  ○ EUROHIP = 65.68 (11.22) years
	  ○ EOC = 70.27 (11.30) years
	  ○ ST HELIER = 66.30 (14.52) years
	• Female:Male
	  ○ EPOS = 92:70
	  ○ EUROHIP = 260:199
	  ○ EOC = 801:428

Reference	Judge 2014[83]
	○ ST HELIER = 53:37 • OHS pre-op ○ EPOS = 15.81 (8.15) ○ EUROHIP = 13.26 (8.43) ○ EOC = 18.38 (8.56) ○ ST HELIER = 17.47 (7.63) **Population source:** People with osteoarthritis who had a hip replacement surgery in four databases: EUROHIP in 2002, EPOS between 1999 and 2002, EOC between 2005-2008, St. Helier Hospital outcome programme between 1995-2007.
Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 24 Healthy weight (BMI 18.5-25 kg/m^2) = 864 Overweight (BMI 25-30 kg/m^2) = 1139 Obesity I (BMI 30-35 kg/m^2) = 502 Obesity II (BMI 35-40 kg/m^2) = 150 Obesity III (BMI >40 kg/m^2) = 47
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, SF-36 mental health, comorbidities, fixed flexion, analgesic use, college education, OA in other joints, expectation of less pain, radiographic K&L grade, ASA grade, years of hip pain.
Outcomes and effect sizes	Post-operative patient-reported outcome measures at 1 year (1 year) **Obesity III (BMI ≥40 kg/m^2), obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), underweight (BMI <18.5 kg/m^2) compared to healthy weight (BMI 18.5-25 kg/m^2)** **Post-operative patient-reported outcome measures at 1 year – mean (95% CI) (final value)** • **Underweight (BMI <18.5 kg/m^2) (n=24) = 39.34 (34.97, 43.71)** • **Healthy weight (BMI 18.5-25 kg/m^2) (n=864) = 39.85 (38.25, 41.45)** • **Overweight (BMI 25-29.9 kg/m^2) (n=1139) = 39.15 (37.56, 40.75)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=502) = 37.66 (35.93, 39.39)** • **Obesity II (BMI 35-39.9 kg/m^2) (n=150) = 36.92 (34.72, 39.11)** • **Obesity III (BMI ≥40 kg/m^2) (n=47) = 37.83 (34.25, 41.41)**

Reference	Judge 2014[83]
Comments	**Post-operative patient-reported outcome measures at 1 year** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH Indirectness: No known indirectness

Reference	Li 2017[98]
Study type and analysis	Prospective cohort study (FORCE-TJR cohort). Multivariate analysis using linear mixed models that adjusted for the clustering of patients within individual clinics, with and without adjustment for other covariates. Adjusting data for differences in baseline function and pain score, sex, age, race, household income, education, living alone, type of insurance, medical comorbidities, low back pain, number of other painful joints, and surgical volume of the hospital People from >100 community orthopedic practices, distributed across 22 states in the United States of America.
Number of participants and characteristics	N=2964 patients who underwent primary unilateral total knee replacement and the first 2040 who underwent primary unilateral total hip replacement between May 2011 and March 2013 and completed the 6-month postoperative questionnaire (treated by a total of 111 orthopaedic surgeons, representing >85% of all enrolled patients). Total hip replacement = 2040 Total knee replacement = 2964 **Inclusion criteria:**

Reference	Li 2017[98]
	A primary diagnosis of osteoarthritis **Exclusion criteria:** Another diagnosis (for example, osteonecrosis or inflammatory arthritis), or had the total joint replacement for an acute fracture or cancer. **Values listed below are presented as mean (SD) or number (%) unless stated otherwise** **Total hip replacement:** • Male (%) = 41.4% • Mean age (SD) = 65.2 (10.4) years • White race (%) = 94.1% • Education (no more than high school) (%) = 25.1% • Household income (no more than $45,000) (%) = 35.0% • Medicare insurance (%) = 50.2% • Living alone (%) = 23.6% • Current smoker (%) = 7.5% • At least 1 medical comorbidities (%) = 42.2% • Moderate or severe low-back pain (%) = 35.0% • At least 1 other painful joint(s) (%) = 34.7% • Baseline MCS score (SD) = 50.9 (12.3) **Total knee replacement:** • Male (%) = 38.9% • Mean age (SD) = 67.0 (9.2) years • White race (%) = 92.7% • Education (no more than high school) (%) = 31.5% • Household income (no more than $45,000) (%) = 38.7% • Medicare insurance (%) = 56.0% • Living alone (%) = 22.8% • Current smoker (%) = 4.5%

Reference	Li 2017[98]
	• At least 1 medical comorbidities (%) = 48.7% • Moderate or severe low-back pain (%) = 26.9% • At least 1 other painful joint(s) (%) = 31.4% • Baseline MCS score (SD) = 52.4 (11.8) **Population source:** People with osteoarthritis from >100 community orthopedic practices, distributed across 22 states in the United States of America who had total joint replacements (including hip and knee replacements)
Prognostic variables	Total hip replacement = 2040: Under or healthy weight* (BMI <25 kg/m^2) = 530 (this group includes people who were underweight or of healthy weight, this will be included as healthy weight but downgraded for indirectness) Overweight (BMI 25-29.99 kg/m^2) = 763 Obesity I (BMI 30-34.99 kg/m^2) = 453 Obesity II (BMI 35-39.99 kg/m^2) = 204 Obesity III (BMI ≥40 kg/m^2) = 90 Total knee replacement = 2964: Under or healthy weight* (BMI <25 kg/m^2) = 396 (this group includes people who were underweight or of healthy weight, this will be included as healthy weight but downgraded for indirectness) Overweight (BMI 25-29.99 kg/m^2) = 978 Obesity I (BMI 30-34.99 kg/m^2) = 861 Obesity II (BMI 35-39.99 kg/m^2) = 457 Obesity III (BMI ≥40 kg/m^2) = 272
Confounders	Multivariable analysis Factors included in the adjusted analysis: differences in baseline function and pain score, sex, age, race, household income, education, living alone, type of insurance, medical comorbidities, low back pain, number of other painful joints, and surgical volume of the hospital
Outcomes and effect sizes	Health-related quality of life at >3 months (6 months)* (only includes one component score of SF-36, and so will be downgraded for indirectness) Post-operative patient-reported outcome measures at 6 months (6 months)* (only includes the pain subscales of HOOS/KOOS, and so will be downgraded for indirectness) **Total hip replacement**

Reference	Li 2017[98]
	Obesity III (BMI ≥40 kg/m^2), obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), compared to healthy weight (BMI <25 kg/m^2) **Health-related quality of life at >3 months – mean (95% CI) (change score)** • **Healthy weight (BMI <25 kg/m^2) (n=530) = 14.0 (13.1, 14.8)** • **Overweight (BMI 25-29.99 kg/m^2) (n=763) = 13.2 (12.5, 13.9)** • **Obesity I (BMI 30-34.99 kg/m^2) (n=453) = 13.3 (12.4, 14.2)** • **Obesity II (BMI 35-39.99 kg/m^2) (n=204) = 10.8 (9.5, 12.0)** • **Obesity III (BMI ≥40 kg/m^2) (n=90) = 9.6 (7.7, 11.4)** **Post-operative patient-reported outcome measures at 6 months – mean (95% CI) (change score)** • **Healthy weight (BMI <25 kg/m^2) (n=515) = 42.4 (41.0, 43.7)** • **Overweight (BMI 25-29.99 kg/m^2) (n=745) = 41.0 (39.8, 42.2)** • **Obesity I (BMI 30-34.99 kg/m^2) (n=442) = 41.0 (39.6, 42.4)** • **Obesity II (BMI 35-39.99 kg/m^2) (n=194) = 40.1 (38.1, 42.1)** • **Obesity III (BMI ≥40 kg/m^2) (n=86) = 41.5 (38.6, 44.4)** **<u>Total knee replacement</u>** **Obesity III (BMI ≥40 kg/m^2), obesity II (BMI 35-39.9 kg/m^2), obesity I (BMI 30-34.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), compared to healthy weight (BMI <25 kg/m^2)** **Health-related quality of life at >3 months – mean (95% CI) (change score)** • **Healthy weight (BMI <25 kg/m^2) (n=396) = 10.8 (9.9, 11.6)** • **Overweight (BMI 25-29.99 kg/m^2) (n=978) = 10.9 (10.3, 11.5)** • **Obesity I (BMI 30-34.99 kg/m^2) (n=861) = 9.6 (9.0, 10.2)** • **Obesity II (BMI 35-39.99 kg/m^2) (n=457) = 9.0 (8.2, 9.8)** • **Obesity III (BMI ≥40 kg/m^2) (n=272) = 9.3 (8.3, 10.3)** **Post-operative patient-reported outcome measures at 6 months – mean (95% CI) (change score)**

Reference	Li 2017[98]
	• **Healthy weight (BMI <25 kg/m^2) (n=371) = 31.7 (30.0, 33.44)** • **Overweight (BMI 25-29.99 kg/m^2) (n=927) = 32.2 (31.0, 33.3)** • **Obesity I (BMI 30-34.99 kg/m^2) (n=817) = 30.3 (29.1, 31.5)** • **Obesity II (BMI 35-39.99 kg/m^2) (n=426) = 31.1 (29.5, 32.6)** • **Obesity III (BMI ≥40 kg/m^2) (n=251) = 30.2 (28.2, 32.2)**
Comments	**Total hip replacement** **Health-related quality of life at >3 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH **Post-operative patient-reported outcome measures at 6 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH **Total knee replacement**

Reference	Li 2017[98]
	Health-related quality of life at >3 months Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH **Post-operative patient-reported outcome measures at 6 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH Indirectness: Prognostic variable indirectness – For healthy weight prognostic variable, group includes people who were underweight or of healthy weight. Due to this, outcomes including this group will be downgraded for indirectness. Outcome indirectness – For both outcome types. In both cases, only subscales of the total scale are reported (for example: only the SF-36 physical component summary for health-related quality of life, only the KOOS pain subscale for post-operative patient-reported outcome measures). Due to this, these outcomes will be downgraded due to indirectness.

Reference	Liao 2017[99]
Study type and analysis	Retrospective cohort study. Multivariate analysis using repeated-measures ANOVA with adjustment for baseline prognostic confounding factors. Adjusting data for differences in age, sex, CIRS score, length of stay, pre-operative knee flexion and pre-operative WOMAC physical function score. People undergoing primary total knee replacement at the Shuang Ho Hospital-Taipei Medical University, Taiwan. Taken from the outpatient rehabilitation centre database.
Number of participants and characteristics	N=434 were potentially eligible for inclusion and underwent a primary total knee replacement procedure between July 2009 and October 2013. 41 were excluded in accordance with the exclusion criteria. 13 and 18 people who failed to attend the 3 and 6 month follow-up visits respectively, were excluded. Therefore, 354 people were included in the statistical analysis. **Inclusion criteria:** People who were diagnosed with osteoarthritis and had undergone a primary unilateral total knee replacement between July 2009 and October 2013. **Exclusion criteria:** People who underwent a revision total knee replacement and those who showed any neurological involvement that impaired motor function of the lower extremities.. **Values listed below are presented as mean (SD) or number (%) unless stated otherwise** **Normal weight (BMI 18.5-23.9 kg/m^2):** • Female (%) = 39 (66.1%) • Mean age (SD) = 75.3 (8.0) years • CIRS score (SD) = 7.3 (5.2) • Total Knee Replacement right side (%) = 35 (59.3%) **Overweight (BMI 24.0-26.9 kg/m^2):** • Female (%) = 67 (70.5%) • Mean age (SD) = 73.5 (6.5) years • CIRS score (SD) = 7.5 (4.9) • Total Knee Replacement right side (%) = 43 (45.3%)

Reference	Liao 2017[99]
	Class I obesity (BMI 27.0-29.9 kg/m^2): • Female (%) = 67 (74.4%) • Mean age (SD) = 70.3 (6.8) years • CIRS score (SD) = 8.1 (4.9) • Total Knee Replacement right side (%) = 51 (56.7%) **Class II obesity (BMI 30.0-34.9 kg/m^2):** • Female (%) = 63 (76.8%) • Mean age (SD) = 69.4 (7.6) years • CIRS score (SD) = 9.6 (4.8) • Total Knee Replacement right side (%) = 40 (48.8%) **Class III obesity (BMI ≥35.0 kg/m^2):** • Female (%) = 23 (82.1%) • Mean age (SD) = 66.0 (5.2) years • CIRS score (SD) = 10.9 (5.8) • Total Knee Replacement right side (%) = 12 (42.9%) **Population source:** People undergoing primary total knee replacement in Taiwan – records gathered from medical chart review.
Prognostic variables	The study uses definitions of classes of obesity that are not those in the protocol. However, the different values are appropriate for use with an Asian population, which this study likely includes. Given that the groups used in the study will be included within the BMI classifications stated in the protocol and will not be downgraded for prognostic variable indirectness. Healthy weight (BMI 18.5-24.0 kg/m^2) = 59 Overweight (BMI 24.0-26.9 kg/m^2) = 95 Obesity I (BMI 27.0-29.9 kg/m^2) = 90 Obesity II (BMI 30.0-34.9 kg/m^2) = 82 Obesity III (BMI ≥35 kg/m^2) = 28
Confounders	Multivariable analysis

Reference	Liao 2017[99]
	Factors included in the adjusted analysis: age, sex, CIRS score, length of stay, pre-operative knee flexion and pre-operative WOMAC physical function score.
Outcomes and effect sizes	Post-operative patient-reported outcome measures at 6 months (6 months)* (only includes the physical function subscale of WOMAC, and so will be downgraded for indirectness) **Obesity II (BMI ≥35kg/m^2), obesity I (BMI 30.0-34.9 kg/m^2), overweight (BMI 24.0-29.9 kg/m^2), compared to healthy weight (BMI 18.5-24.0 kg/m^2)** **Post-operative patient-reported outcome measures at 6 months – mean (95% CI) (change score)** • **Healthy weight* (BMI 18.5-24.0 kg/m^2) (n=59) = -24.6 (-26.2, -22.9)** • **Overweight* (BMI 24.0-26.0 kg/m^2) (n=95) = mean (SD) = -25.4 (-26.6, -24.3)** • **Obesity I (BMI 27.0-29.9 kg/m^2) (n=90) = mean (SD) = -30.3 (-31.4, -29.1)** • **Obesity II (BMI 30-34.9 kg/m^2) (n=82) = -32.9 (-34.2, -31.7)** • **Obesity III (BMI ≥35 kg/m^2) (n=28) = -35.0 (-37.3, -32.7)**
Comments	**Post-operative patient-reported outcome measures at 6 months** Risk of bias: 1. Study participation LOW 2. Study attrition LOW 3. Prognostic factor measurement LOW 4. Outcome Measurement LOW 5. Study confounding HIGH 6. Statistical analysis LOW 7. Other risk of bias LOW OVERALL RISK OF BIAS HIGH Indirectness: Outcome indirectness – Only the subscale value for WOMAC is reported (rather than the aggregate score stated in the protocol)

Reference	Mukka 2020[119]
Study type and analysis	Retrospective cohort study.

Reference	Mukka 2020[119]
	Multivariate analysis using linear regression analyses. Adjusting data for differences in age, sex, ASA class, preoperative health-related quality of life and Charnley classification. Sweden, participants from the Swedish Hip Arthroplasty Register, launched in 1979.

Number of participants and characteristics	N=127,663 primary total hip arthroplasties. 14,853 had arthroplasty on a second hip, 1010 had a resurfacing implant, 23,140 did not have primary osteoarthritis, 5,514 did not have ASA and BMI complete, 19,091 did not have complete PROM data. After excluding participants by the exclusion criteria, 64,055 patients were included for the analysis.
	
	Inclusion criteria:
	Patients with primary osteoarthritis who were treated surgically with total hip arthroplasty using uncemented, cemented, hybrid or reverse hybrid fixation, between January 1, 2008, and December 31, 2015. In people with bilateral total hip arthroplasty, only the first total hip arthroplasty was included.
	
	Exclusion criteria:
	Resurfacing total hip arthroplasty; people who were missing documentation of BMI or ASA class.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	
	Underweight (BMI <18.5 kg/m^2):
	• Mean age: 73.05 years
	• Female (%): 90.4%
	• ASA (%)
	  ○ I = 24.1%
	  ○ II = 57.7%
	  ○ III = 16.7%
	  ○ IV/V = 1.5%
	• Fixation (%)
	  ○ All cemented = 79.7%
	  ○ All uncemented = 8.9%
	  ○ Hybrid = 3.5%
	  ○ Reversed hybrids = 7.8%

Reference	Mukka 2020[119]

	• Surgical approach (%)
	  ○ Posterior = 48.1%
	  ○ Direct lateral = 43.3%
	  ○ Other = 8.6%
	• EQ-5D-3L index = 0.39
	• EQ VAS = 54.6
	
	Healthy weight (BMI 18.5-24.9 kg/m^2):
	• Mean age: 70.41 years
	• Female (%): 65.1%
	• ASA (%)
	  ○ I = 32.6%
	  ○ II = 56/5%
	  ○ III = 10.7%
	  ○ IV/V = 0.2%
	• Fixation (%)
	  ○ All cemented = 70.9%
	  ○ All uncemented = 14.7%
	  ○ Hybrid = 2.3%
	  ○ Reversed hybrids = 12.1%
	• Surgical approach (%)
	  ○ Posterior = 50.6%
	  ○ Direct lateral = 42.6%
	  ○ Other = 6.8%
	• EQ-5D-3L index = 0.45
	• EQ VAS = 57.3
	
	Overweight (BMI 25.0-29.9 kg/m^2):
	• Mean age: 68.88 years
	• Female (%): 50.5%
	• ASA (%)

Reference	Mukka 2020[119]
	○ I = 26.2% ○ II = 61.8% ○ III = 11.7% ○ IV/V = 0.3% • Fixation (%) ○ All cemented = 68.0% ○ All uncemented = 17.7% ○ Hybrid = 1.8% ○ Reversed hybrids = 13.2% • Surgical approach (%) ○ Posterior = 52.5% ○ Direct lateral = 41.7% ○ Other = 5.8% • EQ-5D-3L index = 0.44 • EQ VAS = 57.1 **Class I obesity (BMI 30.0-34.9 kg/m^2):** • Mean age: 67.35 years • Female (%): 54.5% • ASA (%) ○ I = 16.3% ○ II = 65.2% ○ III = 18.1% ○ IV/V = 0.4% • Fixation (%) ○ All cemented = 67.3% ○ All uncemented = 17.7% ○ Hybrid = 1.8% ○ Reversed hybrids = 13.2% • Surgical approach (%) ○ Posterior = 54.0%

Reference	Mukka 2020[119]
	○ Direct lateral = 41.0% ○ Other = 5.1% • EQ-5D-3L index = 0.38 • EQ VAS = 53.7 **Class II obesity (BMI 35-39.9 kg/m^2):** • Mean age: 65.78 years • Female (%): 62.2% • ASA (%) ○ I = 6.8% ○ II = 58.6% ○ III = 34.0% ○ IV/V = 0.6% • Fixation (%) ○ All cemented = 65.6% ○ All uncemented = 19.2% ○ Hybrid = 1.8% ○ Reversed hybrids = 13.3% • Surgical approach (%) ○ Posterior = 53.7% ○ Direct lateral = 41.8% ○ Other = 4.6% • EQ-5D-3L index = 0.32 • EQ VAS = 50.8 **Class III obesity (BMI ≥40 kg/m^2):** • Mean age: 64.23 years • Female (%): 69.4% • ASA (%) ○ I = 6.7% ○ II = 45.9%

Reference	Mukka 2020[119]
	○ III = 46.1% ○ IV/V = 1.3% • Fixation (%) ○ All cemented = 64.1% ○ All uncemented = 22.1% ○ Hybrid = 2.1% ○ Reversed hybrids = 11.8% • Surgical approach (%) ○ Posterior = 55.2% ○ Direct lateral = 41.7% ○ Other = 3.1% • EQ-5D-3L index = 0.27 • EQ VAS = 49.1 **Population source:** Participants from the Swedish Hip Arthroplasty Register, launched in 1979.
Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 395 Healthy weight (BMI 18.5-24.9 kg/m^2) = 19,892 Overweight (BMI 25.0-29.9 kg/m^2) = 28,221 Obesity I (BMI 30.0-34.9 kg/m^2) = 12,036 Obesity II (BMI 35.0-39.9 kg/m^2) = 2,899 Obesity III (BMI ≥40.0 kg/m^2) = 612
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, sex, ASA class, preoperative health-related quality of life and Charnley classification.
Outcomes and effect sizes	Health-related quality of life at >3 months (1 year)* (this study reports EQ-5D-3L and EQ VAS. For this analysis we have extracted the value for EQ-5D-3L). **Obesity III (BMI ≥40.0 kg/m^2), obesity II (BMI 35.0-39.9 kg/m^2), obesity I (BMI 30.0-34.9 kg/m^2), overweight (BMI 25.0-29.9 kg/m^2) and underweight (BMI <18.5 kg/m^2) compared to healthy weight (BMI 18.5-24.9 kg/m^2)** **Health-related quality of life at >3 months – mean (95% CI)**

Reference	Mukka 2020[119]
	• **Underweight (BMI <18.5 kg/m^2) (n=395) = -0.038 (-0.068, -0.0074)** • **Healthy weight (BMI 18.5-24.9 kg/m^2) (n=19,892) = 0 (reference)** • **Overweight (BMI 24.0-29.9 kg/m^2) (n=28,221) = -0.018 (-0.023, -0.012)** • **Obesity I (BMI 30-34.9 kg/m^2) (n=12,036) = -0.060 (-0.066, -0.053)** • **Obesity II (BMI 35.0-39.9 kg/m^2) (n=2,899) = -0.11 (-0.13, -0.10)** • **Obesity III (BMI ≥40 kg/m^2) (n=612) = -0.15 (-0.17, -0.13)**
Comments	**Health-related quality of life at >3 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH Indirectness: No known indirectness

Reference	Peters 2020[135]
Study type and analysis	Retrospective cohort study. Multivariate analysis using logistic regression analyses. Adjusting data for differences in age, gender, American Society of Anaesthesiologists score, body mass index, Charnley score, smoking and previous operations to the hip Sweden, participants from the Dutch Arthroplasty Registry (LORI) between 2007 and 2018
Number of participants	N=259,849 in total. People with metal-on-metal total hip arthroplasties (excluded) = 6635. People with osteoarthritis (included) = 218,214.

Reference	Peters 2020[135]

and characteristics	**Inclusion criteria:**
	People who had hip arthroplasty procedures in the Dutch Arthroplasty Registry between 2007 and 2018. People with bilateral prosthesis were included. Only people who had osteoarthritis were included.
	
	Exclusion criteria:
	Metal-on-metal total hip arthroplasties. People without osteoarthritis.
	
	Values listed below are presented as mean (SD) or number (%) unless stated otherwise
	• Age
	  ○ <60 years = 30,937 (14.2%)
	  ○ 60-74 years = 113,878 (52.2%)
	  ○ At least 75 years = 73,399 (33.6%)
	• Male:Female = 71,447:146,489 (32.8%:67.2%)
	• ASA (%)
	  ○ I = 47,114 (22.3%)
	  ○ II = 136,082 (64.3%)
	  ○ III/IV = 28,269 (13.4%)
	• Previous operation
	  ○ Yes = 4495 (2.2%)
	  ○ No = 203,742 (97.8%)
	• Period
	  ○ 2007-2010 = 53,458 (24.5%)
	  ○ 2011-2014 = 88,132 (40.4%)
	  ○ 2015-2017 = 76,624 (35.1%)
	• Smoking
	  ○ Yes = 11,248 (5.2%)
	  ○ No = 90,149 (41.3%)
	  ○ Not registered; before 2014 = 116,817 (53.5%)
	• Charnley score
	  ○ A = 44,080 (20.4%)
	  ○ B1 = 30,267 (14.1%)

Reference	Peters 2020[135]
	○ B2 = 22,010 (10.2%) ○ C = 2288 (1.1%) • BMI not registered (before 2014) = 108,011 (49.5%) **Population source:** Participants from the Dutch Arthroplasty Registry (LORI) between 2007 and 2018.
Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 649 Healthy weight (BMI 18.5-25.0 kg/m^2) = 33,998 Overweight (BMI >25.0-30 kg/m^2) = 46,507 Obesity I/II (BMI >30.0-40.0 kg/m^2) = 25,453 (this group will not be included in the analysis as it doesn't clearly fit either category) Obesity III (BMI >40.0 kg/m^2) = 1336
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, gender, American Society of Anaesthesiologists score, body mass index, Charnley score, smoking and previous operations to the hip.
Outcomes and effect sizes	Reoperation or revision to the prosthesis at >3 months (3 years) **Obesity III (BMI ≥40.0 kg/m^2), healthy weight (BMI 18.5-24.9 kg/m^2) and underweight (BMI <18.5 kg/m^2) compared to overweight (BMI 25.0-29.9 kg/m^2)** **Reoperation or revision to the prosthesis at >3 months – OR (95% CI)** • **Underweight (BMI <18.5 kg/m^2) (n=649) = 1.73 (0.94, 3.20)** • **Healthy weight (BMI 18.5-24.9 kg/m^2) (n=33,998) = 0.76 (0.65, 0.88)** • **Overweight (BMI 24.0-29.9 kg/m^2) (n=46,507) = 1 (reference)** • **Obesity III (BMI ≥40 kg/m^2) (n=1336) = 1.91 (1.27, 2.86)**
Comments	**<u>Reoperation or revision to the prosthesis at >3 months</u>** Risk of bias: 1. Study participation LOW 2. Study attrition LOW 3. Prognostic factor measurement LOW 4. Outcome Measurement LOW 5. Study confounding HIGH

Reference	Peters 2020[135]	
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	HIGH
	Indirectness:	
	No known indirectness	

Reference	Thornqvist 2014[175]
Study type and analysis	Retrospective cohort study. Multivariate analysis using Cox regression models. Adjusting data for differences in age, gender, hip vs. knee replacement surgery, heart failure, previous myocardial infarction, chronic ischaemic heart disease, atrial fibrillation, peripheral artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, renal disease, diabetes and cemented vs. non-cemented prosthesis. Denmark, participants from the Danish National Patient Register and the Danish Anaesthesia Register, identified between 2005 and 2011.
Number of participants and characteristics	N=37,744 people (45% received a total knee replacement) **Inclusion criteria:** People (aged at least 20 years) who had undergone elective primary hip and knee replacement surgery between 2005 and 2011. **Exclusion criteria:** People with rheumatoid arthritis; people with a hip/knee fracture within 30 days prior to surgery. **Values listed below are presented as mean (SD) or number (%) unless stated otherwise** **Underweight** • Mean age (range) = 75 (65-82) years • Male = 33 • Total hip replacement = 307 • ASA score 1:2:3+ = 68:208:68

Reference	Thornqvist 2014[175]

	• Heart failure = 8
	• Current smoker = 119
	• Cerebrovascular disease = 18
	• Chronic Obstructive Pulmonary Disease = 23
	• Anaemia = 19
	• Renal disease = 3
	• Peripheral artery disease = 5
	• Acute myocardial infarction = 7
	• Atrial fibrillation = 21
	• Statin treatment = 51
	• Diabetes = 10
	• Calcium channel blockers = 40
	• ACE inhibitors = 76
	• Thiazides = 44
	• Aldosterone blockers = 14
	• Clopidogrel = 4
	• Beta blocker = 39
	• Vitamin K antagonists = 15
	• Aspirin = 56
	• Alcohol
	  ○ 0 drinks/week = 160
	  ○ 1-14 drinks/week = 107
	  ○ 15-21 drinks/week = 16
	  ○ >21 drinks/week = 23
	  ○ Unknown = 47
	• No loop diuretics = 319
	
	Normal weight
	• Mean age (range) = 75 (65-82) years
	• Male = 3382

Reference	Thornqvist 2014[175]

	• Total hip replacement = 6676
	• ASA score 1:2:3+ = 3081:5586:1061
	• Heart failure = 196
	• Current smoker = 1786
	• Cerebrovascular disease = 311
	• Chronic Obstructive Pulmonary Disease = 233
	• Anaemia = 266
	• Renal disease = 78
	• Peripheral artery disease = 63
	• Acute myocardial infarction = 155
	• Atrial fibrillation = 444
	• Statin treatment = 1835
	• Diabetes = 360
	• Calcium channel blockers = 1618
	• ACE inhibitors = 2416
	• Thiazides = 1359
	• Aldosterone blockers = 142
	• Clopidogrel = 114
	• Beta blocker = 1277
	• Vitamin K antagonists = 413
	• Aspirin = 1839
	• Alcohol
	  ○ 0 drinks/week = 3649
	  ○ 1-14 drinks/week = 3791
	  ○ 15-21 drinks/week = 499
	  ○ >21 drinks/week = 616
	  ○ Unknown = 1304
	• No loop diuretics = 9255
	
	Overweight

Reference	Thornqvist 2014[175]

	• Mean age (range) = 71 (64-78) years
	• Male = 6625
	• Total hip replacement = 7765
	• ASA score 1:2:3+ = 3610:8532:1491
	• Heart failure = 287
	• Current smoker = 2059
	• Cerebrovascular disease = 351
	• Chronic Obstructive Pulmonary Disease = 264
	• Anaemia = 229
	• Renal disease = 90
	• Peripheral artery disease = 74
	• Acute myocardial infarction = 242
	• Atrial fibrillation = 605
	• Statin treatment = 3454
	• Diabetes = 943
	• Calcium channel blockers = 2636
	• ACE inhibitors = 4398
	• Thiazides = 2512
	• Aldosterone blockers = 237
	• Clopidogrel = 170
	• Beta blocker = 2336
	• Vitamin K antagonists = 642
	• Aspirin = 2912
	• Alcohol
	  ○ 0 drinks/week = 4927
	  ○ 1-14 drinks/week = 5259
	  ○ 15-21 drinks/week = 903
	  ○ >21 drinks/week = 962
	  ○ Unknown = 1734
	• No loop diuretics = 12793

Reference	Thornqvist 2014[175]

	Obesity I
	• Mean age (range) = 67 (62-74) years
	• Male = 3153
	• Total hip replacement = 3250
	• ASA score 1:2:3+ = 1272:5052:1044
	• Heart failure = 185
	• Current smoker = 1033
	• Cerebrovascular disease = 185
	• Chronic Obstructive Pulmonary Disease = 171
	• Anaemia = 108
	• Renal disease = 58
	• Peripheral artery disease = 46
	• Acute myocardial infarction = 146
	• Atrial fibrillation = 342
	• Statin treatment = 2256
	• Diabetes = 907
	• Calcium channel blockers = 1765
	• ACE inhibitors = 3114
	• Thiazides = 1563
	• Aldosterone blockers = 181
	• Clopidogrel = 107
	• Beta blocker = 1525
	• Vitamin K antagonists = 352
	• Aspirin = 1743
	• Alcohol
	  ○ 0 drinks/week = 2981
	  ○ 1-14 drinks/week = 2639
	  ○ 15-21 drinks/week = 403
	  ○ >21 drinks/week = 516

Reference	Thornqvist 2014[175]
	○ Unknown = 911 • No loop diuretics = 6606 **Obesity II** • Mean age (range) = 65 (59-71) years • Male = 1113 • Total hip replacement = 1130 • ASA score 1:2:3+ = 236:2042:980 • Heart failure = 86 • Current smoker = 446 • Cerebrovascular disease = 78 • Chronic Obstructive Pulmonary Disease = 113 • Anaemia = 60 • Renal disease = 29 • Peripheral artery disease = 25 • Acute myocardial infarction = 51 • Atrial fibrillation = 152 • Statin treatment = 961 • Diabetes = 607 • Calcium channel blockers = 425 • ACE inhibitors = 1542 • Thiazides = 808 • Aldosterone blockers = 112 • Clopidogrel = 24 • Beta blocker = 727 • Vitamin K antagonists = 166 • Aspirin = 763 • Alcohol ○ 0 drinks/week = 1582 ○ 1-14 drinks/week = 948

Reference	Thornqvist 2014[175]
	○ 15-21 drinks/week = 127 ○ >21 drinks/week = 228 ○ Unknown = 410 • No loop diuretics = 2713 **Population source:** Participants from the Danish National Patient Register and the Danish Anaesthesia Register, identified between 2005 and 2011.
Prognostic variables	Underweight (BMI <18.5 kg/m^2) = 353 Healthy weight (BMI 18.5-25.0 kg/m^2) = 9589 Overweight (BMI >25.0-30.0 kg/m^2) = 13,787 Obesity I (BMI >30.0-35.0 kg/m^2) = 7450 Obesity II (BMI >35.0-40.0 kg/m^2) = 3295
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, gender, hip vs. knee replacement surgery, heart failure, previous myocardial infarction, chronic ischaemic heart disease, atrial fibrillation, peripheral artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, renal disease, diabetes and cemented vs. non-cemented prosthesis.
Outcomes and effect sizes	Mortality at ≤3 months (30 days) and >3 months (1 year) **Obesity II (BMI >35.0-40.0 kg/m^2), Obesity I (BMI >30.0-35.0 kg/m^2), healthy weight (BMI 18.5-25.0 kg/m^2) and underweight (BMI <18.5 kg/m^2) compared to overweight (BMI >25.0-29.9 kg/m^2)** **Mortality at ≤3 months – HR (95% CI)** • **Underweight (BMI <18.5 kg/m^2) (n=353) = 7.0 (2.8, 15)** • **Healthy weight (BMI 18.5-25.0 kg/m^2) (n=9589) = 2.0 (1.2, 3.2)** • **Overweight (BMI >25.0-30.0 kg/m^2) (n=13,787) = 1 (reference)** • **Obesity I (BMI >30.0-35.0 kg/m^2) (n=7450) = 1.5 (0.87, 2.7)** • **Obesity II (BMI >35.0-40 kg/m^2) (n=3295) = 1.9 (0.9, 4.2)** **Mortality at >3 months – HR (95% CI)** • **Underweight (BMI <18.5 kg/m^2) (n=353) = 5.2 (3.5, 7.8)**

Reference	Thornqvist 2014[175]
	• **Healthy weight (BMI 18.5-25.0 kg/m^2) (n=9589) = 1.6 (1.3, 2.0)** • **Overweight (BMI >25.0-30.0 kg/m^2) (n=13,787) = 1 (reference)** • **Obesity I (BMI >30.0-35.0 kg/m^2) (n=7450) = 1.1 (0.87, 1.4)** • **Obesity II (BMI >35.0-40 kg/m^2) (n=3295) = 1.4 (1.01, 2.0)**
Comments	**Mortality at ≤3 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH **Mortality at >3 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — HIGH 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — VERY HIGH Indirectness: No known indirectness

Reference	Wallace 2014[175]
Study type and analysis	Retrospective cohort study. Multivariate analysis using logistic regression analyses. Adjusting data for differences in age, gender, drinking, smoking, socioeconomic status, year of surgery, previous occurrence of outcome, prior use of statins, antihypertensives, aspirin, antidepressants, anticoagulants, antibiotics, previous diagnosis of diabetes, hypertension, chronic obstructive pulmonary disease, atrial fibrillation, ischaemic heart disease. United Kingdom, participants from Clinical Practice Research Datalink taken between 1995 and 2011 (NHS observational data).
Number of participants and characteristics	N=53,337 people were identified with a first record of a total hip replacement. 505 were excluded due to other joint operations in the 6 months prior. 559 left the practice before the end of the 6 month follow-up period. 20,456 did not have a relevant BMI measure. Total (hip) = 31,817. 49,200 people were identified with a first record of a total knee replacement. 573 were excluded due to other joint operations in the 6 months prior. 411 left the practice before the end of the 6 month follow-up period. 15,731 did not have a relevant BMI measure. Total (knee) = 32,485. **Inclusion criteria:** Total hip replacement patients who had no record of a previous primary hip replacement ever nor any record of a primary total hip or unicompartmental knee replacement in the 6 months prior to total knee replacement. All people must have had no hip or knee revision operation in the 6 months prior to the operation, at least one valid BMI measure (between 10 kg/m^2 and 70 kg/m^2) in the 5 years prior to the total knee replacement or total hip replacement, at least 6 months subsequent follow-up prior to transferring out of the GP practice (unless the reason was dead). **Exclusion criteria:** No additional information. **Values listed below are presented as mean (SD) or number (%) unless stated otherwise** **Hip replacement** **Underweight (BMI <18.5 kg/m^2)** • Mean age (SD) = 73.0 (12.8) years • Male:Female = 68:394 • Drinking (Yes:No:Ex) = 321:69:56 • Smoking (Yes:No:Ex) = 103:230:127

Reference	Wallace 2014[175]

	• Comorbidities:
	  ○ Diabetes = 15
	  ○ Chronic obstructive pulmonary disease = 5
	  ○ Ischaemic heart disease = 38
	  ○ Hypertension = 113
	  ○ Atrial fibrillation = 28
	  ○ Antibiotic use = 307
	  ○ Anticoagulant use = 20
	  ○ Aspirin use = 109
	  ○ Antihypertensive use = 8
	  ○ Statins use = 67
	  ○ Antidepressant use = 178
	  ○ Pulmonary embolism or deep vein thrombosis = 10
	  ○ Wound infection = 13
	  ○ Respiratory infection = 54
	  ○ Urinary tract infection = 99
	  ○ Haemorrhagic stroke = 1
	  ○ Anaemia = 47
	  ○ Myocardial infarction = 19
	  ○ Stroke = 9
	
	Normal (BMI 18.5 – 25 kg/m^2)
	• Mean age (SD) = 70.9 (11.5) years
	• Male:Female = 2786:6220
	• Drinking (Yes:No:Ex) = 6220:6839:1036
	• Smoking (Yes:No:Ex) = 1250:4705:3036
	• Comorbidities:
	  ○ Diabetes = 616
	  ○ Chronic obstructive pulmonary disease = 56
	  ○ Ischaemic heart disease = 823
	  ○ Hypertension = 2684

Reference	Wallace 2014[175]
	○ Atrial fibrillation = 487 ○ Antibiotic use = 6056 ○ Anticoagulant use = 440 ○ Aspirin use = 2409 ○ Antihypertensive use = 244 ○ Statins use = 2099 ○ Antidepressant use = 2737 ○ Pulmonary embolism or deep vein thrombosis = 295 ○ Wound infection = 195 ○ Respiratory infection = 797 ○ Urinary tract infection = 1598 ○ Haemorrhagic stroke = 22 ○ Anaemia = 595 ○ Myocardial infarction = 424 ○ Stroke = 187 **Overweight (BMI 25 – 30 kg/m^2)** • Mean age (SD) = 69.5 (10.3) years • Male:Female = 5520:7099 • Drinking (Yes:No:Ex) = 9799:1318:1170 • Smoking (Yes:No:Ex) = 1252:6267:5091 • Comorbidities: ○ Diabetes = 1258 ○ Chronic obstructive pulmonary disease = 70 ○ Ischaemic heart disease = 1329 ○ Hypertension = 4543 ○ Atrial fibrillation = 647 ○ Antibiotic use = 8705 ○ Anticoagulant use = 677 ○ Aspirin use = 3780 ○ Antihypertensive use = 533

Reference	Wallace 2014[175]
	○ Statins use = 3999 ○ Antidepressant use = 3701 ○ Pulmonary embolism or deep vein thrombosis = 446 ○ Wound infection = 344 ○ Respiratory infection = 1100 ○ Urinary tract infection = 2116 ○ Haemorrhagic stroke = 27 ○ Anaemia = 632 ○ Myocardial infarction = 684 ○ Stroke = 237 **Obese I (BMI 30 – 35 kg/m^2)** • Mean age (SD) = 67.5 (9.9) years • Male:Female = 2764:4045 • Drinking (Yes:No:Ex) = 5178:689:721 • Smoking (Yes:No:Ex) = 643:3207:2950 • Comorbidities: ○ Diabetes = 1039 ○ Chronic obstructive pulmonary disease = 41 ○ Ischaemic heart disease = 779 ○ Hypertension = 2964 ○ Atrial fibrillation = 334 ○ Antibiotic use = 4978 ○ Anticoagulant use = 422 ○ Aspirin use = 2203 ○ Antihypertensive use = 323 ○ Statins use = 2558 ○ Antidepressant use = 2328 ○ Pulmonary embolism or deep vein thrombosis = 315 ○ Wound infection = 259 ○ Respiratory infection = 729

Reference	Wallace 2014[175]
	○ Urinary tract infection = 1245 ○ Haemorrhagic stroke = 12 ○ Anaemia = 334 ○ Myocardial infarction = 377 ○ Stroke = 137 **Obese II (BMI 35 – 40 kg/m^2)** • Mean age (SD) = 65.0 (9.9) years • Male:Female = 784:1440 • Drinking (Yes:No:Ex) = 1568:270:293 • Smoking (Yes:No:Ex) = 226:986:1010 • Comorbidities: ○ Diabetes = 420 ○ Chronic obstructive pulmonary disease = 11 ○ Ischaemic heart disease = 224 ○ Hypertension = 1010 ○ Atrial fibrillation = 113 ○ Antibiotic use = 1694 ○ Anticoagulant use = 150 ○ Aspirin use = 737 ○ Antihypertensive use = 92 ○ Statins use = 853 ○ Antidepressant use = 860 ○ Pulmonary embolism or deep vein thrombosis = 122 ○ Wound infection = 113 ○ Respiratory infection = 214 ○ Urinary tract infection = 434 ○ Haemorrhagic stroke = 5 ○ Anaemia = 121 ○ Myocardial infarction = 118 ○ Stroke = 34

Reference	Wallace 2014[175]

	Obese III (BMI >40 kg/m^2)
	• Mean age (SD) = 62.9 (9.4) years
	• Male:Female = 165:532
	• Drinking (Yes:No:Ex) = 444:116:114
	• Smoking (Yes:No:Ex) = 59:350:287
	• Comorbidities:
	  ○ Diabetes = 161
	  ○ Chronic obstructive pulmonary disease = 4
	  ○ Ischaemic heart disease = 51
	  ○ Hypertension = 334
	  ○ Atrial fibrillation = 32
	  ○ Antibiotic use = 557
	  ○ Anticoagulant use = 52
	  ○ Aspirin use = 196
	  ○ Antihypertensive use = 26
	  ○ Statins use = 257
	  ○ Antidepressant use = 310
	  ○ Pulmonary embolism or deep vein thrombosis = 44
	  ○ Wound infection = 36
	  ○ Respiratory infection = 65
	  ○ Urinary tract infection = 146
	  ○ Haemorrhagic stroke = 1
	  ○ Anaemia = 38
	  ○ Myocardial infarction = 21
	  ○ Stroke = 10
	
	Knee replacement
	
	Underweight (BMI <18.5 kg/m^2)
	• Mean age (SD) = 71.5 (12.5) years

Reference	Wallace 2014[175]

	• Male:Female = 19:119
	• Drinking (Yes:No:Ex) = 82:29:23
	• Smoking (Yes:No:Ex) = 28:72:38
	• Comorbidities:
	  ○ Diabetes = 5
	  ○ Chronic obstructive pulmonary disease = 0
	  ○ Ischaemic heart disease = 9
	  ○ Hypertension = 33
	  ○ Atrial fibrillation = 0
	  ○ Antibiotic use = 12
	  ○ Anticoagulant use = 0
	  ○ Aspirin use = 2
	  ○ Antihypertensive use = 4
	  ○ Statins use = 21
	  ○ Antidepressant use = 61
	  ○ Pulmonary embolism or deep vein thrombosis = 3
	  ○ Wound infection = 6
	  ○ Respiratory infection = 12
	  ○ Urinary tract infection = 37
	  ○ Haemorrhagic stroke = 0
	  ○ Anaemia = 24
	  ○ Myocardial infarction = 4
	  ○ Stroke = 0
	
	Normal (BMI 18.5 – 25 kg/m^2)
	• Mean age (SD) = 72.7 (10.1) years
	• Male:Female = 2119:3277
	• Drinking (Yes:No:Ex) = 4051:614:576
	• Smoking (Yes:No:Ex) = 536:2870:1986
	• Comorbidities:
	  ○ Diabetes = 410

Reference	Wallace 2014[175]
	○ Chronic obstructive pulmonary disease = 27 ○ Ischaemic heart disease = 611 ○ Hypertension = 1720 ○ Atrial fibrillation = 27 ○ Antibiotic use = 360 ○ Anticoagulant use = 38 ○ Aspirin use = 149 ○ Antihypertensive use = 192 ○ Statins use = 1595 ○ Antidepressant use = 1697 ○ Pulmonary embolism or deep vein thrombosis = 202 ○ Wound infection = 153 ○ Respiratory infection = 505 ○ Urinary tract infection = 972 ○ Haemorrhagic stroke = 12 ○ Anaemia = 459 ○ Myocardial infarction = 287 ○ Stroke = 125 **Overweight (BMI 25 – 30 kg/m^2)** • Mean age (SD) = 71.1 (8.9) years • Male:Female = 6063:6340 • Drinking (Yes:No:Ex) = 9602:1247:1214 • Smoking (Yes:No:Ex) = 1022:5915:5451 • Comorbidities: ○ Diabetes = 1464 ○ Chronic obstructive pulmonary disease = 77 ○ Ischaemic heart disease = 1451 ○ Hypertension = 4894 ○ Atrial fibrillation = 53 ○ Antibiotic use = 840

Reference	Wallace 2014[175]
	○ Anticoagulant use = 74 ○ Aspirin use = 341 ○ Antihypertensive use = 769 ○ Statins use = 4622 ○ Antidepressant use = 3812 ○ Pulmonary embolism or deep vein thrombosis = 557 ○ Wound infection = 448 ○ Respiratory infection = 1166 ○ Urinary tract infection = 2193 ○ Haemorrhagic stroke = 12 ○ Anaemia = 716 ○ Myocardial infarction = 669 ○ Stroke = 250 **Obese I (BMI 30 – 35 kg/m^2)** • Mean age (SD) = 68.6 (8.7) years • Male:Female = 3927:5345 • Drinking (Yes:No:Ex) = 6866:1046:1107 • Smoking (Yes:No:Ex) = 690:4419:4160 • Comorbidities: ○ Diabetes = 1635 ○ Chronic obstructive pulmonary disease = 65 ○ Ischaemic heart disease = 1070 ○ Hypertension = 4242 ○ Atrial fibrillation = 45 ○ Antibiotic use = 618 ○ Anticoagulant use = 67 ○ Aspirin use = 268 ○ Antihypertensive use = 602 ○ Statins use = 3905 ○ Antidepressant use = 3202

Reference	Wallace 2014[175]
	○ Pulmonary embolism or deep vein thrombosis = 488 ○ Wound infection = 434 ○ Respiratory infection = 1007 ○ Urinary tract infection = 1743 ○ Haemorrhagic stroke = 8 ○ Anaemia = 522 ○ Myocardial infarction = 506 ○ Stroke = 191 **Obese II (BMI 35 – 40 kg/m^2)** • Mean age (SD) = 66.3 (8.5) years • Male:Female = 1170:2659 • Drinking (Yes:No:Ex) = 2671:506:510 • Smoking (Yes:No:Ex) = 304:1868:1650 • Comorbidities: ○ Diabetes = 803 ○ Chronic obstructive pulmonary disease = 32 ○ Ischaemic heart disease = 370 ○ Hypertension = 1877 ○ Atrial fibrillation = 22 ○ Antibiotic use = 257 ○ Anticoagulant use = 30 ○ Aspirin use = 116 ○ Antihypertensive use = 200 ○ Statins use = 1616 ○ Antidepressant use = 1493 ○ Pulmonary embolism or deep vein thrombosis = 225 ○ Wound infection = 204 ○ Respiratory infection = 459 ○ Urinary tract infection = 781 ○ Haemorrhagic stroke = 7

Reference	Wallace 2014[175]
	○ Anaemia = 243 ○ Myocardial infarction = 147 ○ Stroke = 67 **Obese III (BMI >40 kg/m^2)** • Mean age (SD) = 64.1 (8.4) years • Male:Female = 326:1121: • Drinking (Yes:No:Ex) = 945:217:226 • Smoking (Yes:No:Ex) = 101:719:626 • Comorbidities: ○ Diabetes = 370 ○ Chronic obstructive pulmonary disease = 9 ○ Ischaemic heart disease = 120 ○ Hypertension = 736 ○ Atrial fibrillation = 4 ○ Antibiotic use = 104 ○ Anticoagulant use = 12 ○ Aspirin use = 35 ○ Antihypertensive use = 62 ○ Statins use = 604 ○ Antidepressant use = 639 ○ Pulmonary embolism or deep vein thrombosis = 93 ○ Wound infection = 84 ○ Respiratory infection = 203 ○ Urinary tract infection = 306 ○ Haemorrhagic stroke = 5 ○ Anaemia = 105 ○ Myocardial infarction = 46 ○ Stroke = 24 **Population source:** Participants from Clinical Practice Research Datalink taken between 1995 and 2011 (NHS observational data).

Reference	Wallace 2014[175]
Prognostic variables	**Hip replacement** Underweight (BMI <18.5 kg/m^2) = 462 Healthy weight (BMI 18.5-25.0 kg/m^2) = 9006 Overweight (BMI 25.0-30 kg/m^2) = 12,619 Obesity I (BMI 30.0-35.0 kg/m^2) = 6809 Obesity II (BMI 35.0-40.0 kg/m^2) = 2224 Obesity III (BMI >40.0 kg/m^2) = 697 **Knee replacement** Underweight (BMI <18.5 kg/m^2) = 138 Healthy weight (BMI 18.5-25.0 kg/m^2) = 5396 Overweight (BMI 25.0-30 kg/m^2) = 12,403 Obesity I (BMI 30.0-35.0 kg/m^2) = 9272 Obesity II (BMI 35.0-40.0 kg/m^2) = 3829 Obesity III (BMI >40.0 kg/m^2) = 1447
Confounders	Multivariable analysis Factors included in the adjusted analysis: age, gender, drinking, smoking, socioeconomic status, year of surgery, previous occurrence of outcome, prior use of statins, antihypertensives, aspirin, antidepressants, anticoagulants, antibiotics, previous diagnosis of diabetes, hypertension, chronic obstructive pulmonary disease, atrial fibrillation, ischaemic heart disease.
Outcomes and effect sizes	Mortality at >3 months (6 months) Venous thromboembolic events at >3 months (6 months) Surgical site infection (wound infection) at >3 months (6 months) **Obesity II (BMI 35.0+ kg/m^2)*, obesity I (BMI 30.0-35.0 kg/m^2), overweight (BMI 25.0-30.0 kg/m^2) and underweight (BMI <18.5 kg/m^2) compared to healthy weight (BMI 18.5-25.0 kg/m^2)** ***Study reports people with a BMI of 35+ instead of obesity II and III separately. As the majority of participants in the group has a BMI of 35-40 kg/m^2, this will be included as obesity II, but will be downgraded for indirectness.** **<u>Hip replacement</u>** **Mortality at >3 months – OR (95% CI)**

Reference	Wallace 2014[175]
	• Underweight (BMI <18.5 kg/m^2) (n=462) = 2.71 (1.67, 4.39) • Healthy weight (BMI 18.5-25.0 kg/m^2) (n=9006) = 1 (reference) • Overweight (BMI 25.0-30.0 kg/m^2) (n=12,619) = 0.61 (0.46, 0.81) • Obesity I (BMI 30.0-35.0 kg/m^2) (n=6809) = 0.62 (0.43, 0.90) • Obesity II (BMI ≥35.0 kg/m^2) (n=2921) = 0.65 (0.36, 1.16) Venous thromboembolic events at >3 months – OR (95% CI) • Underweight (BMI <18.5 kg/m^2) (n=443) = 0.75 (0.35, 1.60) • Healthy weight (BMI 18.5-25.0 kg/m^2) (n=8876) = 1 (reference) • Overweight (BMI 25.0-30.0 kg/m^2) (n=12,523) = 1.39 (1.16, 1.66) • Obesity I (BMI 30.0-35.0 kg/m^2) (n=6764) = 1.64 (1.34, 2.00) • Obesity II (BMI ≥35.0 kg/m^2) (n=2904) = 1.51 (1.16, 1.96) Surgical site infection (wound infection) at >3 months – OR (95% CI) • Underweight (BMI <18.5 kg/m^2) (n=443) = 1.03 (0.48, 2.19) • Healthy weight (BMI 18.5-25.0 kg/m^2) (n=8876) = 1 (reference) • Overweight (BMI 25.0-30.0 kg/m^2) (n=12,523) = 1.34 (1.09, 1.64) • Obesity I (BMI 30.0-35.0 kg/m^2) (n=6764) = 1.52 (1.21, 1.90) • Obesity II (BMI ≥35.0 kg/m^2) (n=2904) = 2.18 (1.67, 2.86) <u>Knee replacement</u> Mortality at >3 months – OR (95% CI) • Underweight (BMI <18.5 kg/m^2) (n=138) = 4.61 (1.64, 13.01) • Healthy weight (BMI 18.5-25.0 kg/m^2) (n=5396) = 1 (reference) • Overweight (BMI 25.0-30.0 kg/m^2) (n=12,403) = 1.12 (0.74, 1.70) • Obesity I (BMI 30.0-35.0 kg/m^2) (n=9272) = 1.21 (0.78, 1.88) • Obesity II (BMI ≥35.0 kg/m^2) (n=5276) = 0.95 (0.50, 1.78) Venous thromboembolic events at >3 months – OR (95% CI) • Underweight (BMI <18.5 kg/m^2) (n=134) = No information (was dropped due to zero events)

Reference	Wallace 2014[175]
	• **Healthy weight (BMI 18.5-25.0 kg/m^2) (n=5359) = 1 (reference)** • **Overweight (BMI 25.0-30.0 kg/m^2) (n=12,326) = 1.41 (1.13, 1.75)** • **Obesity I (BMI 30.0-35.0 kg/m^2) (n=9224) = 1.59 (1.26, 1.99)** • **Obesity II (BMI ≥35.0 kg/m^2) (n=5260) = 1.93 (1.45, 2.57)** **Surgical site infection (wound infection) at >3 months – OR (95% CI)** • **Underweight (BMI <18.5 kg/m^2) (n=134) = 0.97 (0.36, 2.67)** • **Healthy weight (BMI 18.5-25.0 kg/m^2) (n=5359) = 1 (reference)** • **Overweight (BMI 25.0-30.0 kg/m^2) (n=12,326) = 0.98 (0.81, 1.19)** • **Obesity I (BMI 30.0-35.0 kg/m^2) (n=9224) = 1.23 (1.01, 1.50)** • **Obesity II (BMI ≥35.0 kg/m^2) (n=5260) = 1.39 (1.11, 1.72)**
Comments	**Hip and knee replacement** **Mortality at >3 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — LOW 6. Statistical analysis — LOW 7. Other risk of bias — LOW OVERALL RISK OF BIAS — HIGH **Venous thromboembolic events at >3 months** Risk of bias: 1. Study participation — LOW 2. Study attrition — HIGH 3. Prognostic factor measurement — LOW 4. Outcome Measurement — LOW 5. Study confounding — LOW

Reference	Wallace 2014[175]	
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	HIGH
	Surgical site infection (wound infection) at >3 months	
	Risk of bias:	
	1. Study participation	LOW
	2. Study attrition	HIGH
	3. Prognostic factor measurement	LOW
	4. Outcome Measurement	LOW
	5. Study confounding	LOW
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	HIGH
	Indirectness:	
	Prognostic variable indirectness – The obesity II group includes people with obesity II and obesity III. As the majority have obesity II it has been included in this group, but will be downgraded for indirectness.	

Appendix E – Forest plots

E.1 Knee osteoarthritis

E.1.1 People who are underweight compared to people who are of healthy weight

Figure 2: Mortality at ≤3 months

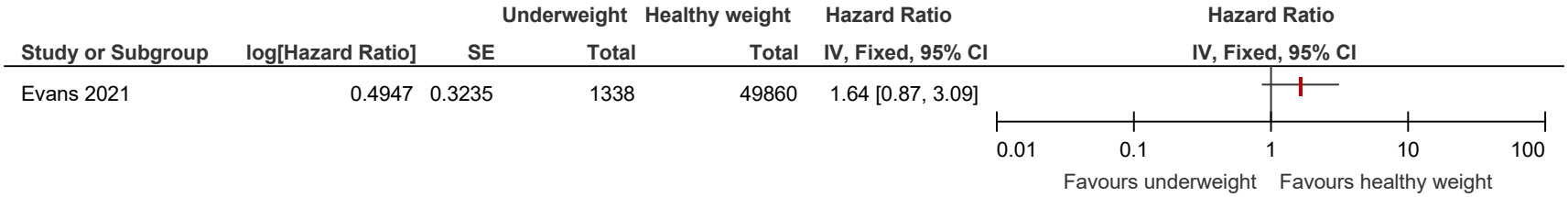


Figure 3: Mortality at >3 months

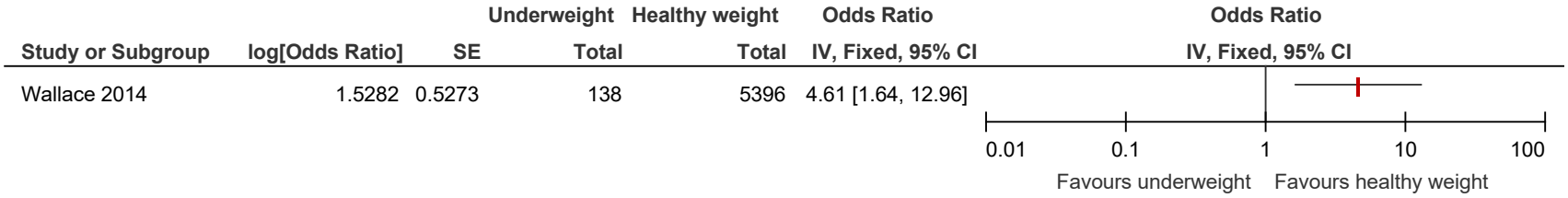


Figure 4: Reoperation or revision to the prosthesis at >3 months

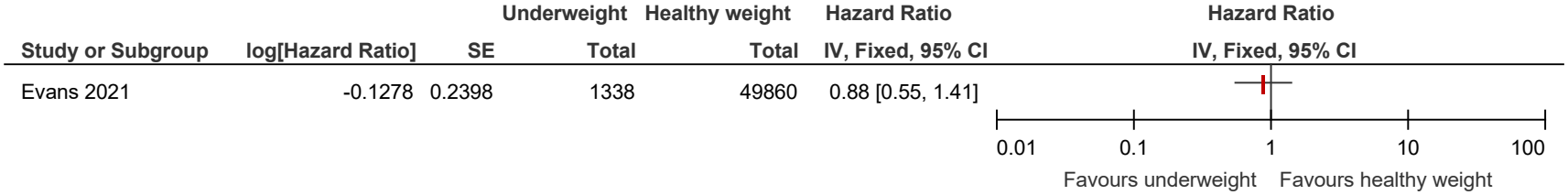
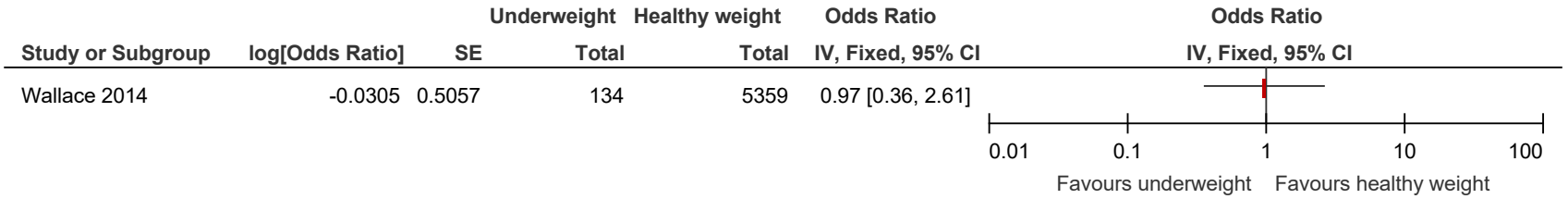


Figure 5: Surgical site infection (wound infection) at >3 months



E.1.2 People who are overweight compared to people who are of healthy weight

Figure 6: Mortality at ≤3 months

Study or Subgroup	log[Hazard Ratio]	SE	Overweight Total	Healthy weight Total	Hazard Ratio IV, Fixed, 95% CI
Evans 2021	-0.2744	0.0798	168947	49860	0.76 [0.65, 0.89]

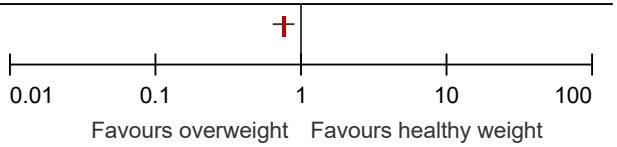


Figure 7: Mortality at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	-0.0305	0.3084	41155	14989	0.97 [0.53, 1.78]

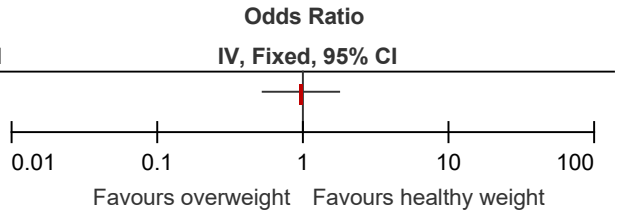


Figure 8: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Overweight Mean	SD	Total	Healthy weight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-23	20.2324	203	-18.1	19.9162	120	-4.90 [-9.42, -0.38]

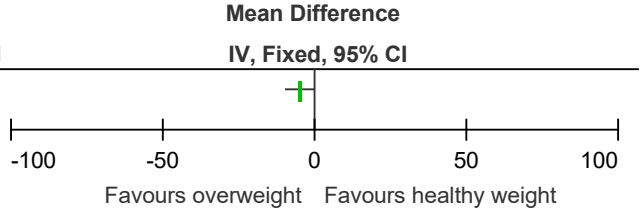


Figure 9: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

	Overweight			Healthy weight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Collins 2017	-23	18.0647	203	-19.5	17.7033	120	-3.50 [-7.53, 0.53]	

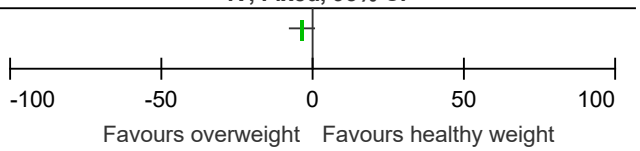


Figure 10: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

	Overweight			Healthy weight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Liao 2017	-25.4	5.8907	95	-24.6	6.1396	59	-0.80 [-2.76, 1.16]	

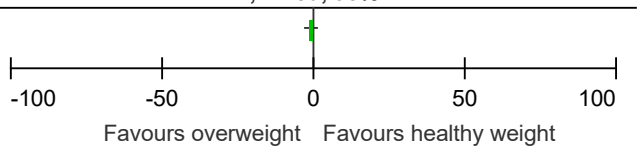


Figure 11: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

	Overweight			Healthy weight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	41	16.6842	745	42.4	16.1719	515	-1.40 [-3.24, 0.44]	

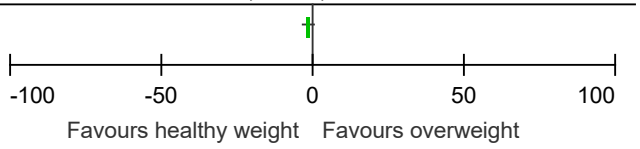


Figure 12: Reoperation or revision to the prosthesis at ≤3 months

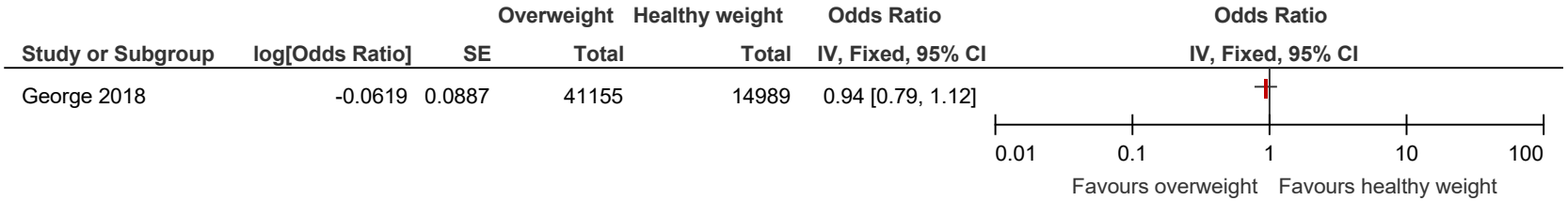


Figure 13: Total adverse events up to 90 days

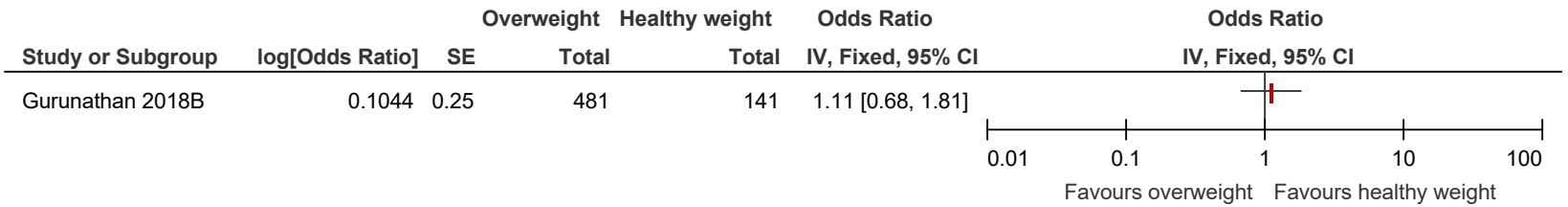


Figure 14: Surgical site infection (superficial infection) at ≤3 months

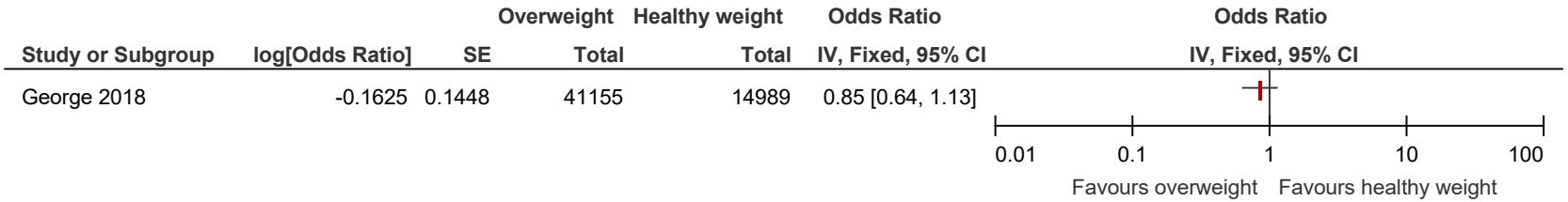


Figure 15: Surgical site infection (periprosthetic joint infection) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	-0.1054	0.1984	41155	14989	0.90 [0.61, 1.33]

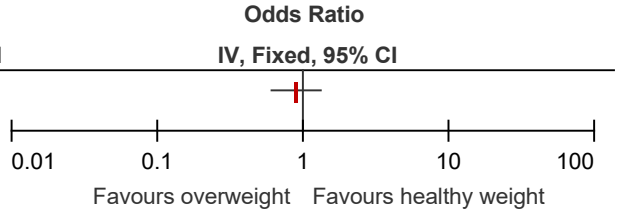


Figure 16: Venous thromboembolic events (deep vein thrombosis) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	0.0953	0.1024	41155	14989	1.10 [0.90, 1.34]

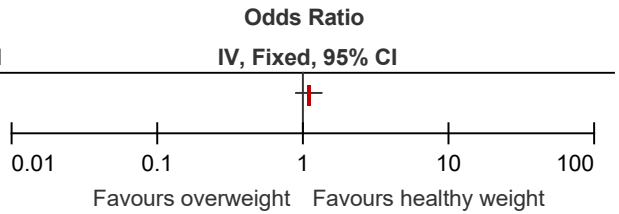


Figure 17: Venous thromboembolic events (pulmonary embolism) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	0.3988	0.1456	41155	14989	1.49 [1.12, 1.98]

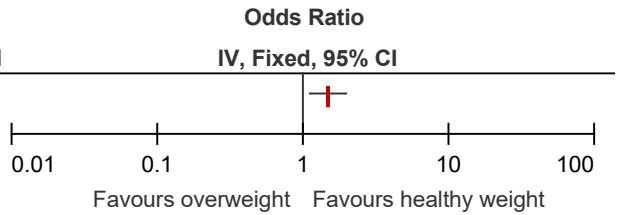


Figure 18: Mortality at >3 months

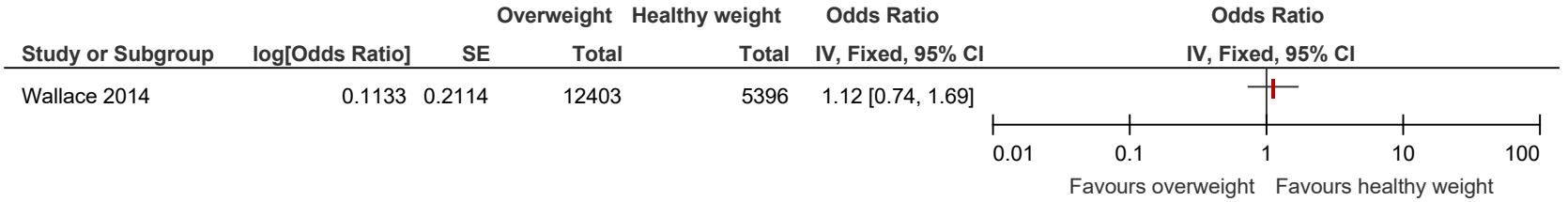


Figure 19: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

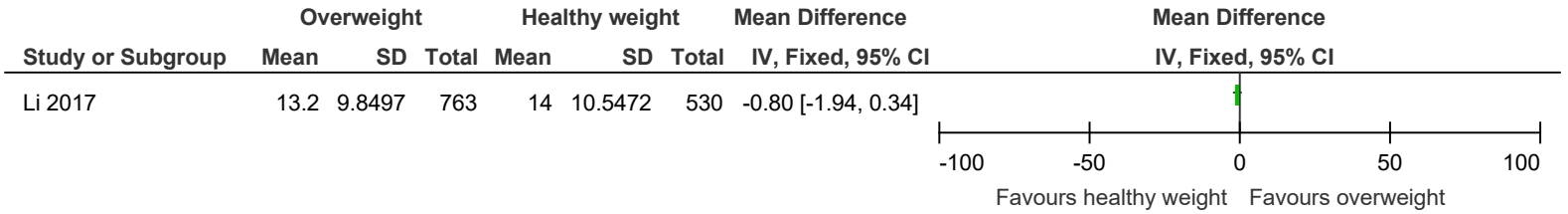


Figure 20: Reoperation or revision to the prosthesis at >3 months

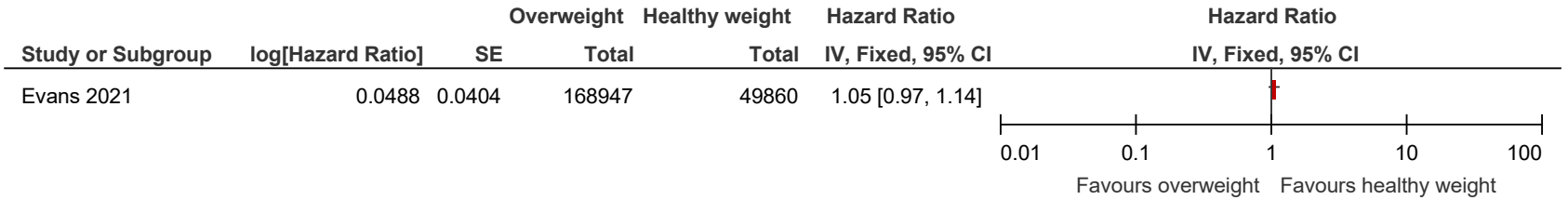


Figure 21: Venous thromboembolic events at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.4637	0.1187	12326	5359	1.59 [1.26, 2.01]

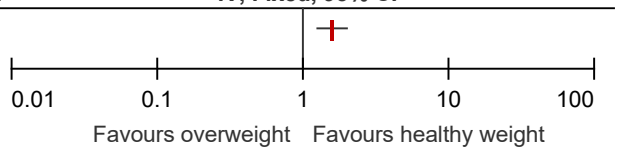
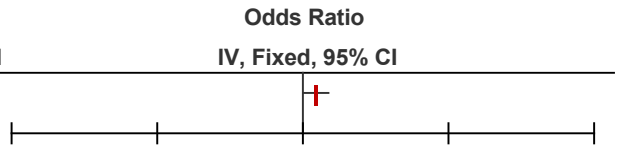


Figure 22: Surgical site infection (wound infection) at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.207	0.1005	12326	5359	1.23 [1.01, 1.50]



E.1.3 People who have obesity I compared to people who are of healthy weight

Figure 23: Mortality at ≤3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity I Total	Healthy weight Total	Hazard Ratio IV, Fixed, 95% CI
Evans 2021	-0.3711	0.0886	159056	49860	0.69 [0.58, 0.82]

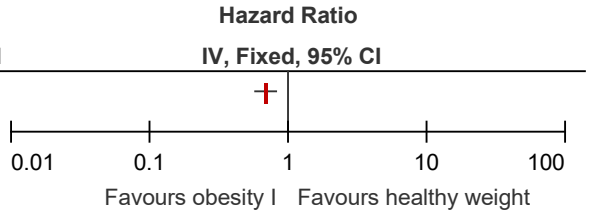


Figure 24: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

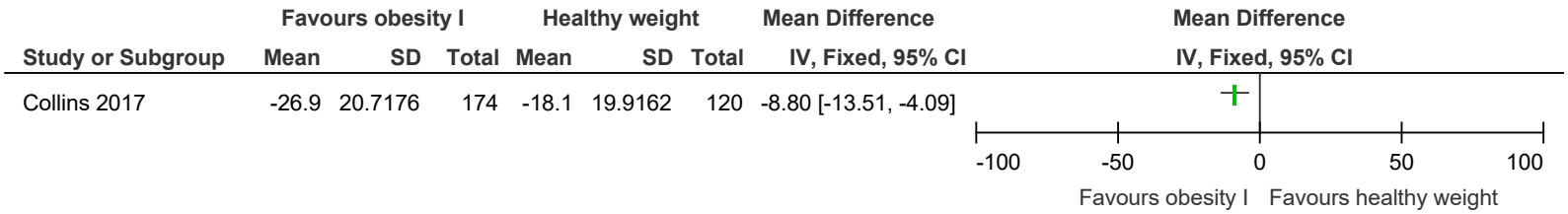


Figure 25: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

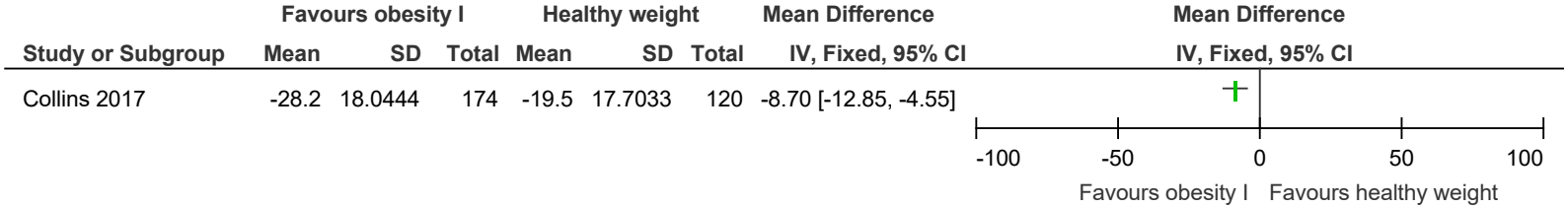


Figure 26: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

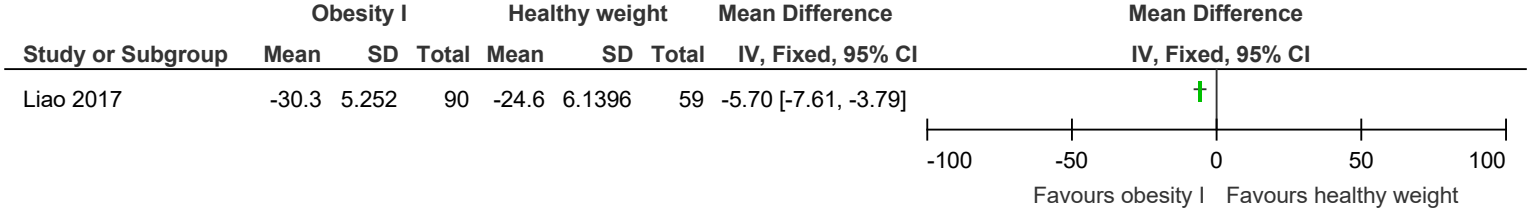


Figure 27: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

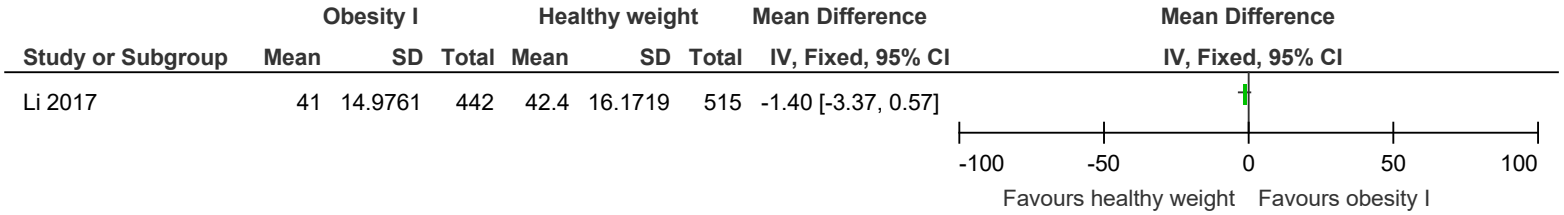


Figure 28: Total adverse events up to 90 days

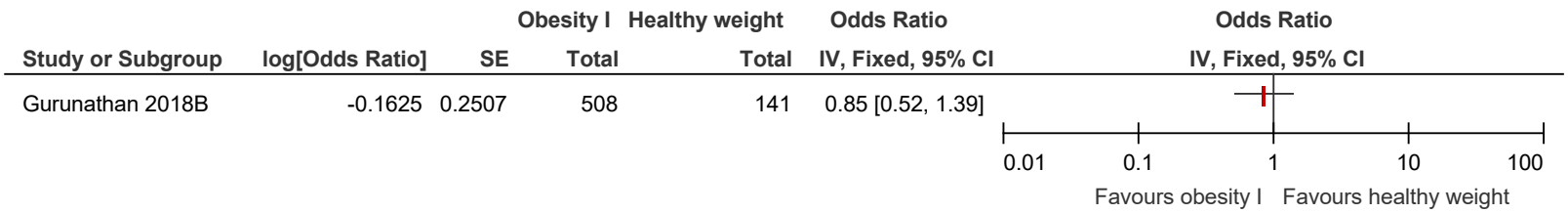


Figure 29: Mortality at >3 months

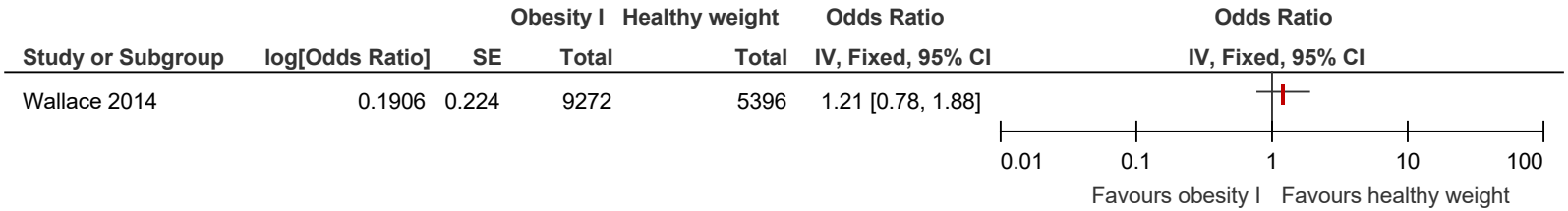


Figure 30: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

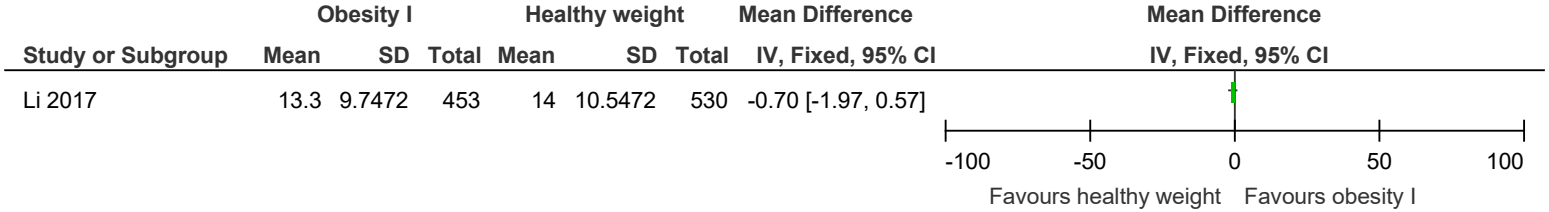


Figure 31: Reoperation or revision to the prosthesis at >3 months

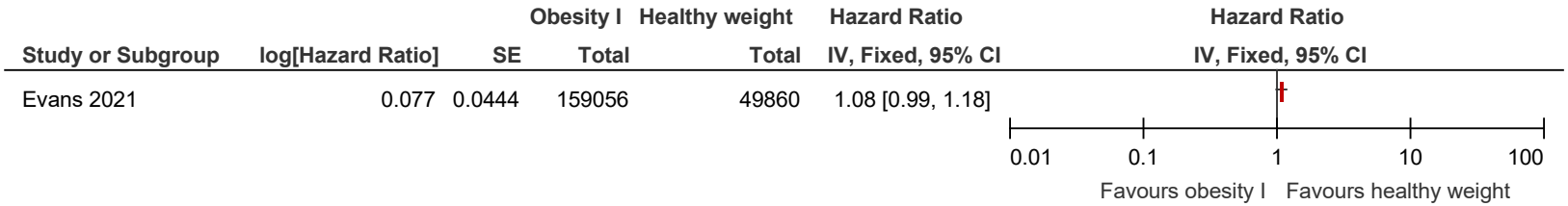


Figure 32: Venous thromboembolic events at >3 months

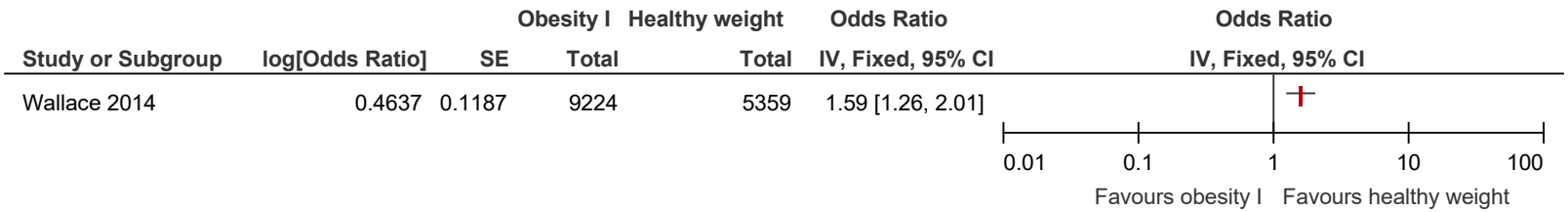
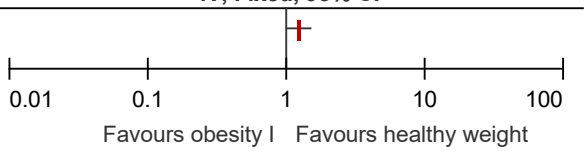


Figure 33: Surgical site infection (wound infection) at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity I Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.207	0.1005	9224	5359	1.23 [1.01, 1.50]



E.1.4 People who have obesity I compared to people who are overweight

Figure 34: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Favours obesity I Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-26.9	20.7176	174	-23	20.2324	203	-3.90 [-8.05, 0.25]

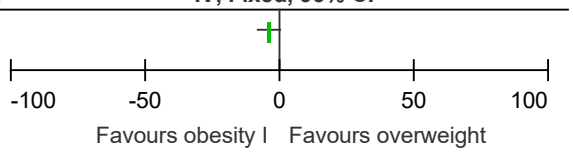


Figure 35: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Favours obesity I Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-28.2	18.0444	174	-23	18.0647	203	-5.20 [-8.86, -1.54]

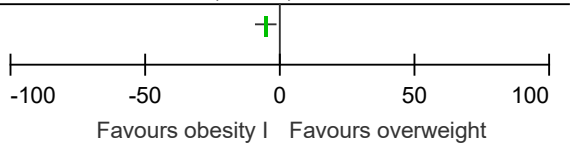


Figure 36: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

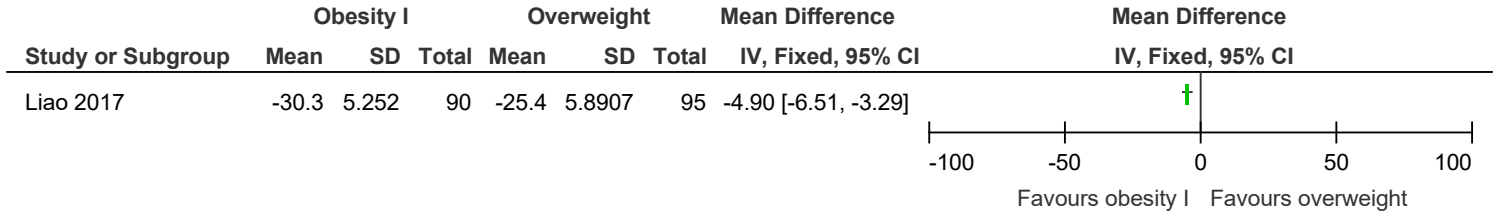


Figure 37: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

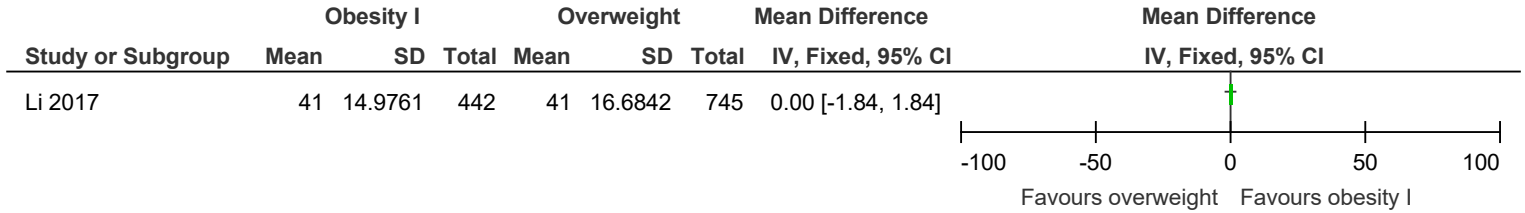
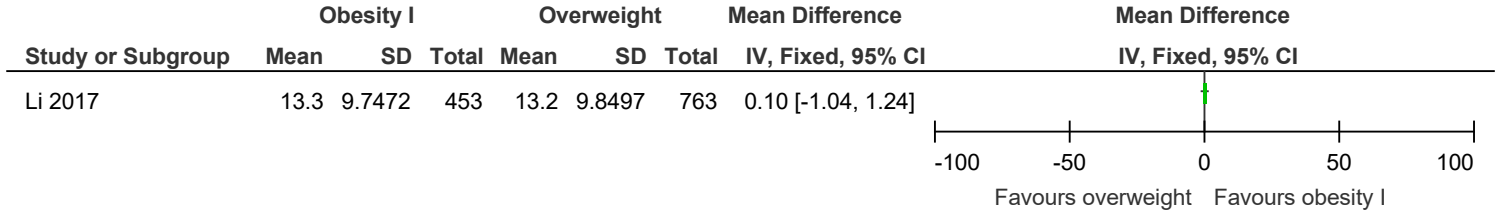


Figure 38: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months



E.1.5 People who have obesity II compared to people who are of healthy weight

Figure 39: Mortality at ≤3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity II Total	Healthy weight Total	Hazard Ratio IV, Fixed, 95% CI
Evans 2021	-0.1278	0.1024	80166	49860	0.88 [0.72, 1.08]

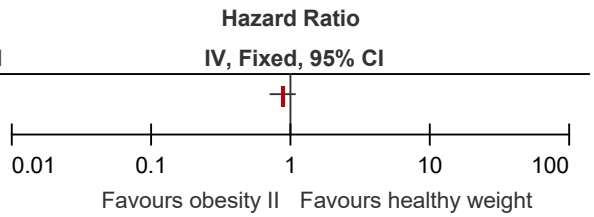


Figure 40: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Obesity II Mean	SD	Total	Healthy weight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-30.6	19.6439	79	-18.1	19.9162	120	-12.50 [-18.11, -6.89]

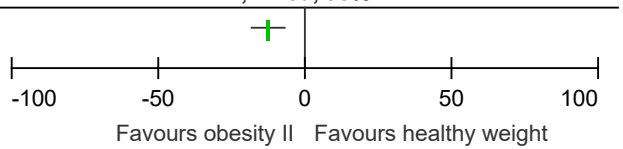


Figure 41: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Obesity II Mean	SD	Total	Healthy weight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-29.6	17.4117	79	-19.5	17.7033	120	-10.10 [-15.08, -5.12]

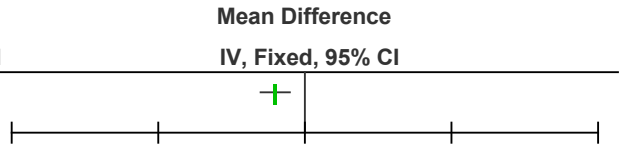


Figure 42: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

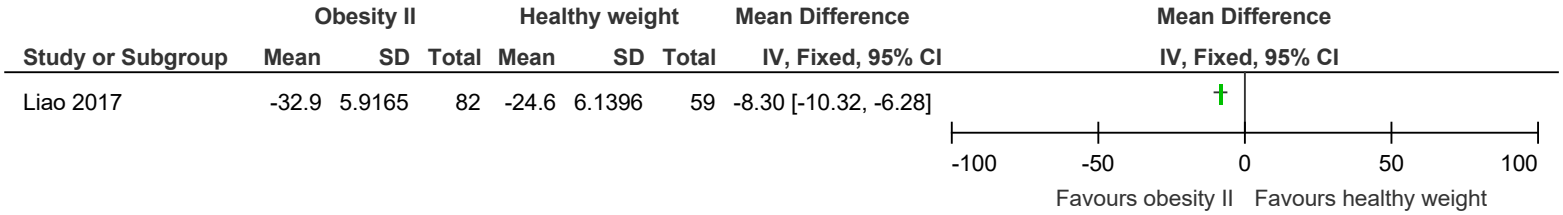


Figure 43: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

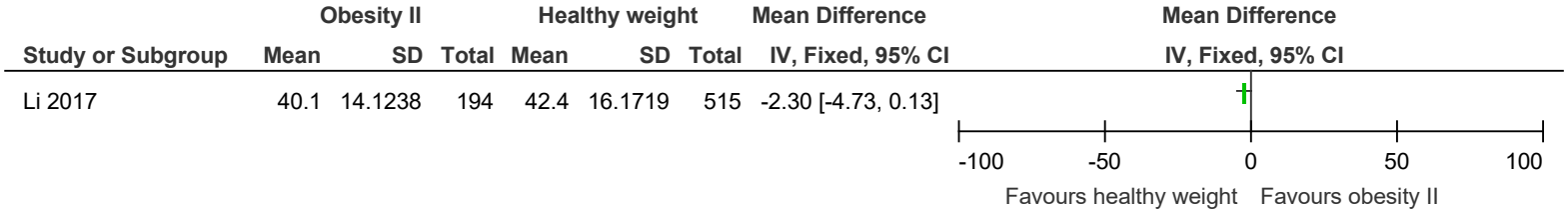


Figure 44: Total adverse events up to 90 days

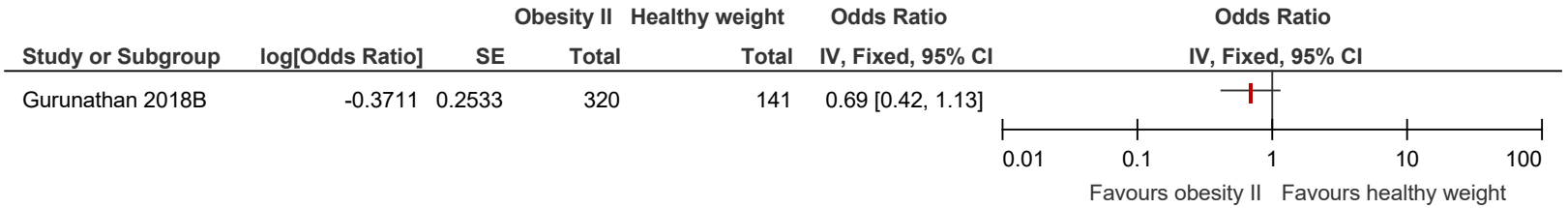


Figure 45: Mortality at >3 months

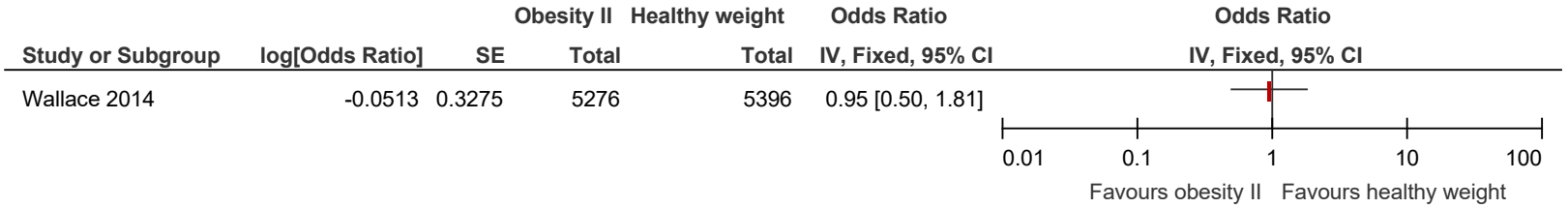


Figure 46: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

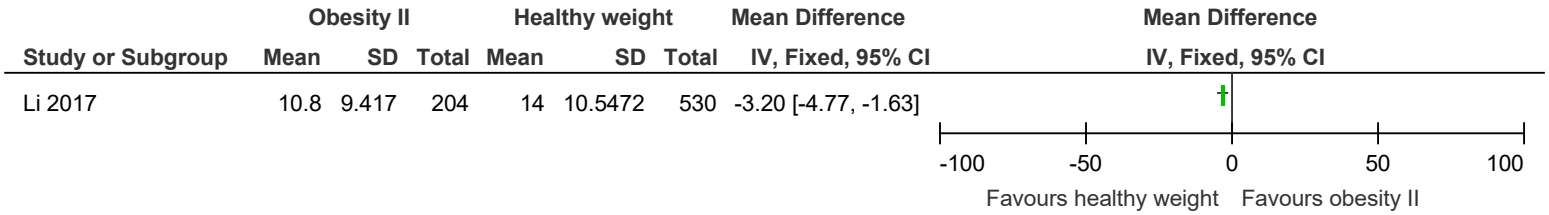


Figure 47: Reoperation or revision to the prosthesis at >3 months

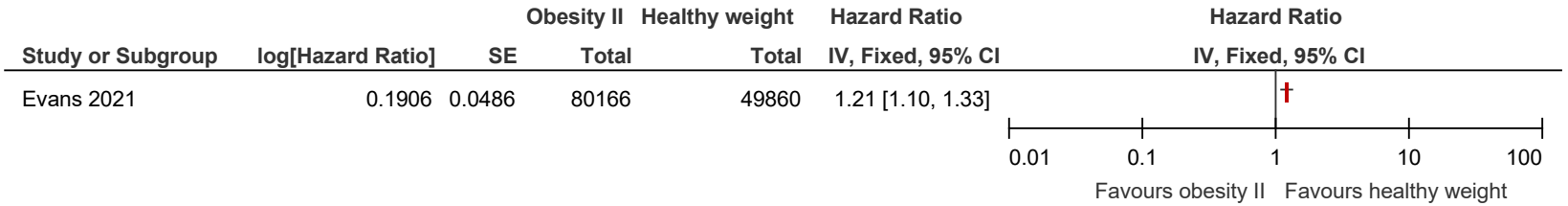


Figure 48: Venous thromboembolic events at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity II Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.6575	0.1459	5260	5359	1.93 [1.45, 2.57]

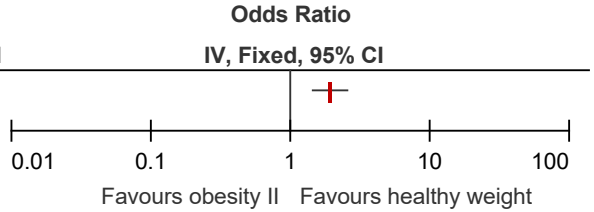
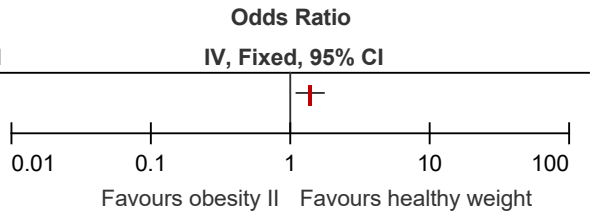


Figure 49: Surgical site infection (wound infection) at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity II Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.3293	0.1148	5260	5359	1.39 [1.11, 1.74]



E.1.6 People who have obesity II compared to people who are overweight

Figure 50: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Obesity II Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-30.6	19.6439	79	-23	20.2324	203	-7.60 [-12.75, -2.45]

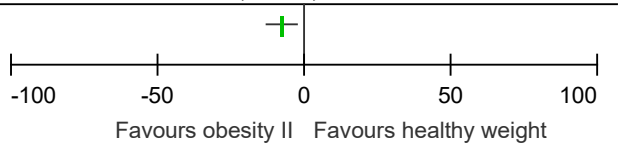


Figure 51: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

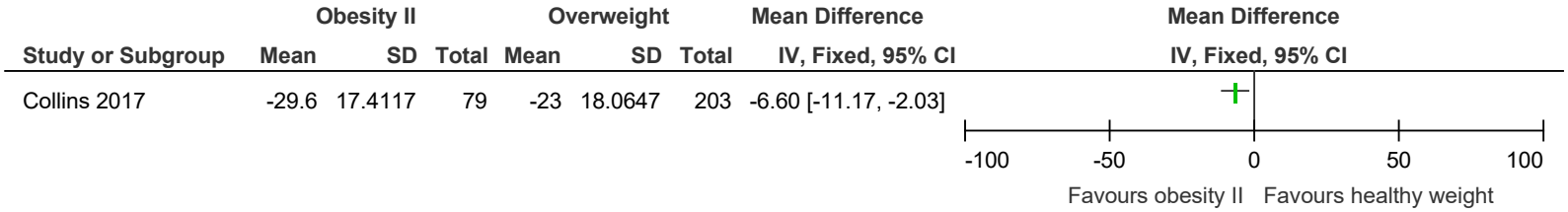


Figure 52: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

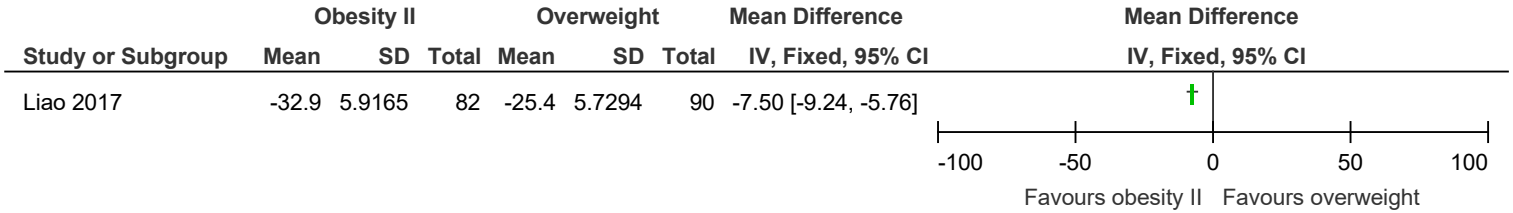


Figure 53: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

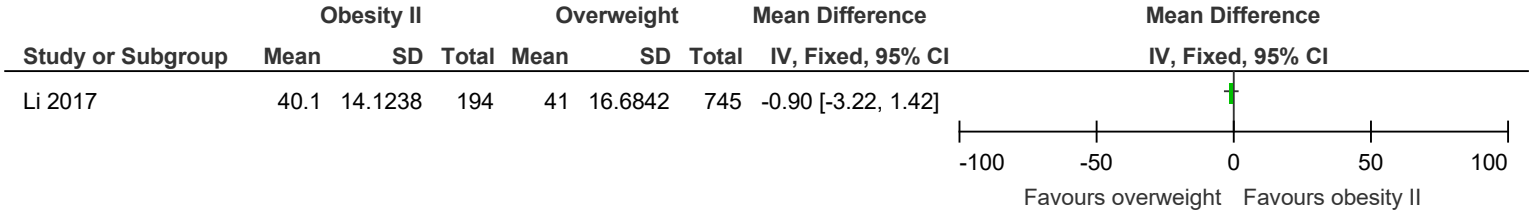
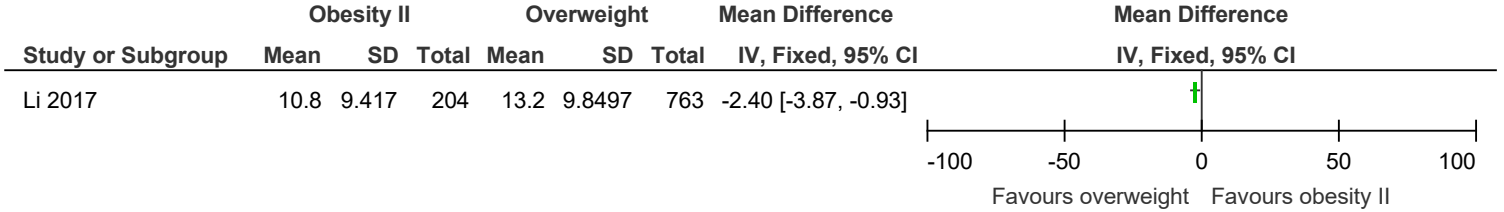


Figure 54: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months



E.1.7 People who have obesity II compared to people who have obesity I

Figure 55: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

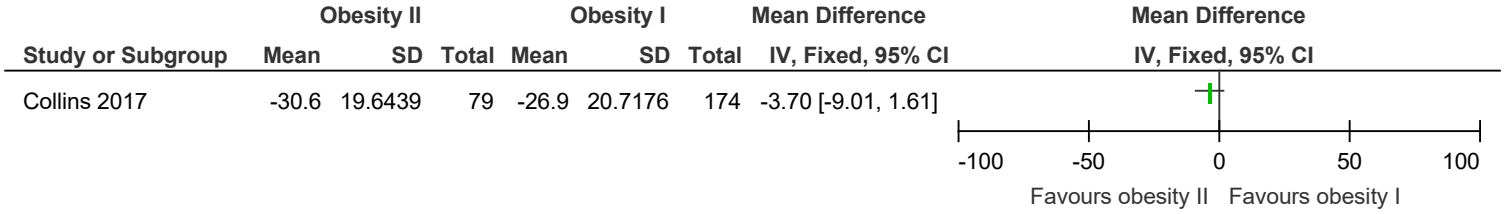


Figure 56: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

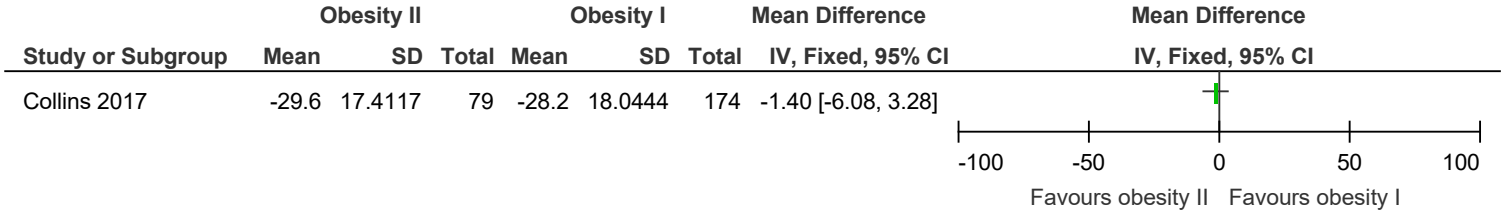


Figure 57: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

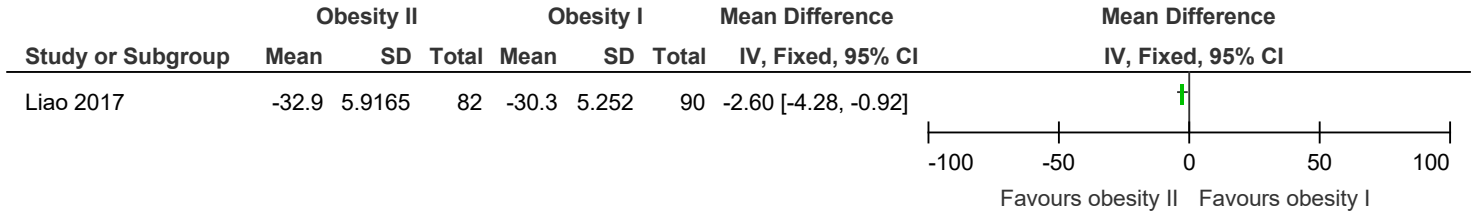


Figure 58: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

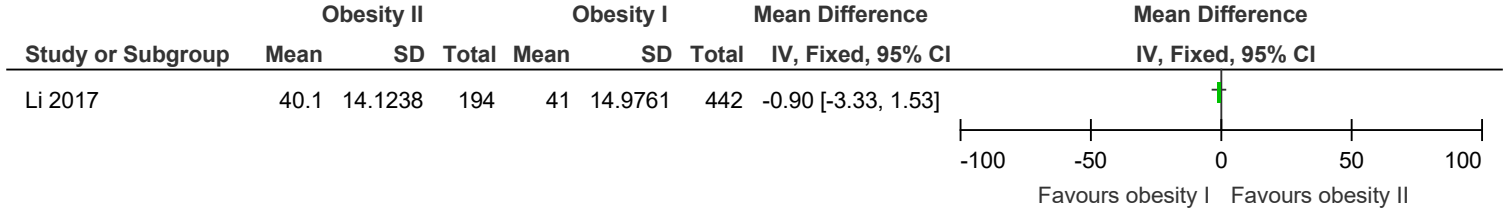
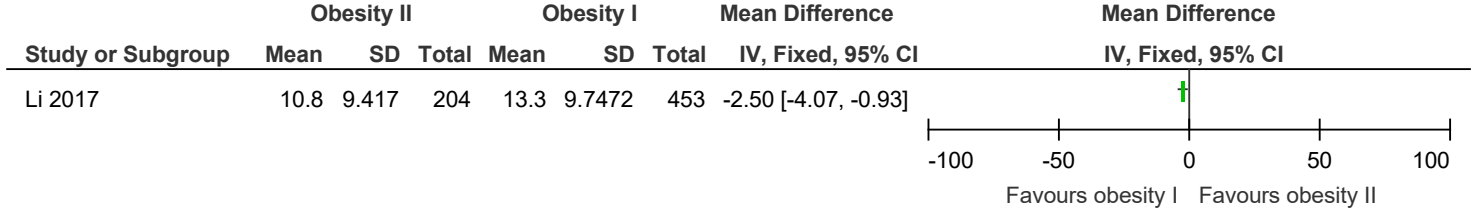


Figure 59: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months



E.1.8 People who have obesity III compared to people who are of healthy weight

Figure 60: Mortality at ≤3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity III Total	Healthy weight Total	Hazard Ratio IV, Fixed, 95% CI
Evans 2021	0.157	0.1339	34343	49860	1.17 [0.90, 1.52]

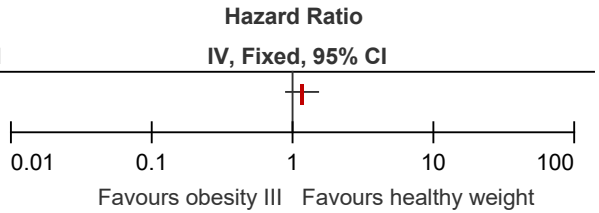


Figure 61: Mortality at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity III Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	0.2231	0.3182	23081	14989	1.25 [0.67, 2.33]

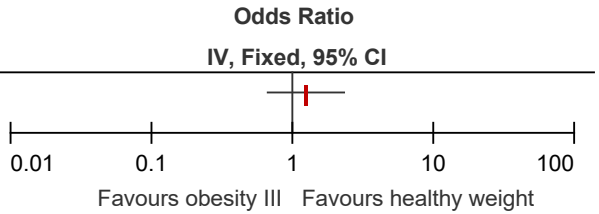


Figure 62: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Obesity III Mean	SD	Total	Healthy weight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-32.2	19.9747	57	-18.1	19.9162	120	-14.10 [-20.39, -7.81]

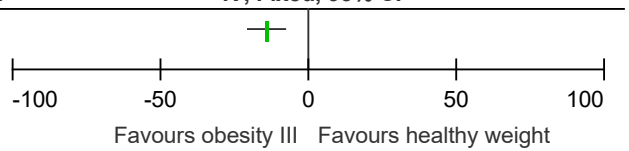


Figure 63: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

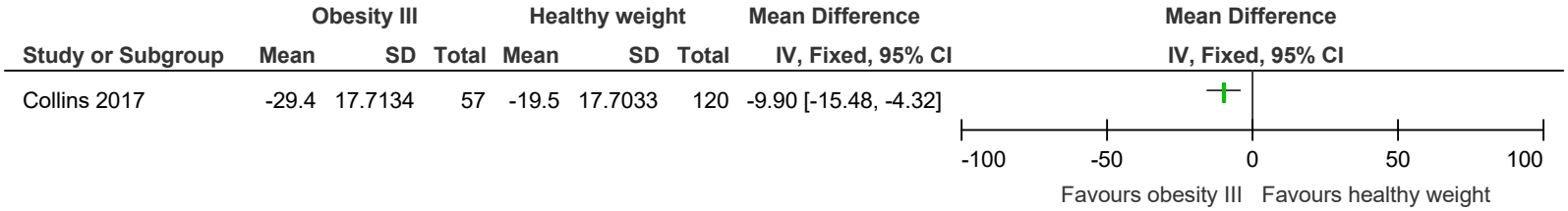


Figure 64: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

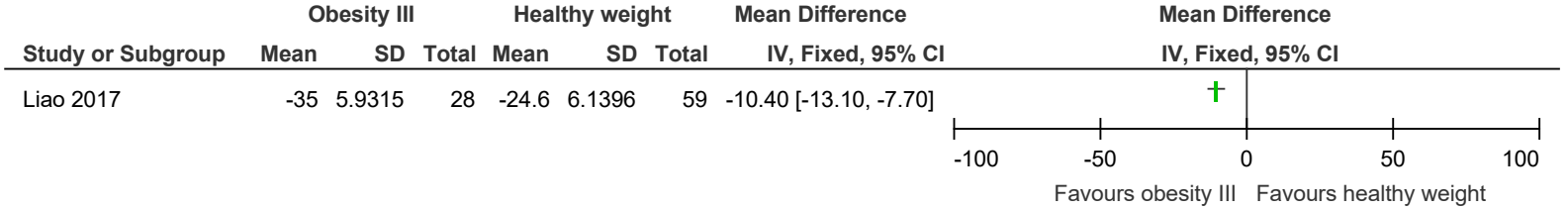


Figure 65: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

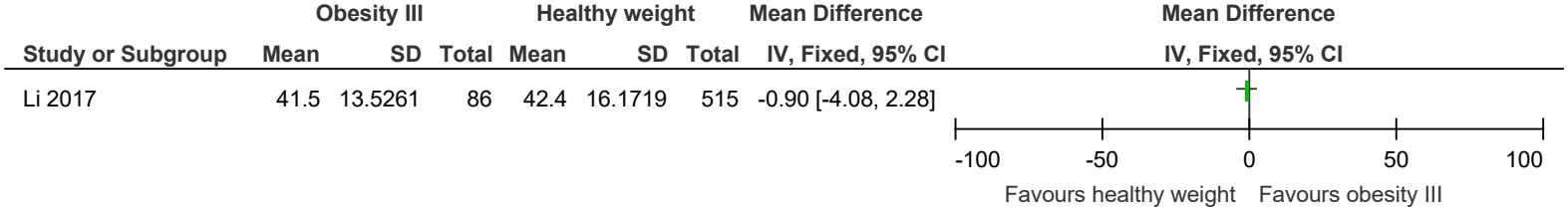


Figure 66: Reoperation or revision to the prosthesis at ≤3 months

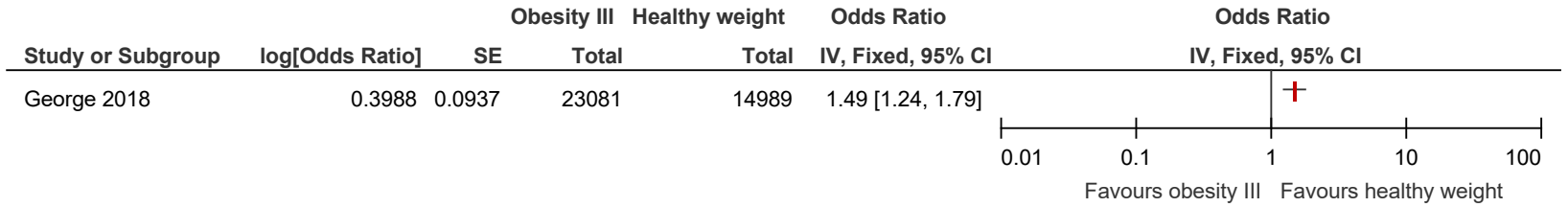


Figure 67: Total adverse events up to 90 days

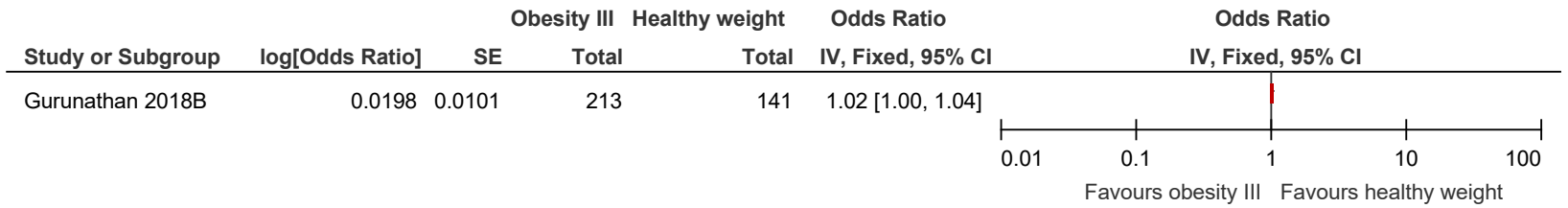


Figure 68: Surgical site infection (superficial infection) at ≤3 months

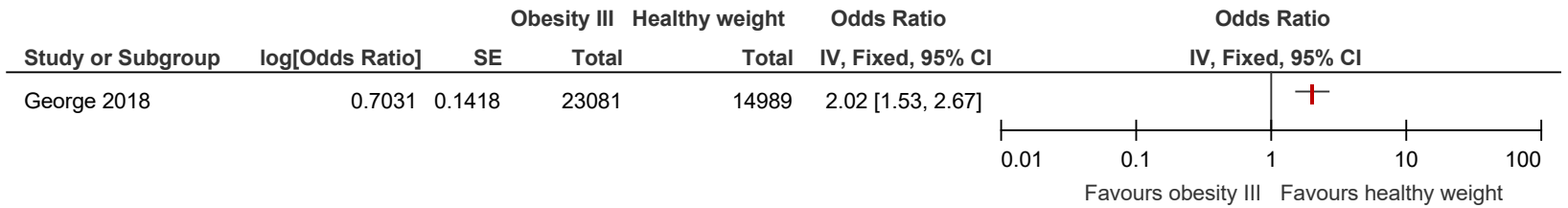


Figure 69: Surgical site infection (periprosthetic joint infection) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity III Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	0.7608	0.1881	23081	14989	2.14 [1.48, 3.09]

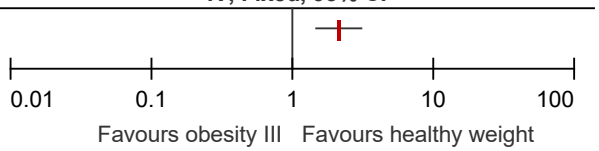


Figure 70: Venous thromboembolic events (deep vein thrombosis) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity III Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	-0.2231	0.1139	23081	14989	0.80 [0.64, 1.00]

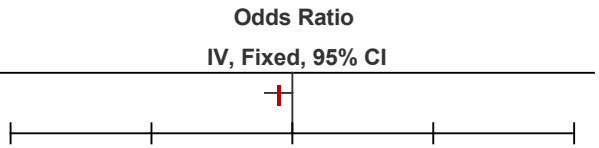


Figure 71: Venous thromboembolic events (pulmonary embolism) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity III Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
George 2018	0.6523	0.1539	23081	14989	1.92 [1.42, 2.60]

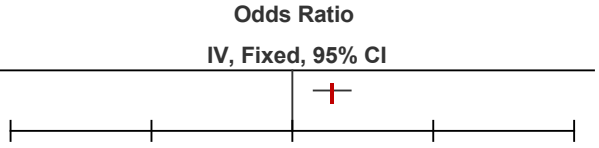


Figure 72: Health-related quality of life (EQ-5D, -0.11-1, higher is better, change score) at >3 months

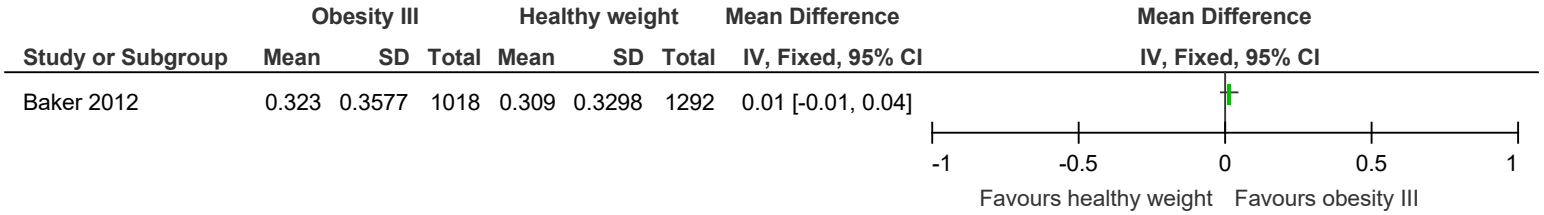


Figure 73: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

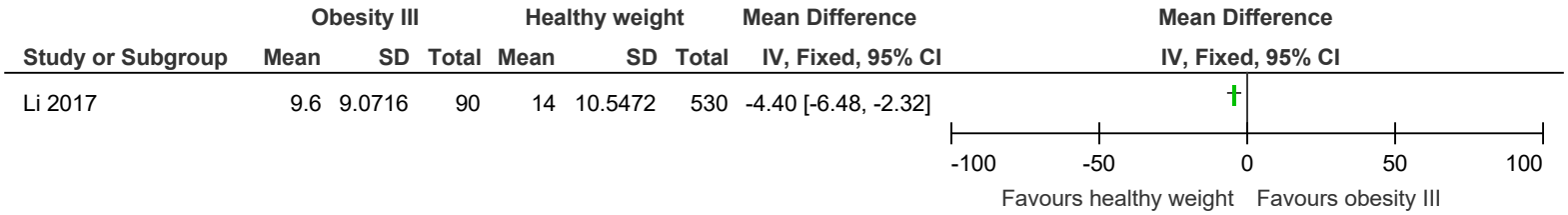


Figure 74: Post-operative Patient Reported Outcome Measures (OKS, 0-48, higher is better, change score) at 1 year

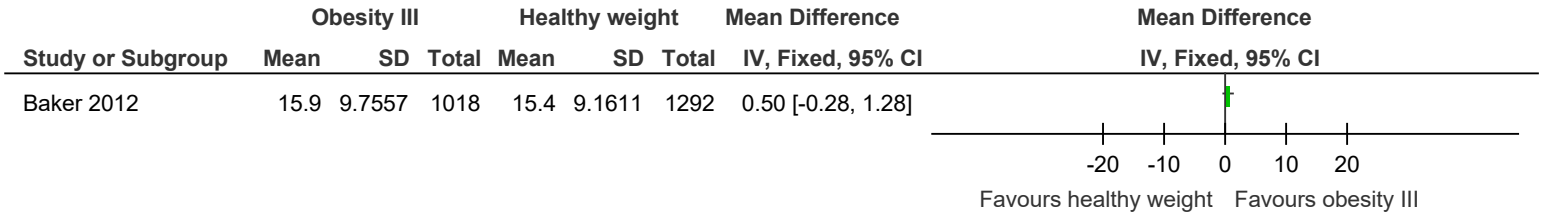
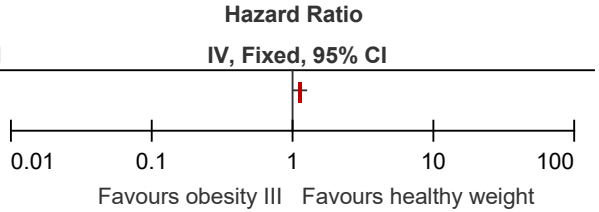


Figure 75: Reoperation or revision to the prosthesis at >3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity III Total	Healthy weight Total	Hazard Ratio IV, Fixed, 95% CI
Evans 2021	0.1222	0.0523	34343	49860	1.13 [1.02, 1.25]



E.1.9 People who have obesity III compared to people who are overweight

Figure 76: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Obesity III Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-32.2	19.9747	57	-23	20.2324	203	-9.20 [-15.09, -3.31]

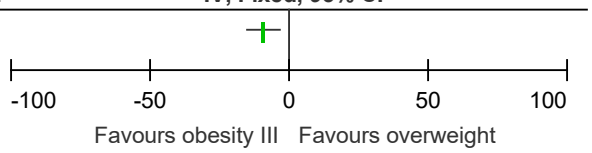


Figure 77: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

Study or Subgroup	Obesity III Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Collins 2017	-29.4	17.7134	57	-23	18.0647	203	-6.40 [-11.63, -1.17]

Figure 78: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

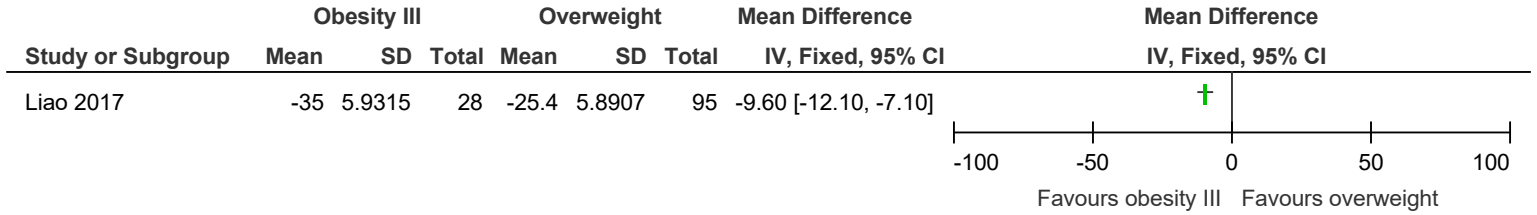


Figure 79: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

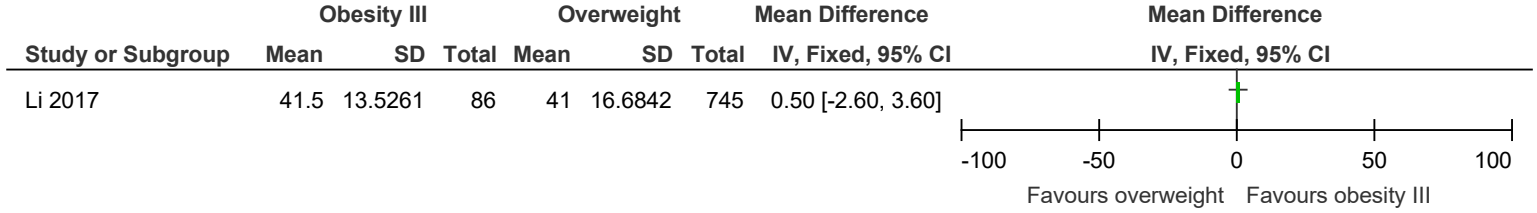
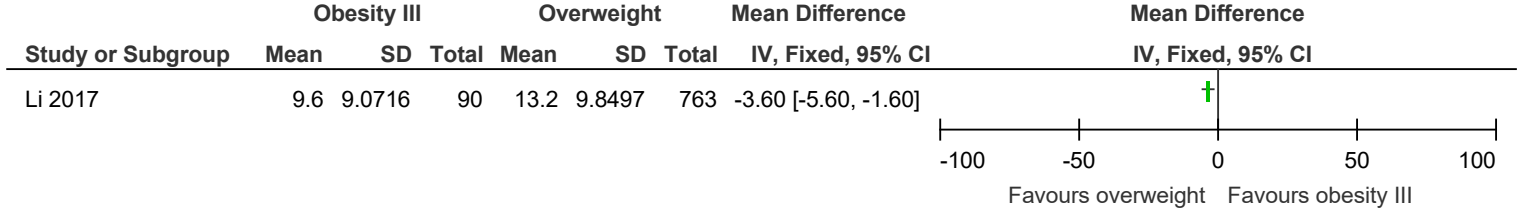


Figure 80: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months



E.1.10 People who have obesity III compared to people who have obesity I

Figure 81: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

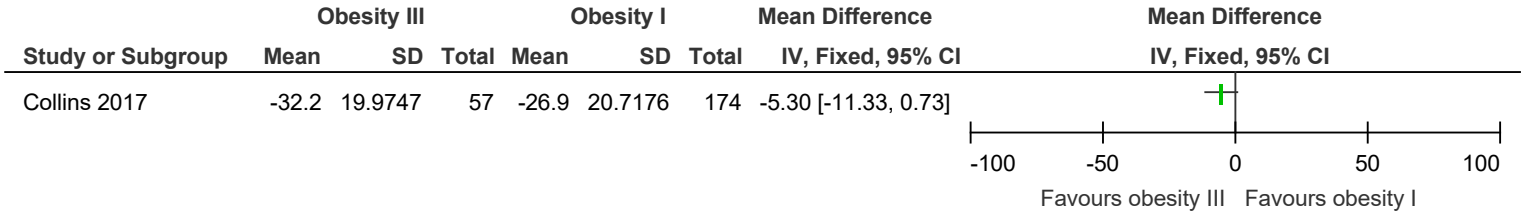


Figure 82: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

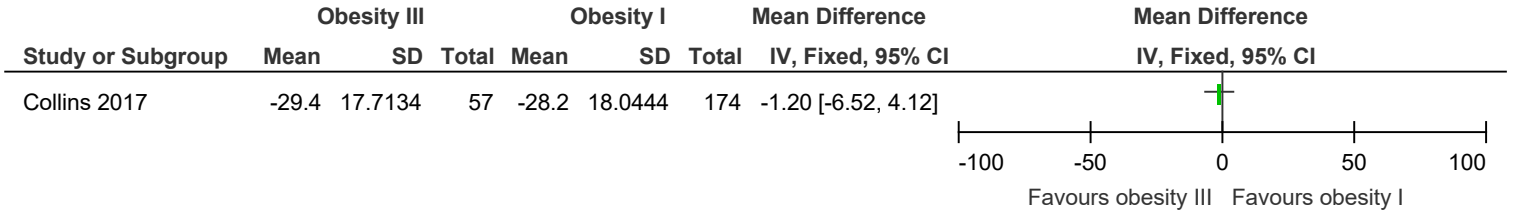


Figure 83: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

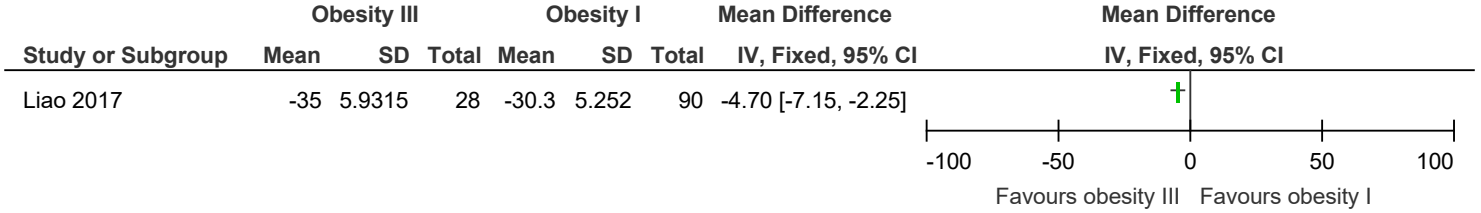


Figure 84: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

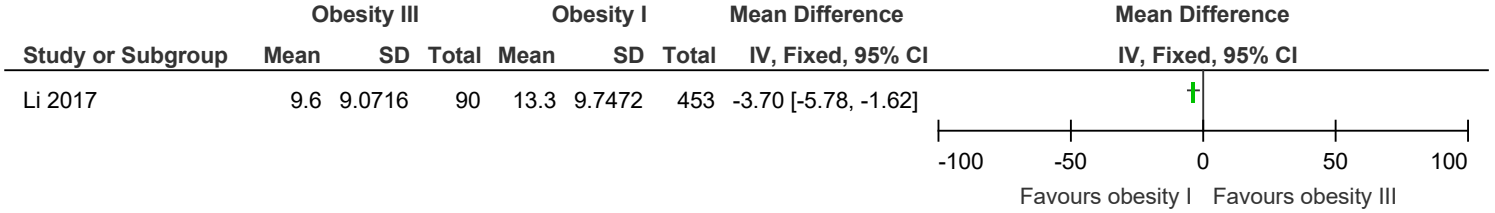
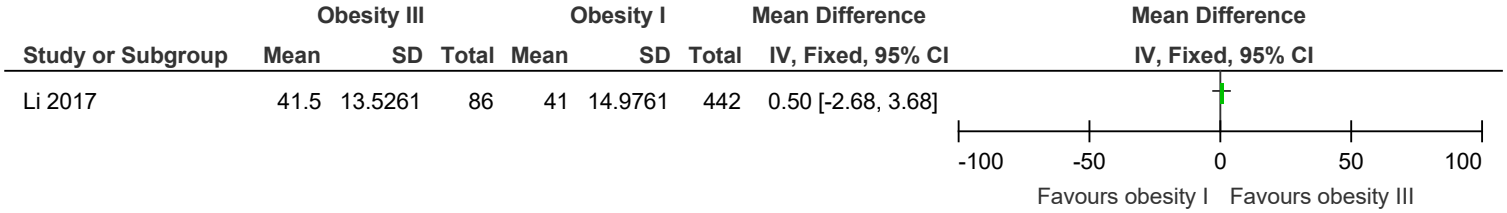


Figure 85: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months



E.1.11 People who have obesity III compared to people who have obesity II

Figure 86: Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months

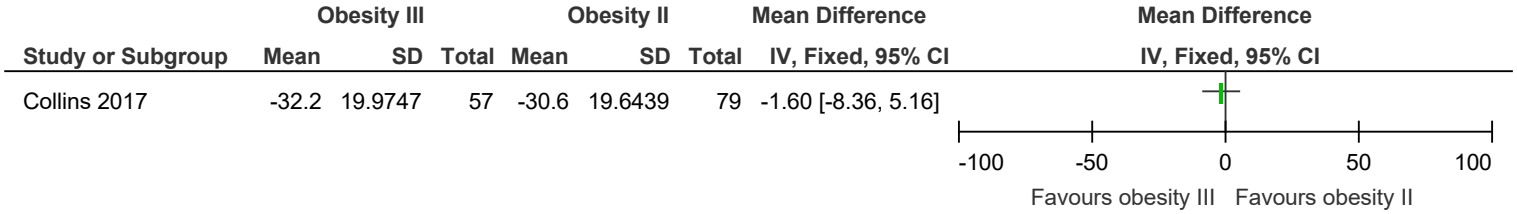


Figure 87: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

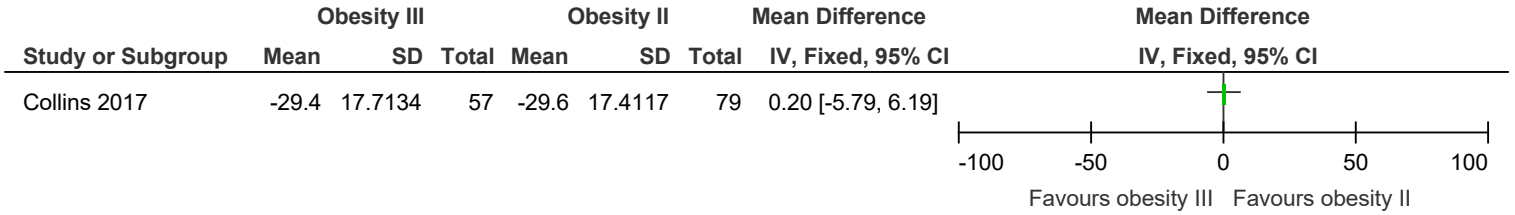


Figure 88: Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months

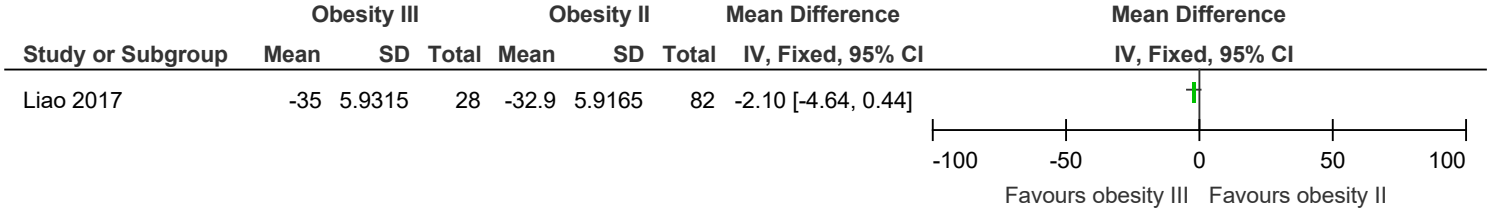


Figure 89: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

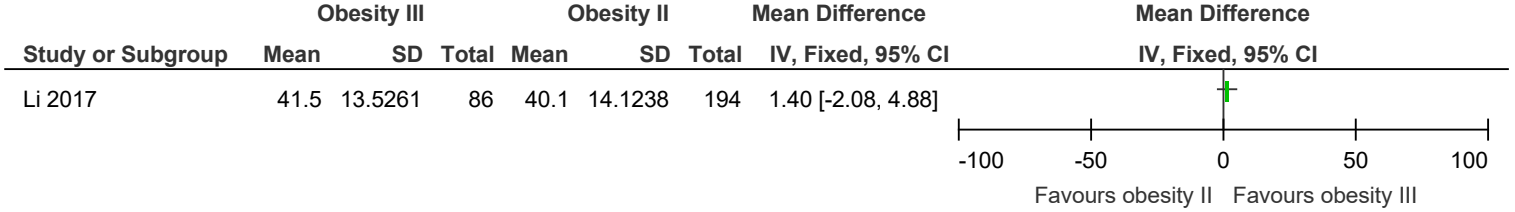
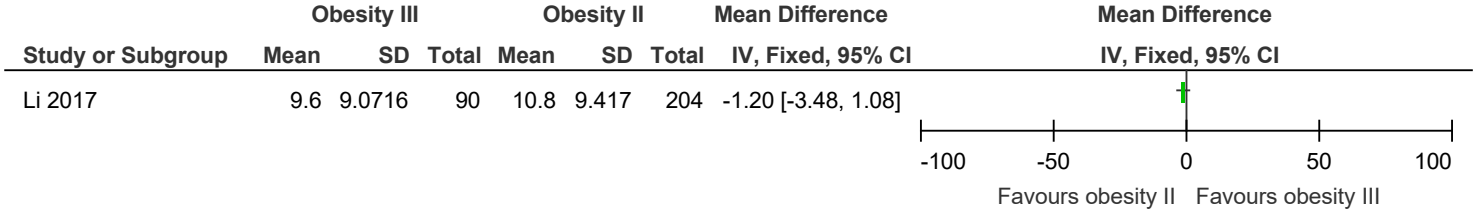


Figure 90: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months



E.2 Hip osteoarthritis

E.2.1 People who are underweight compared to people who are of healthy weight

Figure 91: Mortality at >3 months

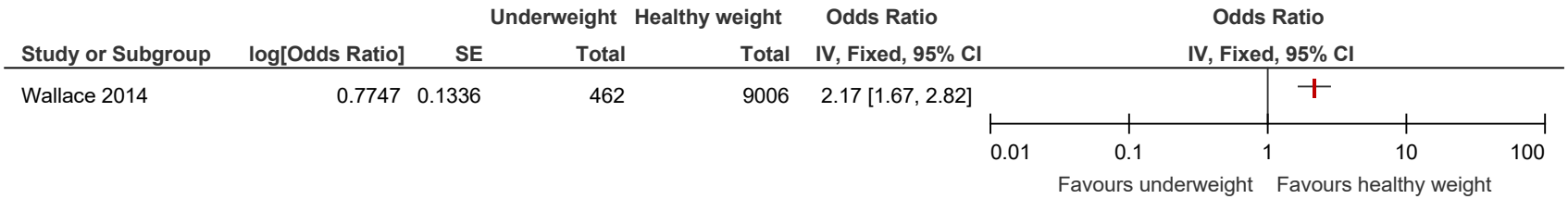


Figure 92: Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months

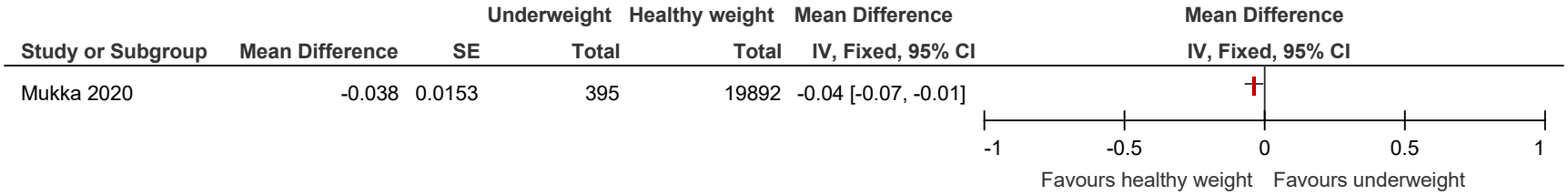


Figure 93: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

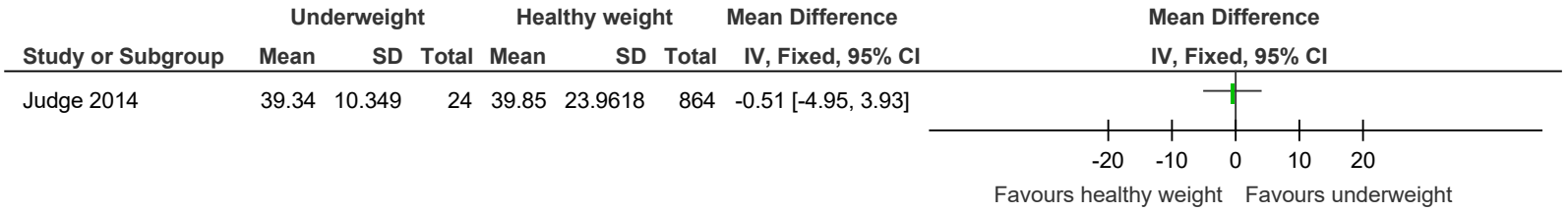


Figure 94: Venous thromboembolic events at >3 months

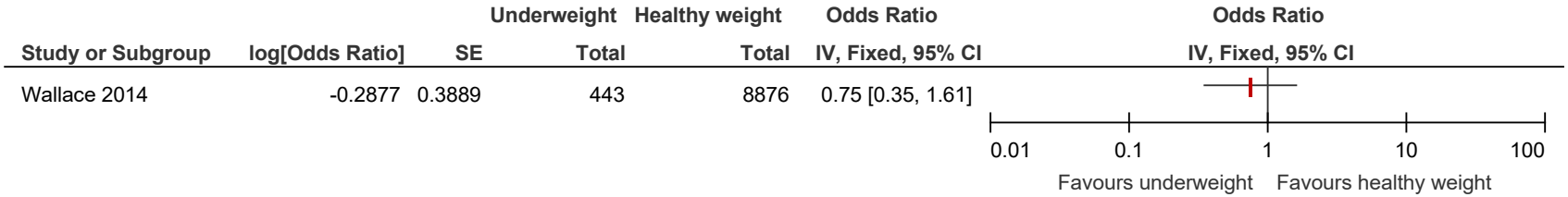
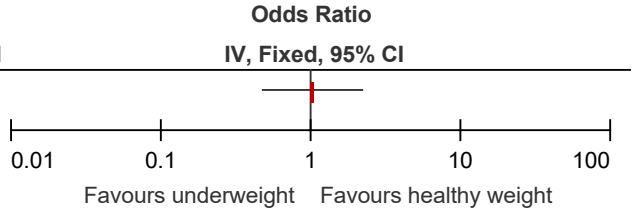


Figure 95: Surgical site infection (wound infection) at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Underweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.0296	0.3896	443	8876	1.03 [0.48, 2.21]



E.2.2 People who are underweight compared to people who are overweight

Figure 96: Reoperation or revision to the prosthesis at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Underweight Total	Overweight Total	Odds Ratio IV, Fixed, 95% CI
Peters 2020	0.5481	0.3112	649	46507	1.73 [0.94, 3.18]

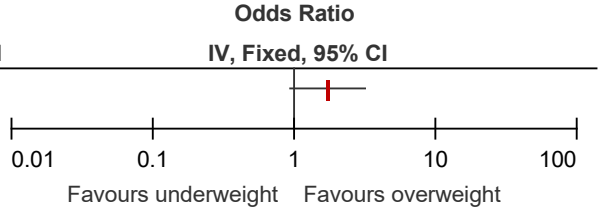
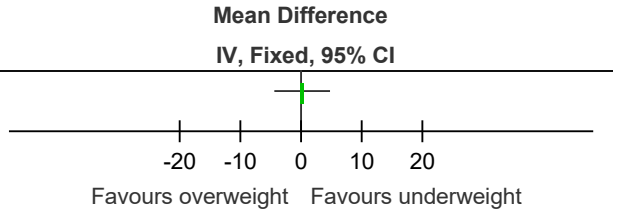


Figure 97: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

Study or Subgroup	Underweight Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Judge 2014	39.34	10.349	24	39.15	27.3495	1139	0.19 [-4.24, 4.62]



E.2.3 People who are overweight compared to people who are of healthy weight

Figure 98: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

	Overweight			Healthy weight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	32.2	18.6168	927	31.7	16.6519	371	0.50 [-1.58, 2.58]	

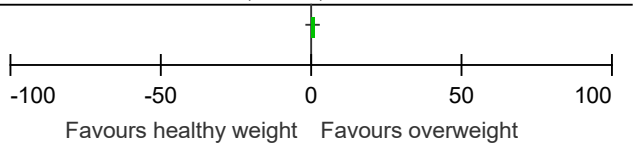


Figure 99: Total adverse events at up to 90 days

			Overweight	Healthy weight	Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gurunathan 2018A	-0.478	0.1867	378	191	0.62 [0.43, 0.89]	

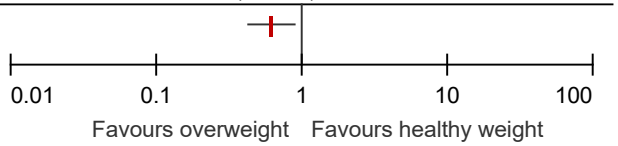


Figure 100: Surgical site infection (wound infection) at ≤3 months

			Overweight	Healthy weight	Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gurunathan 2018A	0.1989	0.3454	378	191	1.22 [0.62, 2.40]	

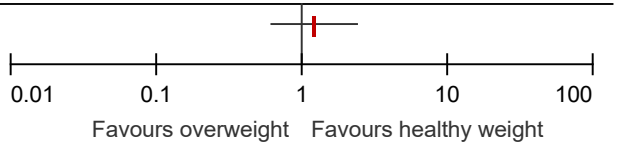


Figure 101: Venous thromboembolic events at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Gurunathan 2018A	-0.9676	0.6325	378	191	0.38 [0.11, 1.31]

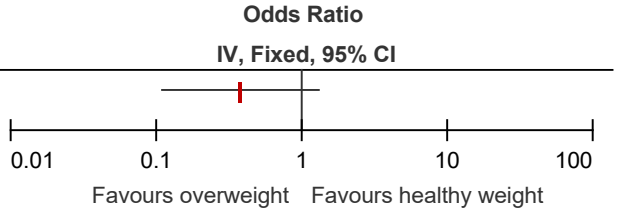


Figure 102: Mortality at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Overweight Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	-0.4943	0.144	12619	9006	0.61 [0.46, 0.81]

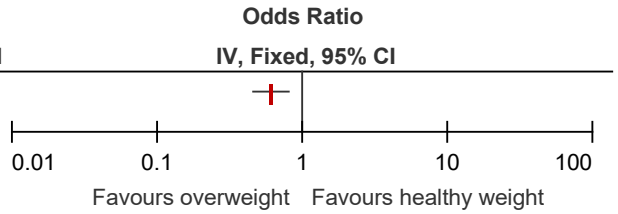


Figure 103: Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months

Study or Subgroup	Mean Difference	SE	Overweight Total	Healthy weight Total	Mean Difference IV, Fixed, 95% CI
Mukka 2020	-0.018	0.0026	28221	19892	-0.02 [-0.02, -0.01]

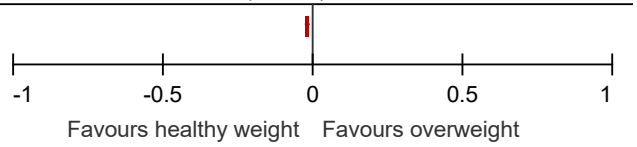


Figure 104: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

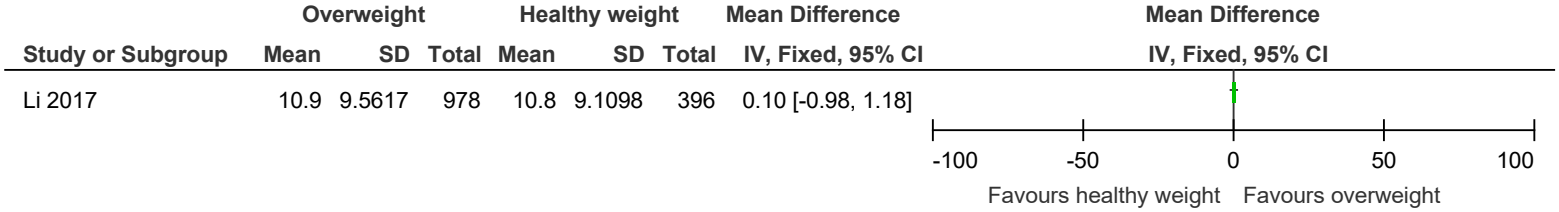


Figure 105: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

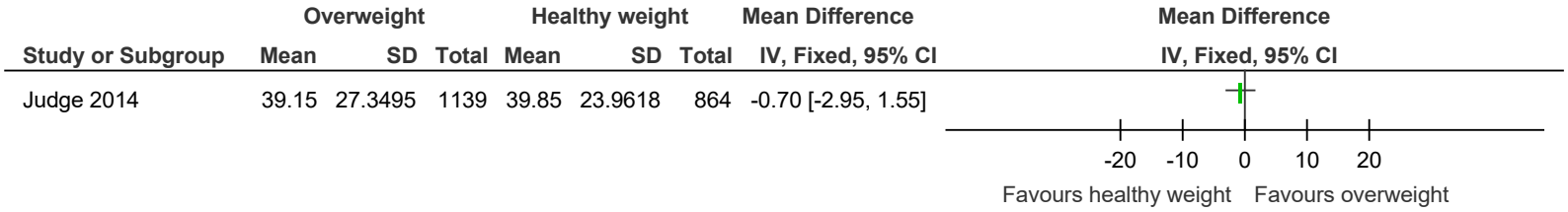


Figure 106: Venous thromboembolic events at >3 months

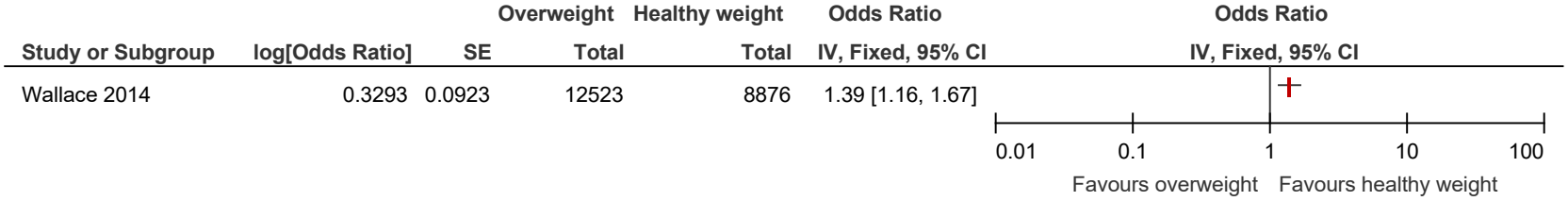


Figure 107: Reoperation or revision to the prosthesis at >3 months

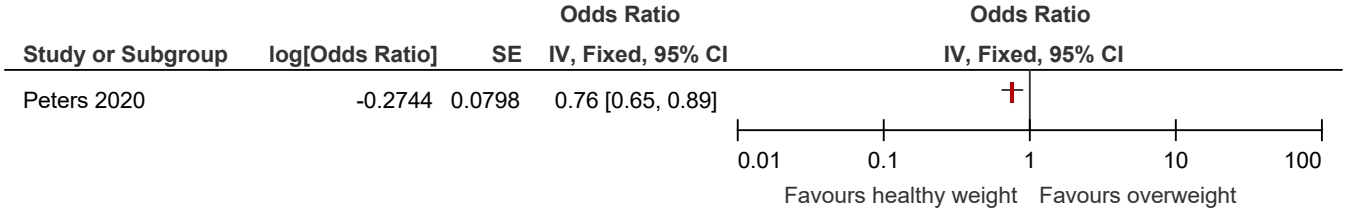
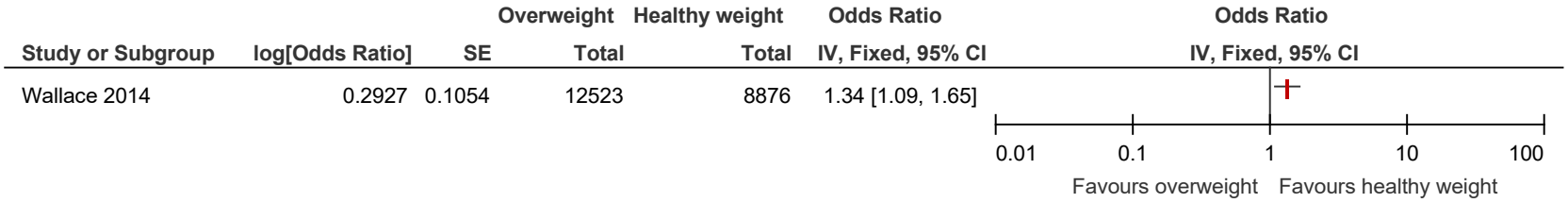


Figure 108: Surgical site infection (wound infection) at >3 months



E.2.4 People who have obesity I compared to people who are of healthy weight

Figure 109: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

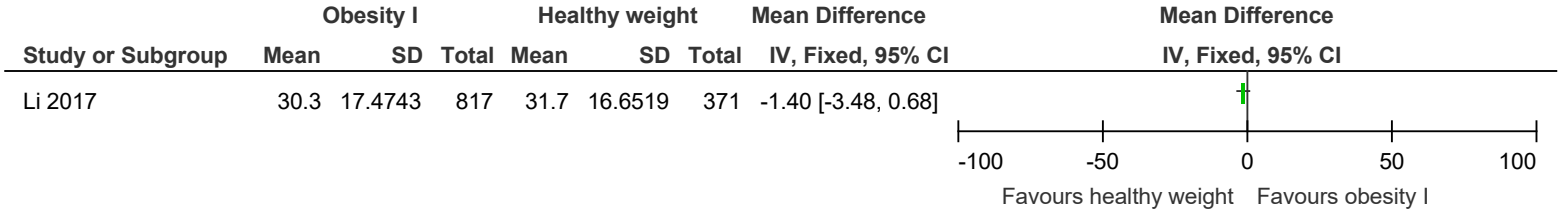


Figure 110: Total adverse events at up to 90 days

Study or Subgroup	log[Odds Ratio]	SE	Obesity I Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Gurunathan 2018A	-0.3567	0.2142	219	191	0.70 [0.46, 1.07]

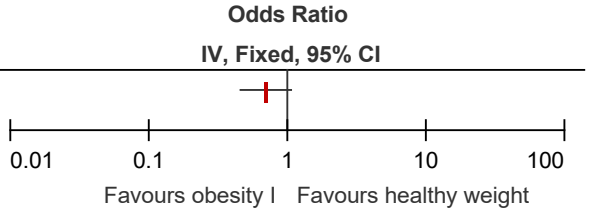


Figure 111: Surgical site infection (wound infection) at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity I Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Gurunathan 2018A	0.3716	0.3789	219	191	1.45 [0.69, 3.05]

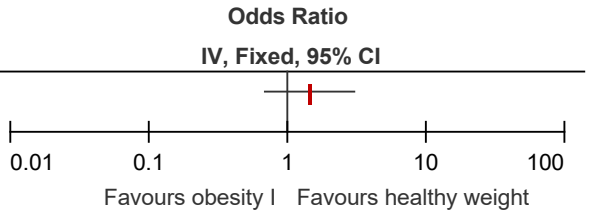


Figure 112: Venous thromboembolic events at ≤3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity I Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Gurunathan 2018A	0.077	0.5605	219	191	1.08 [0.36, 3.24]

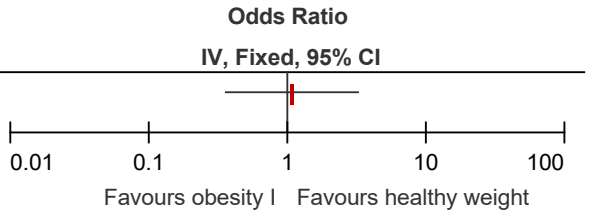


Figure 113: Mortality at >3 months

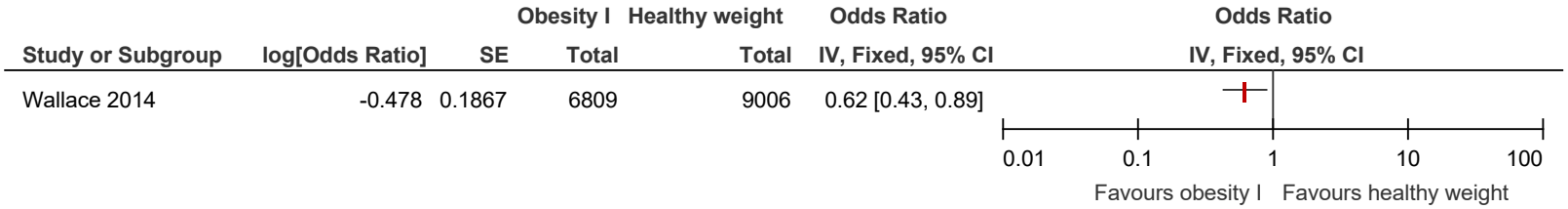


Figure 114: Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months

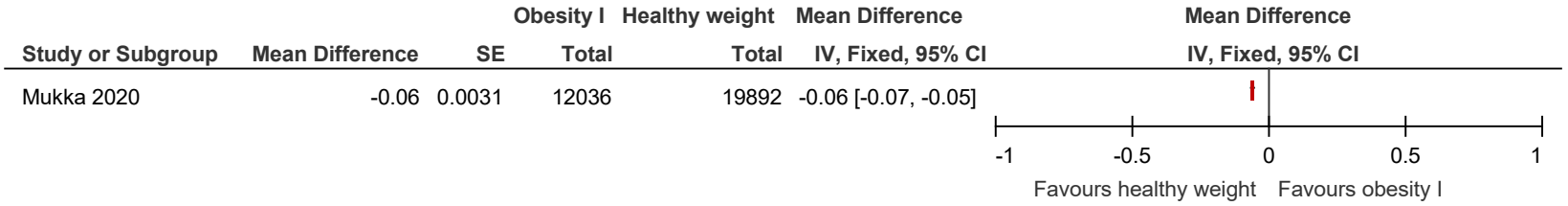


Figure 115: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

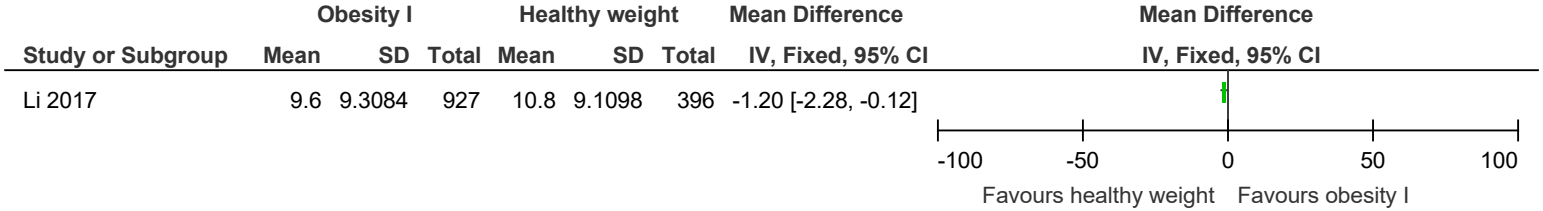


Figure 116: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

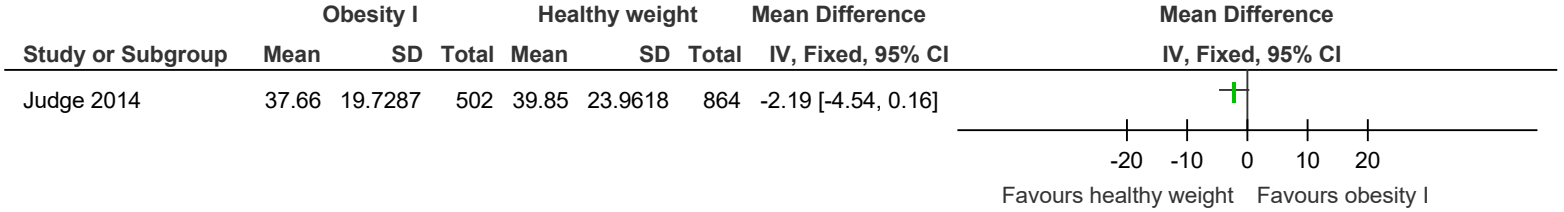


Figure 117: Venous thromboembolic events at >3 months

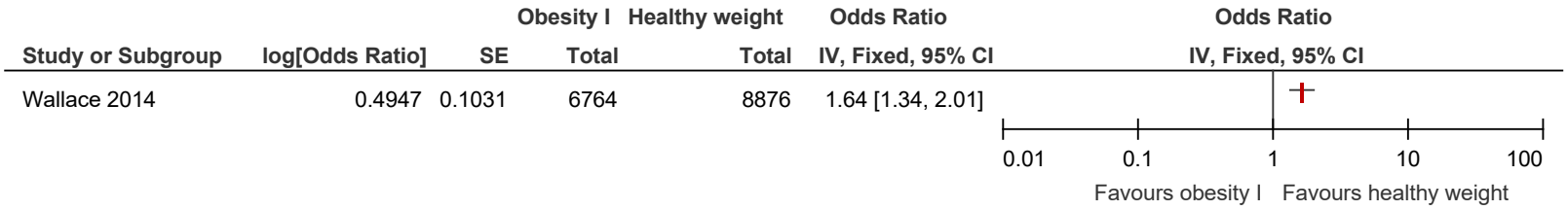
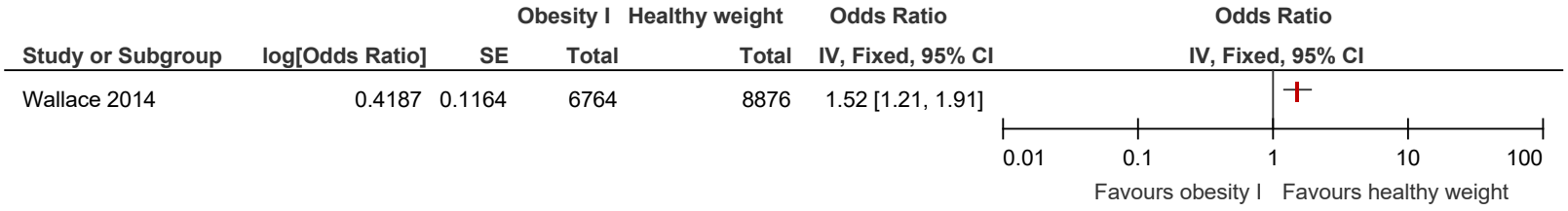


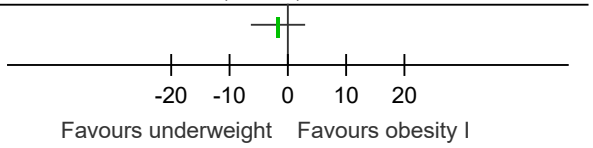
Figure 118: Surgical site infection (wound infection) at >3 months



E.2.5 People who have obesity I compared to people who are underweight

Figure 119: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

	Obesity I			Underweight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Judge 2014	37.66	19.7287	502	39.34	10.349	24	-1.68 [-6.17, 2.81]	



E.2.6 People who have obesity I compared to people who are overweight

Figure 120: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

	Obesity I			Overweight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	30.3	17.4743	817	32.2	18.6168	927	-1.90 [-3.59, -0.21]	

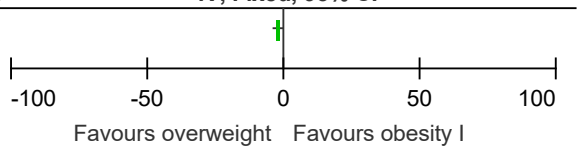


Figure 121: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

	Obesity I			Overweight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	9.6	9.3084	927	10.9	9.5617	978	-1.30 [-2.15, -0.45]	

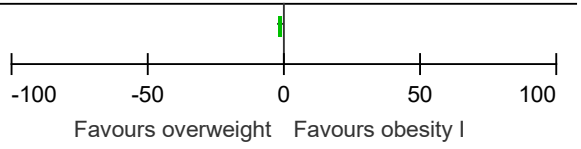
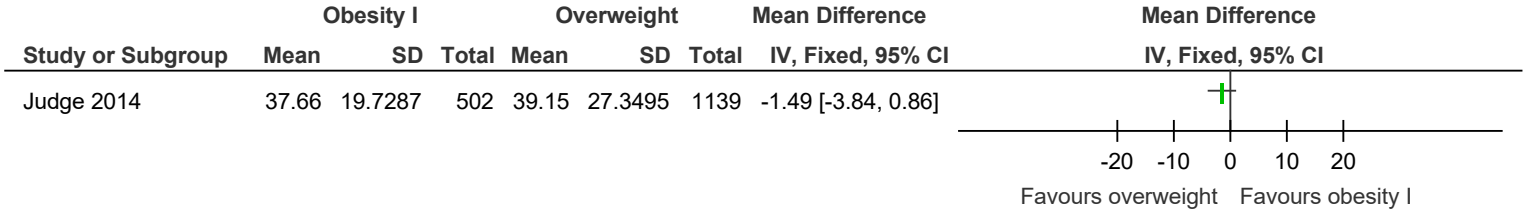


Figure 122: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year



E.2.7 People who have obesity II compared to people who are of healthy weight

Figure 123: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

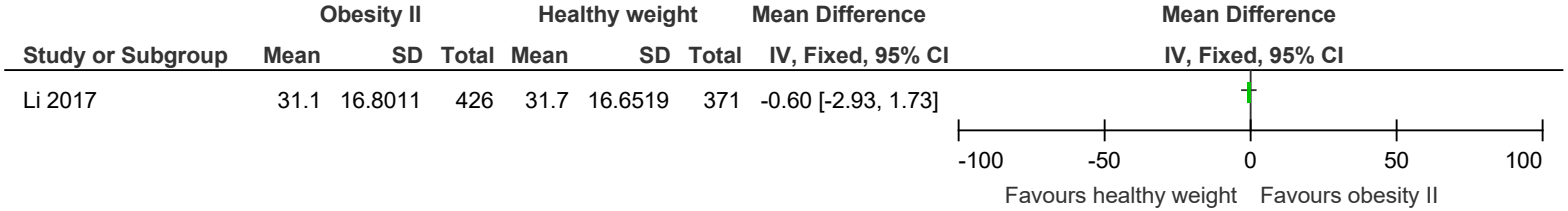


Figure 124: Total adverse events at up to 90 days

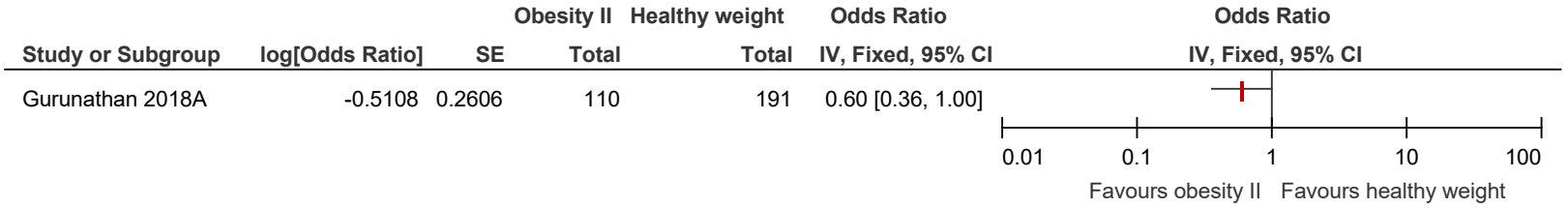


Figure 125: Surgical site infection (wound infection) at ≤3 months

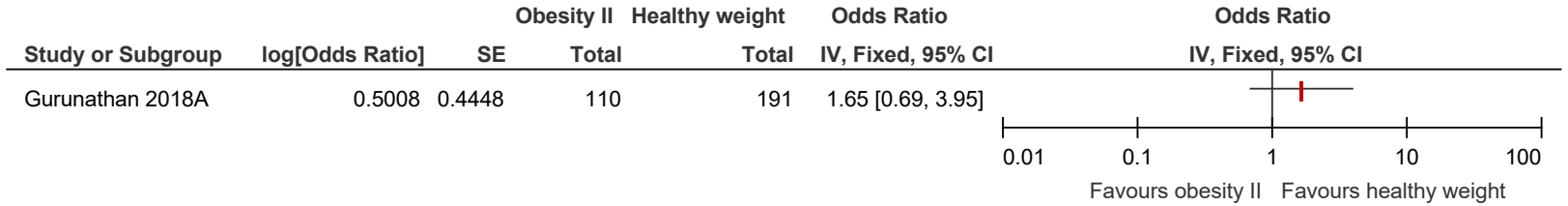


Figure 126: Venous thromboembolic events at ≤3 months

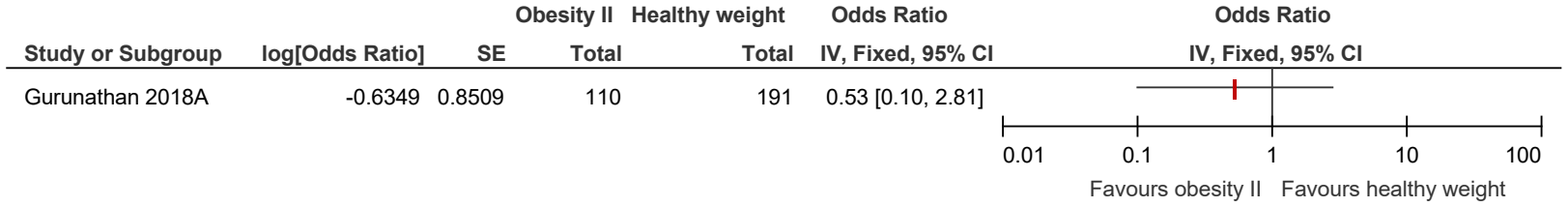


Figure 127: Mortality at >3 months

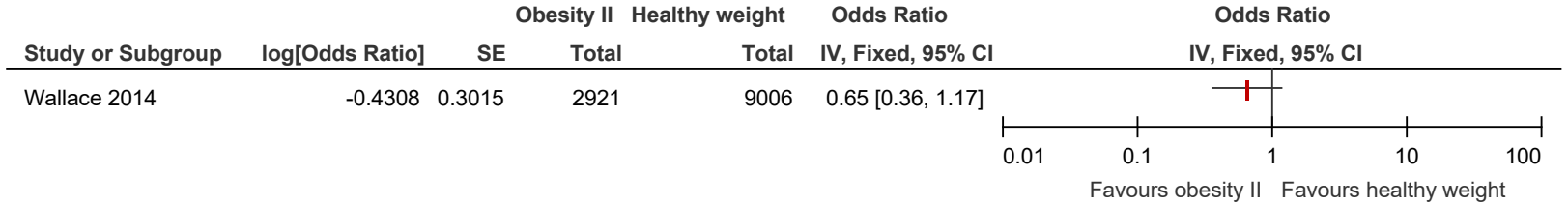


Figure 128: Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months

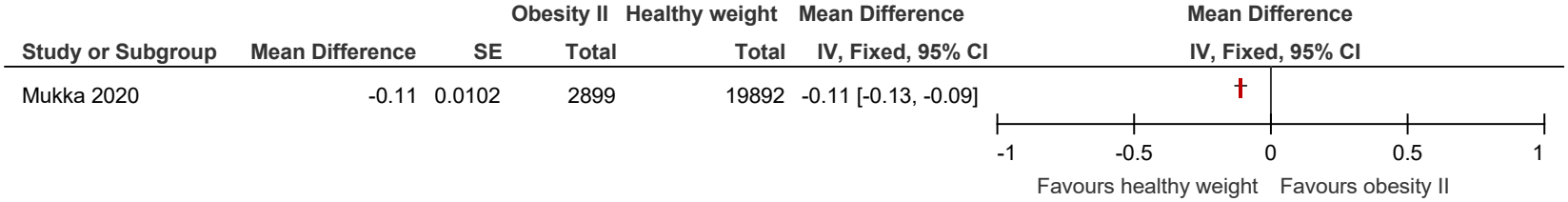


Figure 129: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

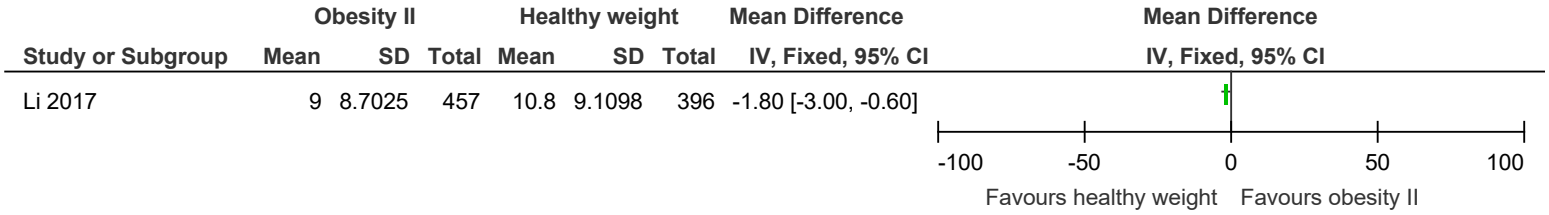


Figure 130: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

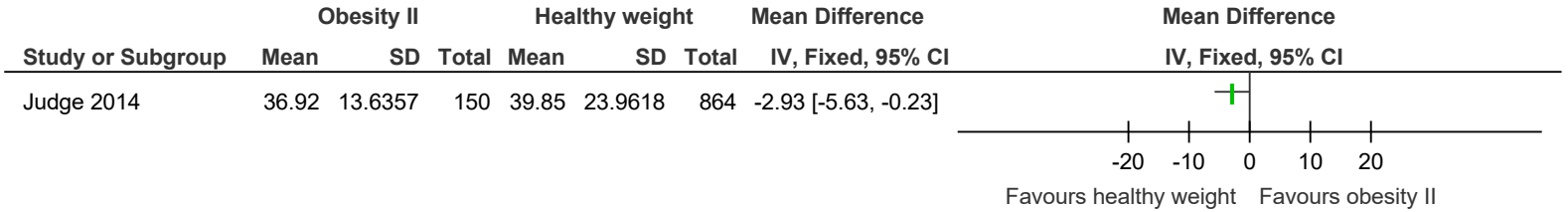


Figure 131: Venous thromboembolic events at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity II Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.4121	0.1345	2904	8876	1.51 [1.16, 1.97]

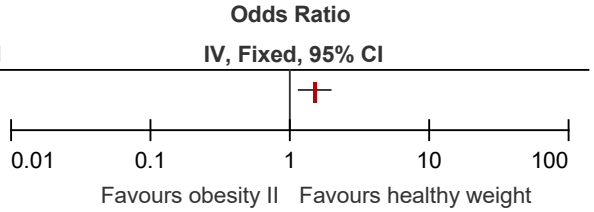
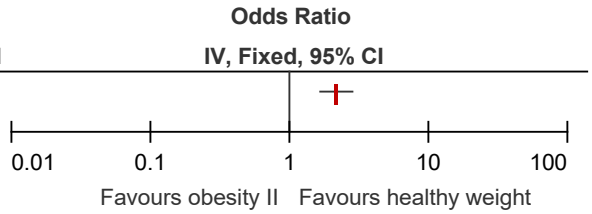


Figure 132: Surgical site infection (wound infection) at >3 months

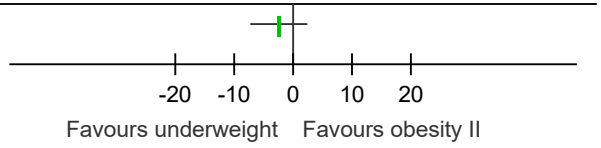
Study or Subgroup	log[Odds Ratio]	SE	Obesity II Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Wallace 2014	0.7793	0.136	2904	8876	2.18 [1.67, 2.85]



E.2.8 People who have obesity II compared to people who are underweight

Figure 133: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

Study or Subgroup	Obesity II Mean	SD	Total	Underweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Judge 2014	36.92	13.6357	150	39.34	10.349	24	-2.42 [-7.10, 2.26]



E.2.9 People who have obesity II compared to people who are overweight

Figure 134: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

	Obesity II			Overweight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	31.1	16.8011	426	32.2	18.6168	927	-1.10 [-3.10, 0.90]	

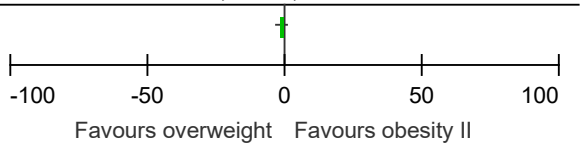


Figure 135: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

	Obesity II			Overweight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	9	8.7025	457	10.9	9.5617	978	-1.90 [-2.90, -0.90]	

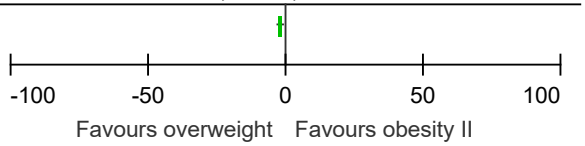
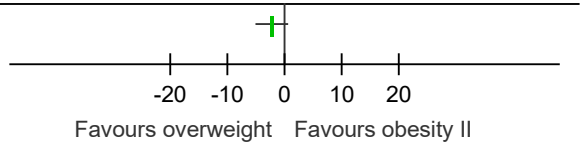


Figure 136: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

	Obesity II			Overweight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Judge 2014	36.92	13.6357	150	39.15	27.3495	1139	-2.23 [-4.93, 0.47]	



E.2.10 People who have obesity II compared to people who have obesity I

Figure 137: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

Study or Subgroup	Obesity II Mean	SD	Total	Obesity I Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Li 2017	31.1	16.8011	426	30.3	17.4743	817	0.80 [-1.20, 2.80]

Figure 138: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

Study or Subgroup	Obesity II Mean	SD	Total	Obesity I Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Li 2017	9	8.7025	457	9.6	9.3084	927	-0.60 [-1.60, 0.40]

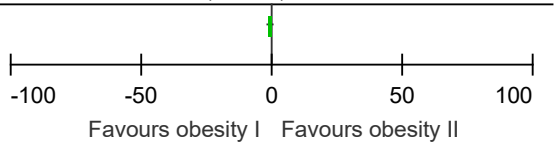
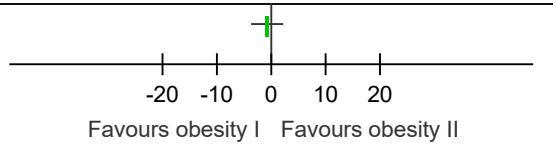


Figure 139: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

Study or Subgroup	Obesity II Mean	SD	Total	Obesity I Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Judge 2014	36.92	13.6357	150	37.66	19.7287	502	-0.74 [-3.52, 2.04]



E.2.11 People who have obesity III compared to people who are of healthy weight

Figure 140: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

	Obesity III			Healthy weight			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Li 2017	30.2	16.0883	251	31.7	16.6519	371	-1.50 [-4.11, 1.11]	

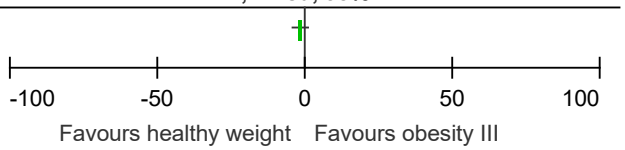


Figure 141: Total adverse events at up to 90 days

			Obesity III	Healthy weight	Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gurunathan 2018A	0.27	0.3655	55	191	1.31 [0.64, 2.68]	

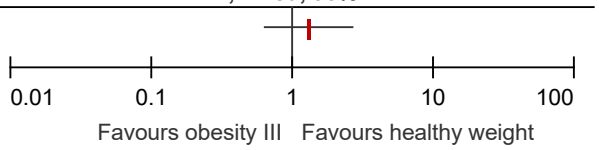


Figure 142: Surgical site infection (wound infection) at ≤3 months

			Obesity III	Healthy weight	Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Gurunathan 2018A	0.9042	0.5095	55	191	2.47 [0.91, 6.70]	

Figure 143: Venous thromboembolic events at ≤3 months

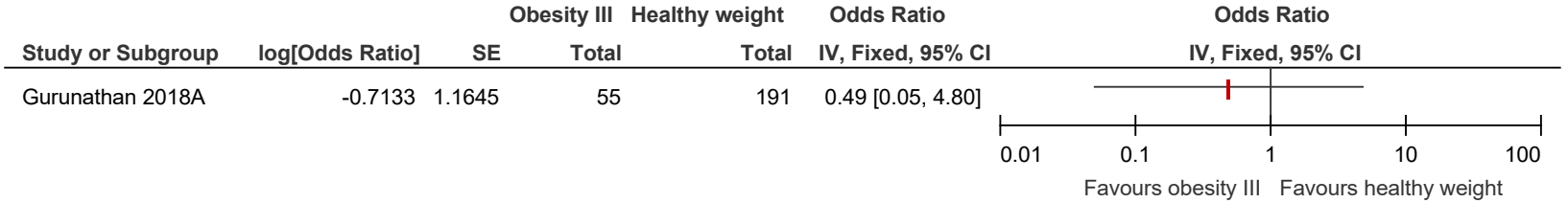


Figure 144: Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months

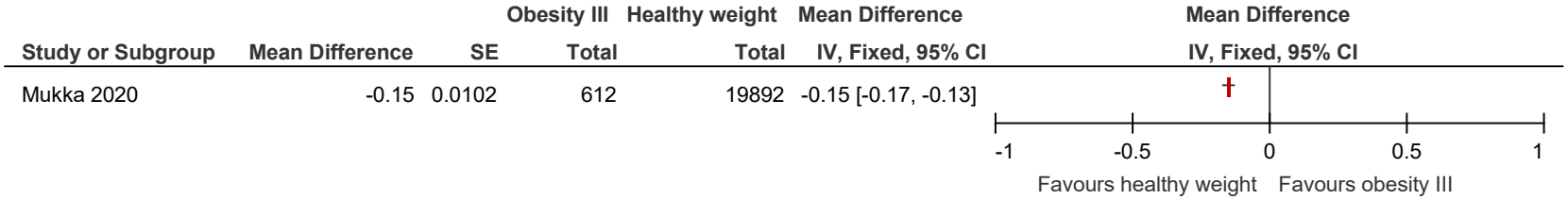


Figure 145: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

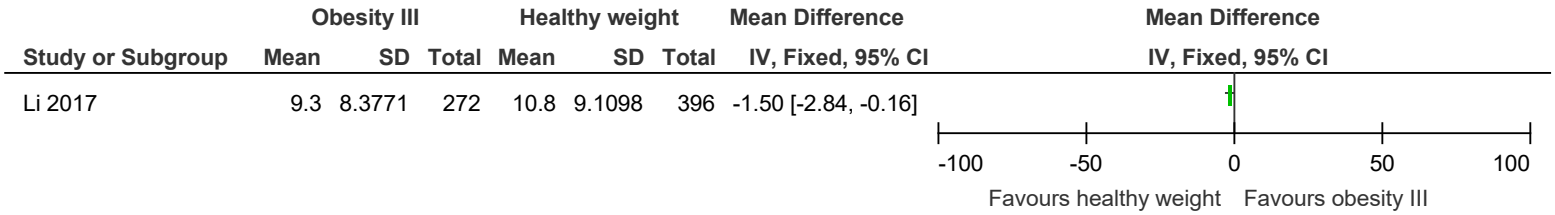
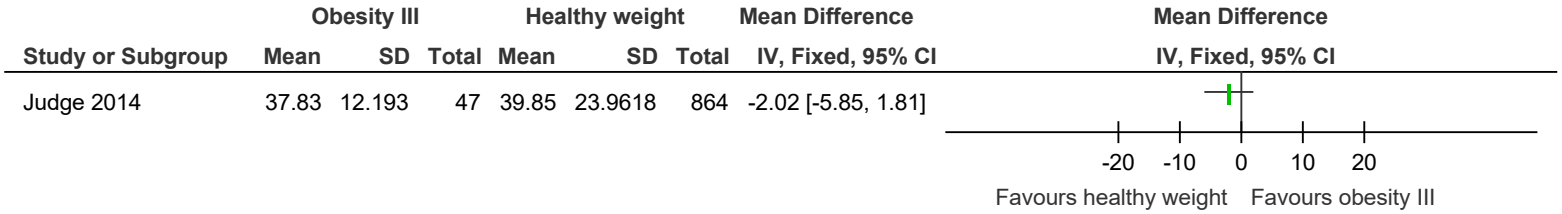
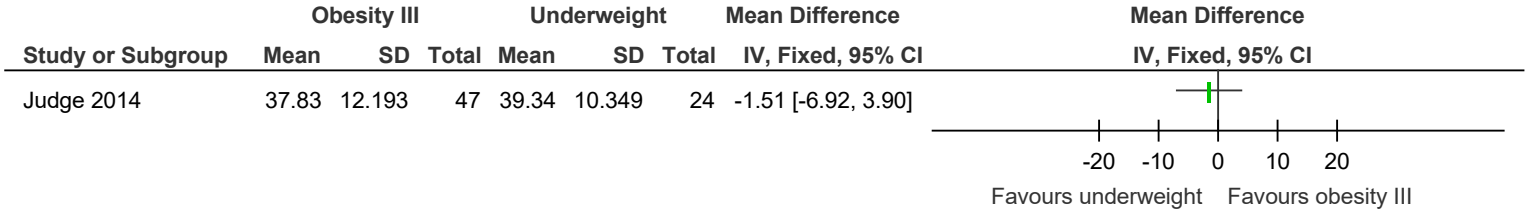


Figure 146: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year



E.2.12 People who have obesity III compared to people who are underweight

Figure 147: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year



E.2.13 People who have obesity III compared to people who are overweight

Figure 148: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

Study or Subgroup	Obesity III Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Li 2017	30.2	16.0883	251	32.2	18.6168	927	-2.00 [-4.32, 0.32]

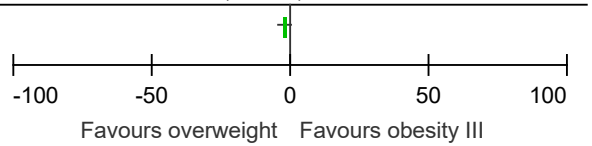


Figure 149: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

Study or Subgroup	Obesity III Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Li 2017	9.3	8.3771	272	10.9	9.5617	978	-1.60 [-2.76, -0.44]

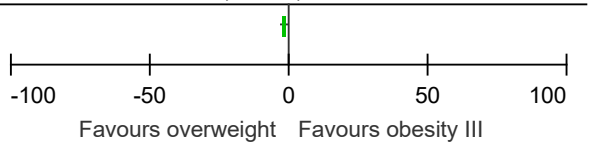


Figure 150: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year

Study or Subgroup	Obesity III Mean	SD	Total	Overweight Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Judge 2014	37.83	12.193	47	39.15	27.3495	1139	-1.32 [-5.15, 2.51]

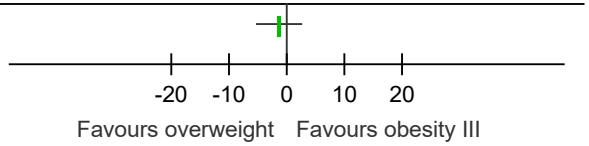
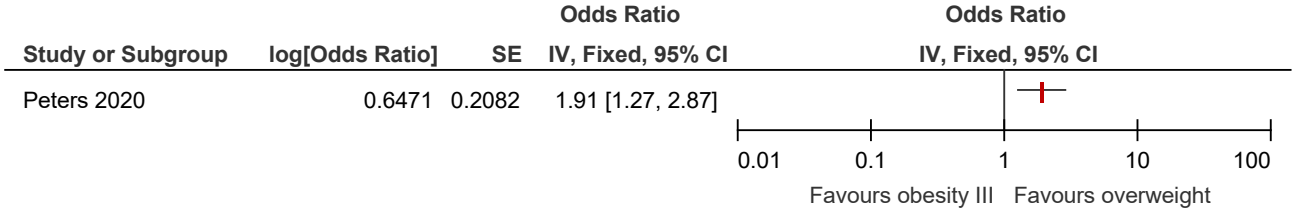


Figure 151: Reoperation or revision to the prosthesis at >3 months



E.2.14 People who have obesity III compared to people who have obesity I

Figure 152: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

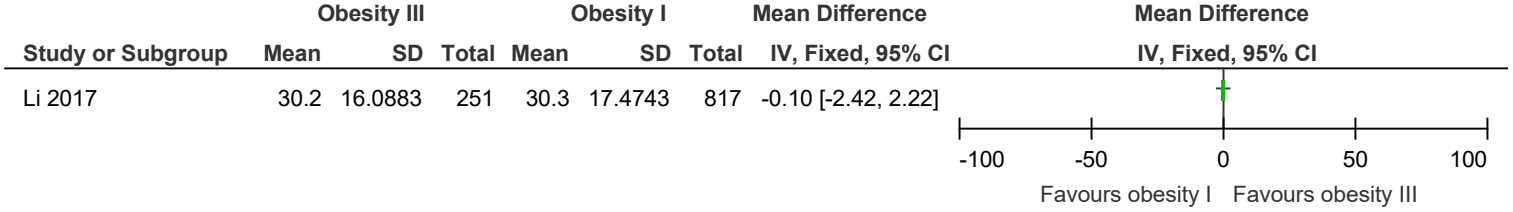


Figure 153: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

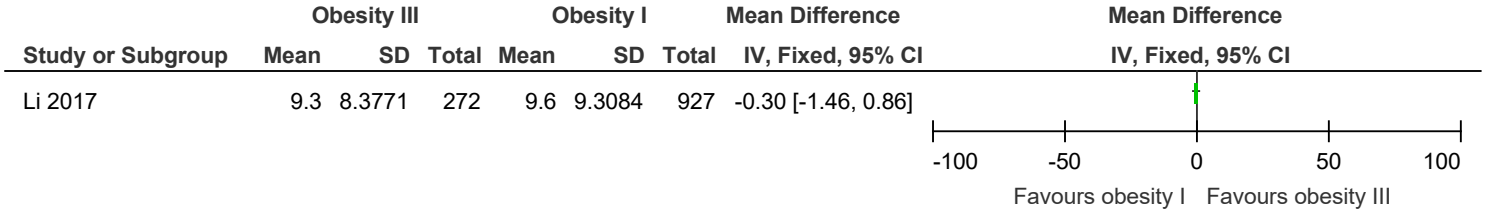
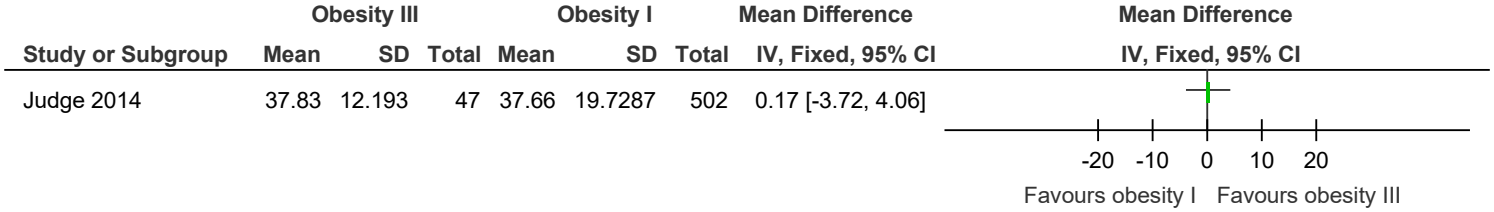


Figure 154: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year



E.2.15 People who have obesity III compared to people who have obesity II

Figure 155: Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months

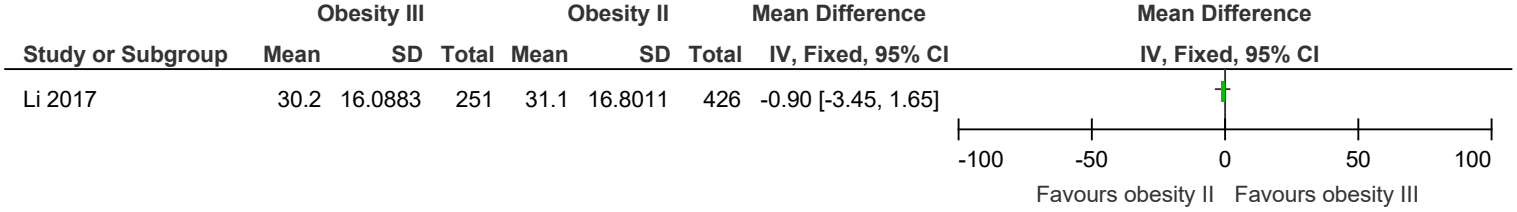


Figure 156: Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months

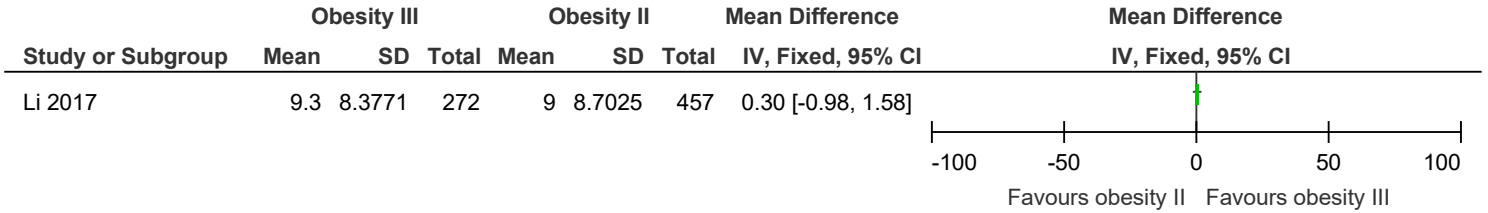
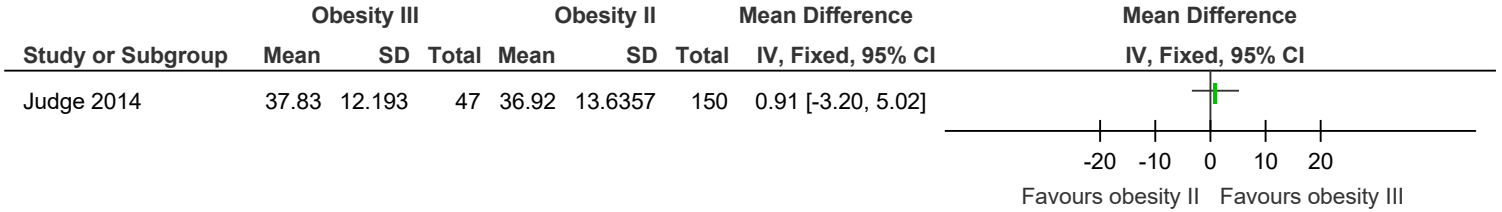


Figure 157: Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year



E.3 Mixed osteoarthritis (hip and knee)

E.3.1 People who are underweight compared to people who are of healthy weight

Figure 158: Mortality at ≤3 months

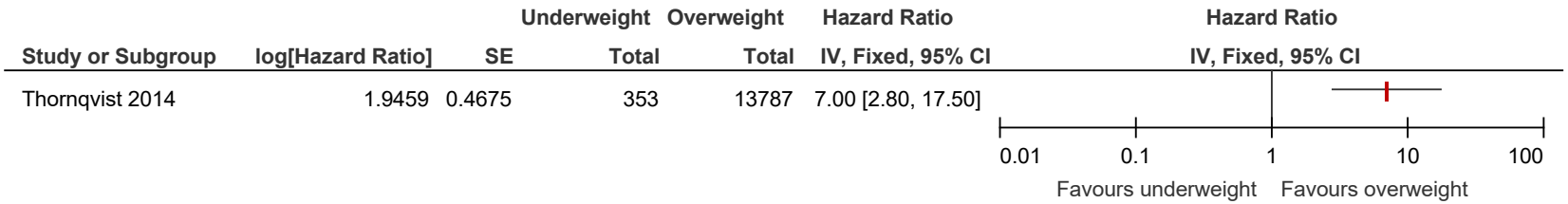
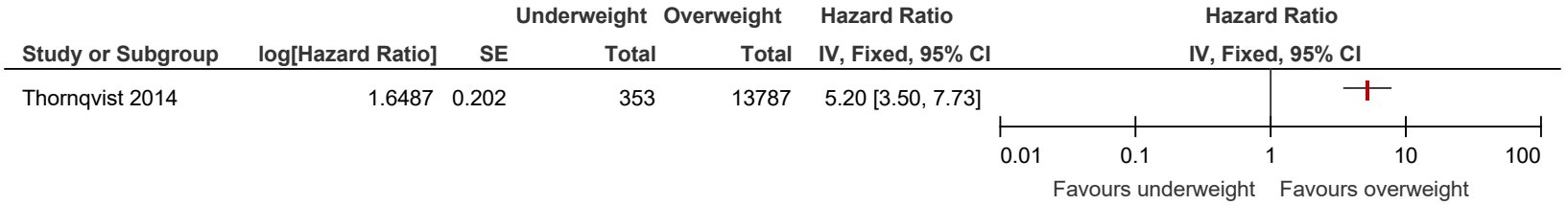


Figure 159: Mortality at >3 months



E.3.2 People who are overweight compared to people who are of healthy weight

Figure 160: Mortality at ≤3 months

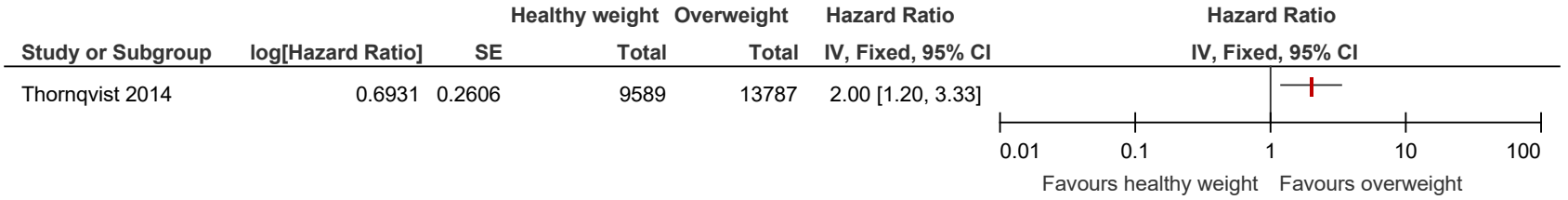


Figure 161: Mortality at >3 months

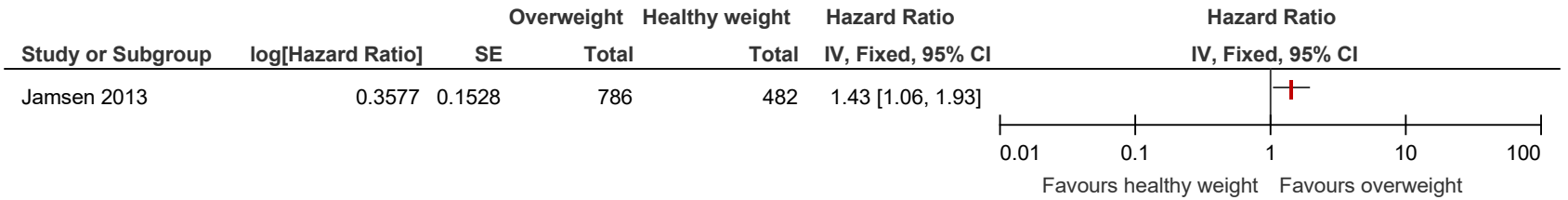


Figure 162: Mortality at >3 months

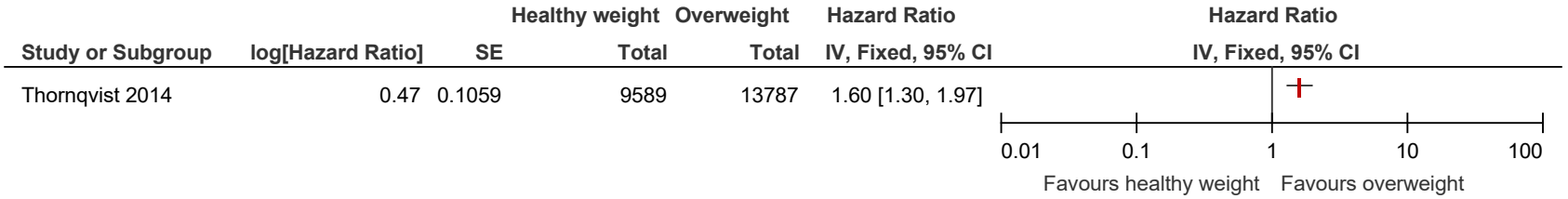
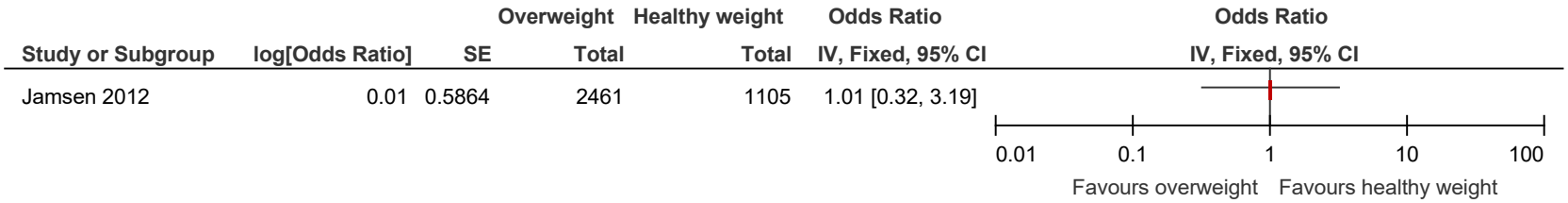
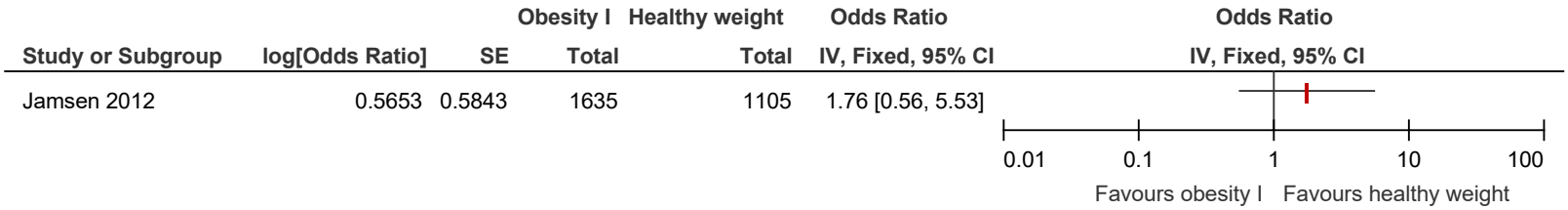


Figure 163: Surgical site infection (wound infection) at >3 months



E.3.3 People who have obesity I compared to people who are of healthy weight

Figure 164: Surgical site infection (wound infection) at >3 months



E.3.4 People who have obesity I compared to people who are overweight

Figure 165: Mortality at ≤3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity I Total	Overweight Total	Hazard Ratio IV, Fixed, 95% CI
Thornqvist 2014	0.4055	0.2779	7450	13787	1.50 [0.87, 2.59]

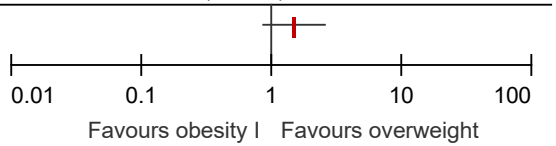


Figure 166: Mortality at >3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity I Total	Overweight Total	Hazard Ratio IV, Fixed, 95% CI
Jamsen 2013	-0.1165	0.1603	482	786	0.89 [0.65, 1.22]

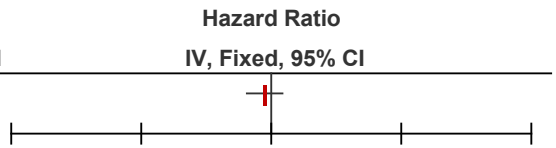
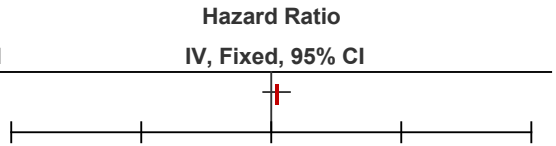


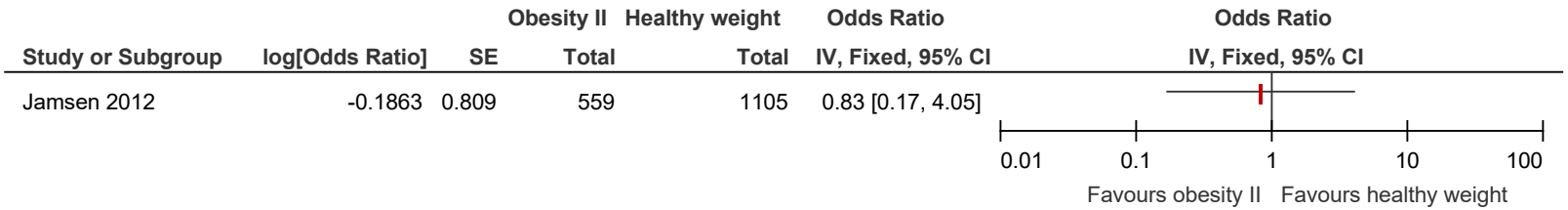
Figure 167: Mortality at >3 months

Study or Subgroup	log[Hazard Ratio]	SE	Obesity I Total	Overweight Total	Hazard Ratio IV, Fixed, 95% CI
Thornqvist 2014	0.0953	0.1197	7450	13787	1.10 [0.87, 1.39]



E.3.5 People who have obesity II compared to people who are of healthy weight

Figure 168: Surgical site infection (wound infection) at >3 months



E.3.6 People who have obesity II compared to people who are overweight

Figure 169: Mortality at ≤3 months

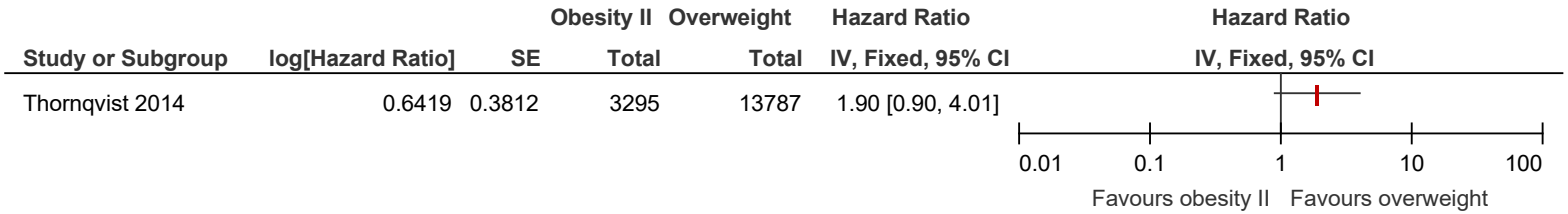
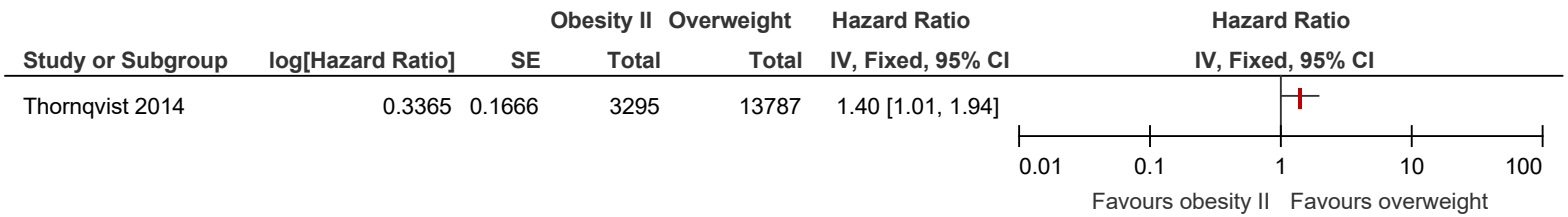


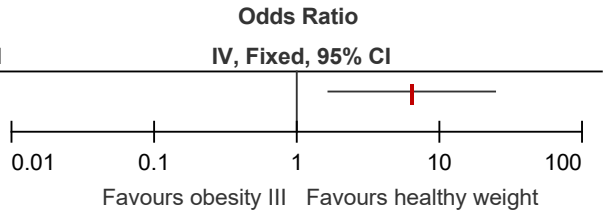
Figure 170: Mortality at >3 months



E.3.7 People who have obesity III compared to people who are of healthy weight

Figure 171: Surgical site infection (wound infection) at >3 months

Study or Subgroup	log[Odds Ratio]	SE	Obesity III Total	Healthy weight Total	Odds Ratio IV, Fixed, 95% CI
Jamsen 2012	1.8579	0.6863	193	1105	6.41 [1.67, 24.61]



Appendix F – GRADE tables

F.1 Knee osteoarthritis

Table 39: Clinical evidence profile: joint replacement for people who are underweight compared to people who are of healthy weight with knee osteoarthritis

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are underweight	joint replacement for people who are of healthy weight	Relative (95% CI)		
Mortality at ≤3 months (follow up: 90 days)											
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	1338	49860	**HR 1.64** (0.87 to 3.09)	⨁◯◯◯ VERY LOW	CRITICAL
Mortality at >3 months (follow up: 6 months)											
1	cohort study	serious [a]	not serious	not serious	not serious	none	138	5396	**OR 4.61** (1.64 to 12.96)	⨁⨁⨁◯ MODERATE	CRITICAL
Reoperation or revision to the prosthesis at >3 months (follow up: 11 years)											
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	1338	49860	**HR 0.88** (0.55 to 1.41)	⨁◯◯◯ VERY LOW	CRITICAL
Surgical site infection (wound infection) at >3 months (follow up: 6 months)											
1	cohort study	serious [a]	not serious	not serious	serious [b]	none	134	5359	**OR 0.97** (0.36 to 2.61)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because of population indirectness

c. Downgraded as 95% CI around the effect size crosses null line

Table 40: Clinical evidence profile: joint replacement for people who are overweight compared to people who are of healthy weight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow up: 90 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	168947	49860	**HR 0.75** (0.65 to 0.89)	-	⨁◯◯◯ VERY LOW	CRITICAL
Mortality at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	41155	14989	**OR 0.97** (0.53 to 1.78)	-	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [d]	not serious	none	203	120	-	MD **4.9 lower** (9.42 lower to 0.38 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [d]	serious [c]	none	203	120	-	MD **3.5 lower** (7.53 lower to 0.53 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	serious [c]	none	95	59	-	MD **0.8 lower** (2.76 lower to 1.16 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [e]	serious [c]	none	745	515	-	MD **1.4 lower** (3.24 lower to 0.44 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Reoperation or revision to the prosthesis at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	41155	14989	**OR 0.94** (0.79 to 1.12)	-	⨁◯◯◯ VERY LOW	CRITICAL
Total adverse events up to 90 days (follow up: 30 days)												
1	cohort study	serious [a]	not serious	not serious	serious [c]	none	481	141	**OR 1.11** (0.68 to 1.81)	-	⨁⨁◯◯ LOW	IMPORTANT
Surgical site infection (superficial infection) at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	41155	14989	**OR 0.85** (0.64 to 1.13)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Surgical site infection (periprosthetic joint infection) at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	41155	14989	**OR 0.90** (0.61 to 1.33)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events (deep vein thrombosis) at ≤3 months (follow up: 30 days)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	41155	14989	**OR 1.10** (0.90 to 1.34)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events (pulmonary embolism) at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	41155	14989	**OR 1.49** (1.12 to 1.98)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Mortality at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	serious [c]	none	12403	5396	**OR 1.12** (0.74 to 1.69)	-	⨁⨁◯◯ LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [e]	serious [c]	none	763	530	-	MD **0.8 lower** (1.94 lower to 0.34 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Reoperation or revision to the prosthesis at >3 months (follow up: 11 years)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	168947	49860	**HR 1.05** (0.97 to 1.14)	-	⨁◯◯◯ VERY LOW	CRITICAL
Venous thromboembolic events at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	12326	5359	**OR 1.59** (1.26 to 2.01)	-	⨁⨁⨁◯ MODERATE	IMPORTANT
Surgical site infection (wound infection) at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	12326	5359	**OR 1.23** (1.01 to 1.50)	-	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to population indirectness

c. Downgraded as 95% CI around the effect size crosses null line

d. Downgraded by 2 increments due to prognostic variable and outcome indirectness

e. Downgraded by 1 or 2 increments due to outcome indirectness

Table 41: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are of healthy weight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow up: 90 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	159056	49860	**HR 0.69** (0.58 to 0.82)	-	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	174	120	-	MD **8.8 lower** (13.51 lower to 4.09 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	174	120	-	MD **8.7 lower** (12.85 lower to 4.55 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	82	120	-	MD **5.7 lower** (7.61 lower to 3.79 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [d]	serious [e]	none	442	515	-	MD **1.4 lower** (3.37 lower to 0.57 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Total adverse events up to 90 days (follow up: 30 days)												
1	cohort study	serious [a]	not serious	not serious	serious [e]	none	508	141	**OR 0.85** (0.52 to 1.39)	-	⨁⨁◯◯ LOW	IMPORTANT
Mortality at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	serious [e]	none	9272	5396	**OR 1.21** (0.78 to 1.88)	-	⨁⨁◯◯ LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [d]	serious [e]	none	453	530	-	MD **0.7 lower** (1.97 lower to 0.57 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Reoperation or revision to the prosthesis at >3 months (follow up: 11 years)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [e]	none	159056	49860	**HR 1.08** (0.99 to 1.18)	-	⨁◯◯◯ VERY LOW	CRITICAL
Venous thromboembolic events at >3 months (follow up: 6 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	not serious	not serious	none	9224	5359	**OR 1.59** (1.26 to 2.01)	-	⨁⨁⨁◯ MODERATE	IMPORTANT
Surgical site infection (wound infection) at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	9224	5359	**OR 1.23** (1.01 to 1.50)	-	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **HR:** Hazard Ratio; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to population indirectness

c. Downgraded by 2 increments due to prognostic variable and outcome indirectness

d. Downgraded by 1 or 2 increments due to outcome indirectness

e. Downgraded as 95% CI around the effect size crosses null line

Table 42: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are overweight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	174	203	-	MD **3.9 lower** (8.05 lower to 0.25 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	not serious	none	174	203	-	MD **5.2 lower** (8.86 lower to 1.54 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	not serious	none	90	95	-	MD **4.9 lower** (6.51 lower to 3.29 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	442	745	-	MD **0** (1.84 lower to 1.84 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	453	763	-	MD **0.1 higher** (1.04 lower to 1.24 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to outcome indirectness

c. Downgraded as 95% CI around the effect size crosses null line

d. Downgraded by 1 or 2 increments due to prognostic variable indirectness

Table 43: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are of healthy weight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow up: 90 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	80166	49860	**HR 0.88** (0.72 to 1.08)	-	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [d]	not serious	none	79	120	-	MD **12.5 lower** (18.11 lower to 6.89 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [d]	not serious	none	79	120	-	MD **10.1 lower** (15.08 lower to 5.12 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [f]	not serious	none	82	59	-	MD **8.3 lower** (10.32 lower to 6.28 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [f]	serious [c]	none	194	515	-	MD **2.3 lower** (4.73 lower to 0.13 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Total adverse events up to 90 days (follow up: 30 days)												
1	cohort study	serious [a]	not serious	not serious	serious [c]	none	320	141	**OR 0.69** (0.42 to 1.13)	-	⨁⨁◯◯ LOW	IMPORTANT
Mortality at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	serious [d]	serious [c]	none	5276	5396	**OR 0.95** (0.50 to 1.81)	-	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [f]	not serious	none	204	530	-	MD **3.2 lower** (4.77 lower to 1.63 lower)	⨁⨁◯◯ LOW	CRITICAL
Reoperation or revision to the prosthesis at >3 months (follow up: 11 years)												
1	cohort study	serious [a]	not serious	serious [b]	not serious	none	80166	49860	**HR 1.21** (1.10 to 1.33)	-	⨁⨁◯◯ LOW	CRITICAL
Venous thromboembolic events at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	5260	5359	**OR 1.93** (1.45 to 2.57)	-	⨁⨁◯◯ LOW	IMPORTANT
Surgical site infection (wound infection) at >3 months (follow up: 6 months)												
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	5260	5359	**OR 1.39** (1.11 to 1.74)	-	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **HR:** Hazard Ratio; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to population indirectness

c. Downgraded as 95% CI around the effect size crosses null line

d. Downgraded by 1 or 2 increments due to prognostic variable indirectness

e. Downgraded by 2 increments due to prognostic variable and outcome indirectness

f. Downgraded by 1 or 2 increments due to outcome indirectness

Table 44: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are overweight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	not serious	none	79	203	-	MD **7.6 lower** (12.75 lower to 2.45 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	not serious	none	79	203	-	MD **6.6 lower** (11.17 lower to 2.03 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [c]	not serious	none	82	90	-	MD **7.5 lower** (9.24 lower to 5.76 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	serious [c]	serious [d]	none	194	745	-	MD **0.9 lower** (3.22 lower to 1.42 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [c]	not serious	none	204	763	-	MD **2.4 lower** (3.87 lower to 0.93 lower)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 2 increments due to prognostic variable and outcome indirectness

c. Downgraded by 1 or 2 increments due to outcome indirectness

d. Downgraded as 95% CI around the effect size crosses null line

Table 45: Clinical evidence profile: joint replacement for people who have obesity II compared to people who have obesity I with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	79	174	-	MD **3.7 lower** (9.01 lower to 1.61 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	79	174	-	MD **1.4 lower** (6.08 lower to 3.28 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	82	90	-	MD **2.6 lower** (4.28 lower to 0.92 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [d]	serious [c]	none	194	442	-	MD **0.9 lower** (3.33 lower to 1.53 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	204	453	-	MD **2.5 lower** (4.07 lower to 0.93 lower)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 2 increments due to prognostic variable and outcome indirectness

c. Downgraded as 95% CI around the effect size crosses null line

d. Downgraded by 1 or 2 increments due to outcome indirectness

Table 46: Clinical evidence profile: joint replacement for people who have obesity III compared to people who are of healthy weight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow up: 90 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	34343	49860	**HR 1.17** (0.90 to 1.52)	-	⨁◯◯◯ VERY LOW	CRITICAL
Mortality at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	23081	14989	**OR 1.25** (0.67 to 2.33)	-	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [d]	not serious	none	57	120	-	MD **14.1 lower** (20.39 lower to 7.81 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [d]	not serious	none	57	120	-	MD **9.9 lower** (15.48 lower to 4.32 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [e]	not serious	none	28	59	-	MD **10.4 lower** (13.1 lower to 7.7 lower)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [e]	serious [c]	none	86	515	-	MD 0.9 **lower** (4.08 lower to 2.28 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Reoperation or revision to the prosthesis at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	23081	14989	**OR 1.49** (1.24 to 1.79)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Total adverse events up to 90 days (follow up: 30 days)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	213	141	**OR 1.02** (1.00 to 1.04)	-	⨁⨁⨁◯ MODERATE	IMPORTANT
Surgical site infection (superficial infection) at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	23081	14989	**OR 2.02** (1.53 to 2.67)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Surgical site infection (periprosthetic joint infection) at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	23081	14989	**OR 2.14** (1.48 to 3.09)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events (deep vein thrombosis) at ≤3 months (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	23081	14989	**OR 0.80** (0.64 to 1.00)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events (pulmonary embolism) at ≤3 months (follow up: 30 days)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	23081	14989	**OR 1.92** (1.42 to 2.60)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Health-related quality of life (EQ-5D, -0.11-1, higher is better, change score) at >3 months (follow up: 7 months; assessed with: EQ-5D; Scale from: -0.11 to 1)												
1	cohort study	very serious [a]	not serious	serious [f]	serious [c]	none	1018	1292	-	MD **0.01 higher** (0.01 lower to 0.04 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [e]	not serious	none	90	530	-	MD **4.4 lower** (6.48 lower to 2.32 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (OKS, 0-48, higher is better, change score) at 1 year (follow up: 7 months; assessed with: OKS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	serious [f]	serious [c]	none	1018	1292	-	MD **0.5 higher** (0.28 lower to 1.28 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Reoperation or revision to the prosthesis at >3 months (follow up: 11 years)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	34343	49860	**HR 1.13** (1.02 to 1.25)	-	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to population indirectness

c. Downgraded as 95% CI around the effect size crosses null line

d. Downgraded by 2 increments due to prognostic variable and outcome indirectness

e. Downgraded by 1 or 2 increments due to outcome indirectness

f. Downgraded by 1 or 2 increments due to prognostic variable indirectness

Table 47: Clinical evidence profile: joint replacement for people who have obesity III compared to people who are overweight with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	not serious	none	57	203	-	MD **9.2 lower** (15.09 lower to 3.31 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	not serious	none	57	203	-	MD **6.4 lower** (11.63 lower to 1.17 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	not serious	none	28	95	-	MD **9.6 lower** (12.1 lower to 7.1 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	86	745	-	MD **0.5 higher** (2.6 lower to 3.6 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	serious [b]	not serious	none	90	763	-	MD **3.6 lower** (5.6 lower to 1.6 lower)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to outcome indirectness

c. Downgraded as 95% CI around the effect size crosses null line

Table 48: Clinical evidence profile: joint replacement for people who have obesity III compared to people who have obesity I with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	57	174	-	MD **5.3 lower** (11.33 lower to 0.73 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	57	174	-	MD **1.2 lower** (6.52 lower to 4.12 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)

1	cohort study	serious [a]	not serious	serious [b]	not serious	none	28	90	-	MD **4.7 lower** (7.15 lower to 2.25 lower)	⨁⨁◯◯ LOW	CRITICAL

Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)

1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	86	442	-	MD **0.5 higher** (2.68 lower to 3.68 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (Scale from: 0 to 100)

1	cohort study	serious [a]	not serious	serious [b]	not serious	none	90	453	-	MD **3.7 lower** (5.78 lower to 1.62 lower)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to outcome indirectness

c. Downgraded as 95% CI around the effect size crosses null line

Table 49: Clinical evidence profile: joint replacement for people who have obesity III compared to people who have obesity II with knee osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who have obesity II	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (WOMAC pain, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	57	79	-	MD **1.6 lower** (8.36 lower to 5.16 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 3 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [b]	serious [c]	none	57	79	-	MD **0.2 higher** (5.79 lower to 6.19 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (WOMAC function, 0-100, lower is better, change score) at 6 months (follow up: 6 months; assessed with: WOMAC function; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	28	82	-	MD **2.1 lower** (4.64 lower to 0.44 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	86	194	-	MD **1.4 higher** (2.08 lower to 4.88 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	serious [b]	serious [c]	none	90	204	-	MD **1.2 lower** (3.48 lower to 1.08 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to outcome indirectness

c. Downgraded as 95% CI around the effect size crosses null line

F.2 Hip osteoarthritis

Table 50: Clinical evidence profile: joint replacement for people who are underweight compared to people who are of healthy weight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are underweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Mortality at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	462	9006	**OR 2.17** (1.67 to 2.82)	-	⨁⨁⨁◯ MODERATE	CRITICAL
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months (follow up: 1 years; assessed with: EQ-5D; Scale from: -0.11 to 1)												
1	cohort study	very serious [a]	not serious	not serious	not serious	none	395	19892	-	MD **0.04 lower** (0.07 lower to 0.01 lower)	⨁⨁◯◯ LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	serious [a]	not serious	not serious	serious [b]	none	24	864	-	MD **0.51 lower** (4.95 lower to 3.93 higher)	⨁⨁◯◯ LOW	CRITICAL
Venous thromboembolic events at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	serious [b]	none	443	8876	**OR 0.75** (0.35 to 1.61)	-	⨁⨁◯◯ LOW	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are underweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Surgical site infection (wound infection) at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	serious [b]	none	443	8876	**OR 1.03** (0.48 to 2.21)	-	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

Table 51: Clinical evidence profile: joint replacement for people who are underweight compared to people who are overweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are underweight	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Reoperation or revision to the prosthesis at >3 months (follow up: 3 years)												
1	cohort study	serious [a]	not serious	not serious	serious [b]	none	649	46507	**OR 1.73** (0.94 to 3.18)	-	⨁⨁◯◯ LOW	CRITICAL

Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are underweight	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	24	1139	-	MD **0.19 higher** (4.24 lower to 4.62 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

Table 52: Clinical evidence profile: joint replacement for people who are overweight compared to people who are of healthy weight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain,; Scale from: 0 to 100)												
1	cohort study	very serious [a]	not serious	very serious [d]	not serious	none	927	371	-	MD **0.5 higher** (1.58 lower to 2.58 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Total adverse events at up to 90 days (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	378	191	**OR 0.62** (0.43 to 0.89)	**-**	⨁◯◯◯ VERY LOW	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Surgical site infection (wound infection) at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	378	191	**OR 1.22** (0.62 to 2.40)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	378	191	**OR 0.38** (0.11 to 1.31)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Mortality at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	12619	9006	**OR 0.61** (0.46 to 0.81)	-	⨁⨁⨁◯ MODERATE	CRITICAL
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months (follow up: 1 years; assessed with: EQ-5D; Scale from: -0.11 to 1)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	28221	19892	-	MD **0.02 lower** (0.02 lower to 0.01 lower)	⨁⨁⨁◯ MODERATE	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	serious [c]	none	978	396	-	MD **0.1 higher** (0.98 lower to 1.18 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [c]	none	1139	864	-	MD **0.7 lower** (2.95 lower to 1.55 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Venous thromboembolic events at >3 months (OR) (follow up: 6 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	not serious	not serious	none	12523	8876	**OR 1.39** (1.16 to 1.67)	-	⨁⨁⨁◯ MODERATE	IMPORTANT

Reoperation or revision to the prosthesis at >3 months (follow up: 3 years)

1	cohort study	serious [a]	not serious	not serious	not serious	none	46507	33998	**OR 0.76** (0.65 to 0.89)		⨁⨁⨁◯ MODERATE	CRITICAL

Surgical site infection (wound infection) at >3 months (OR) (follow up: 6 months)

1	cohort study	serious [a]	not serious	not serious	not serious	none	12523	8876	**OR 1.34** (1.09 to 1.65)	-	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Not clear if patients have osteoarthritis

c. Downgraded as 95% CI around the effect size crosses null line

d. Downgraded by 2 increments for population and outcome indirectness

Table 53: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are of healthy weight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	serious [b]	none	817	371	-	MD **1.4 lower** (3.48 lower to 0.68 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Total adverse events at up to 90 days (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	serious [b]	none	219	191	**OR 0.70** (0.46 to 1.07)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Surgical site infection (wound infection) at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	very serious [c,d]	serious [b]	none	219	191	**OR 1.45** (0.69 to 3.05)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	serious [b]	none	219	191	**OR 1.08** (0.36 to 3.24)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Mortality at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	6809	9006	**OR 0.62** (0.43 to 0.89)	-	⨁⨁⨁◯ MODERATE	CRITICAL
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months (follow up: 1 years; assessed with: EQ-5D; Scale from: -0.11 to 1)												
1	cohort study	very serious [a]	not serious	not serious	not serious	none	12036	19892	-	MD **0.06 lower** (0.07 lower to 0.05 lower)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	not serious	none	927	396	-	MD **1.2 lower** (2.28 lower to 0.12 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	502	864	-	MD **2.19 lower** (4.54 lower to 0.16 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Venous thromboembolic events at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	6764	8876	**OR 1.64** (1.34 to 2.01)	-	⨁⨁⨁◯ MODERATE	IMPORTANT
Surgical site infection (wound infection) at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	6764	8876	**OR 1.52** (1.21 to 1.91)	-	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Not clear if population have osteoarthritis

d. May be non-site infection

e. Downgraded by 2 increments for population and outcome indirectness

Table 54: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are underweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are underweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	502	24	-	MD **1.68 lower** (6.17 lower to 2.81 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

Table 55: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are overweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	817	927	-	MD **1.9 lower** (3.59 lower to 0.21 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	927	978	-	MD **1.3 lower** (2.15 lower to 0.45 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	502	1139	-	MD **1.49 lower** (3.84 lower to 0.86 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Downgraded by 2 increments for population and outcome indirectness

Table 56: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are of healthy weight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	serious [b]	none	426	371	-	MD **0.6 lower** (2.93 lower to 1.73 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Total adverse events at up to 90 days (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	not serious	none	110	191	**OR 0.60** (0.36 to 1.00)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Surgical site infection (wound infection) at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	serious [b]	none	110	191	**OR 1.65** (0.69 to 3.95)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	serious [b]	none	110	191	**OR 0.53** (0.10 to 2.81)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Mortality at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	serious [d]	serious [b]	none	2921	9006	**OR 0.65** (0.36 to 1.17)	-	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months (follow up: 1 years; assessed with: EQ-5D; Scale from: -0.11 to 1)												
1	cohort study	very serious [a]	not serious	not serious	not serious	none	2899	19892	-	MD **0.11 lower** (0.13 lower to 0.09 lower)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	not serious	none	457	396	-	MD **1.8 lower** (3 lower to 0.6 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	not serious	none	150	864	-	MD **2.93 lower** (5.63 lower to 0.23 lower)	⨁⨁◯◯ LOW	CRITICAL
Venous thromboembolic events at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	2904	8876	**OR 1.51** (1.16 to 1.97)	-	⨁⨁◯◯ LOW	IMPORTANT
Surgical site infection (wound infection) at >3 months (OR) (follow up: 6 months)												
1	cohort study	serious [a]	not serious	serious [d]	not serious	none	2904	8876	**OR 2.18** (1.67 to 2.85)	-	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Not clear if population is osteoarthritis

d. Prognostic variable indirectness

e. Downgraded by 2 increments for population and outcome indirectness

Table 57: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are underweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are underweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	150	24	-	MD **2.42 lower** (7.1 lower to 2.26 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

Table 58: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are overweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	426	927	-	MD **1.1 lower** (3.1 lower to 0.9 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	457	978	-	MD **1.9 lower** (2.9 lower to 0.9 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	150	1139	-	MD **2.23 lower** (4.93 lower to 0.47 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Downgraded by 2 increments for population and outcome indirectness

Table 59: Clinical evidence profile: joint replacement for people who have obesity II compared to people who have obesity I with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	426	817	-	MD **0.8 higher** (1.2 lower to 2.8 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	457	927	-	MD **0.6 lower** (1.6 lower to 0.4 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	150	502	-	MD **0.74 lower** (3.52 lower to 2.04 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Downgraded by 2 increments for population and outcome indirectness

Table 60: Clinical evidence profile: joint replacement for people who have obesity III compared to people who are of healthy weight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	serious [b]	none	251	371	-	MD **1.5 lower** (4.11 lower to 1.11 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Total adverse events at up to 90 days (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	serious [b]	none	-/55	-/191	**OR 1.31** (0.64 to 2.68)	**-**	⨁◯◯◯ VERY LOW	IMPORTANT
Surgical site infection (wound infection) at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	very serious [c,d]	serious [b]	none	55	191	**OR 2.47** (0.91 to 6.70)	**-**	⨁◯◯◯ VERY LOW	IMPORTANT
Venous thromboembolic events at ≤3 months (OR) (follow up: 30 days)												
1	cohort study	very serious [a]	not serious	serious [c]	serious [b]	none	55	191	**OR 0.49** (0.05 to 4.80)	**-**	⨁◯◯◯ VERY LOW	IMPORTANT
Health-related quality of life (EQ-5D, -0.11-1, higher is better, mean difference) at >3 months (follow up: 1 years; assessed with: EQ-5D; Scale from: -0.11 to 1)												
1	cohort study	very serious [a]	not serious	not serious	not serious	none	612	19892	-	MD **0.15 lower** (0.17 lower to 0.13 lower)	⨁⨁◯◯ LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [e]	not serious	none	272	396	-	MD **1.5 lower** (2.84 lower to 0.16 lower)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are of healthy weight	Relative (95% CI)	Absolute (95% CI)		
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	47	864	-	MD **2.02 lower** (5.85 lower to 1.81 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Not clear whether population have osteoarthritis

d. May be non-site infection

e. Downgraded by 2 increments for population and outcome indirectness

Table 61: Clinical evidence profile: joint replacement for people who have obesity III compared to people who are underweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are underweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are underweight	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	47	24	-	MD **1.51 lower** (6.92 lower to 3.9 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

Table 62: Clinical evidence profile: joint replacement for people who have obesity III compared to people who are overweight with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	251	927	-	MD **2 lower** (4.32 lower to 0.32 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	not serious	none	272	978	-	MD **1.6 lower** (2.76 lower to 0.44 lower)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are overweight	Relative (95% CI)	Absolute (95% CI)		
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	47	1139	-	MD **1.32 lower** (5.15 lower to 2.51 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Reoperation or revision to the prosthesis at >3 months (follow up: 3 years)												
1	cohort study	serious [a]	not serious	not serious	not serious	none	1336	46507	**OR 1.91** (1.27 to 2.87)	-	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Downgraded by 2 increments for population and outcome indirectness

Table 63: Clinical evidence profile: joint replacement for people who have obesity III compared to people who have obesity I with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who have obesity I	Relative (95% CI)	Absolute (95% CI)		
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	251	817	-	MD **0.1 lower** (2.42 lower to 2.22 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component,; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	272	927	-	MD **0.3 lower** (1.46 lower to 0.86 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	47	502	-	MD **0.17 higher** (3.72 lower to 4.06 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Downgraded by 2 increments for population and outcome indirectness

Table 64: Clinical evidence profile: joint replacement for people who have obesity III compared to people who have obesity II with hip osteoarthritis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who have obesity II	Relative (95% CI)	Absolute (95% CI)		
Post-operative Patient Reported Outcome Measures (KOOS pain, 0-100, higher is better, change score) at 6 months (follow up: 6 months; assessed with: KOOS pain; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	251	426	-	MD **0.9 lower** (3.45 lower to 1.65 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Health-related quality of life (SF-36 physical component, 0-100, higher is better, change score) at >3 months (follow up: 6 months; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	cohort study	serious [a]	not serious	very serious [c]	serious [b]	none	272	457	-	MD **0.3 higher** (0.98 lower to 1.58 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Post-operative patient-reported outcome measures (OHS, 0-48, higher is better, final value) at 1 year (follow up: 1 years; assessed with: OHS; Scale from: 0 to 48)												
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	47	150	-	MD **0.91 higher** (3.2 lower to 5.02 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

c. Downgraded by 2 increments for population and outcome indirectness

F.3 Mixed osteoarthritis (hip and knee)

Table 65: Clinical evidence profile: joint replacement for people who are underweight compared to people who are overweight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are underweight	joint replacement for people who are overweight	Relative (95% CI)		
Mortality at ≤3 months (follow up: 30 days)											
1	cohort study	very serious [a]	not serious	not serious	not serious	none	353	13787	**HR 7.0** (2.8 to 17.5)	⨁⨁◯◯ LOW	CRITICAL
Mortality at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	not serious	not serious	none	353	13787	**HR 5.20** (3.50 to 7.73)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **HR:** Hazard Ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 66: Clinical evidence profile: joint replacement for people who are overweight compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who are overweight	joint replacement for people who are of healthy weight	Relative (95% CI)		
Mortality at ≤3 months (follow up: 30 days)											
1	cohort study	very serious [a]	not serious	not serious	not serious	none	9589	13787	**HR 2.00** (1.20 to 3.33)	⨁⨁◯◯ LOW	CRITICAL
Mortality at >3 months (follow up: 5 years)											
1	cohort study	very serious [a]	not serious	serious [b]	not serious	none	786	482	**HR 1.43** (1.06 to 1.93)	⨁◯◯◯ VERY LOW	CRITICAL
Mortality at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	not serious	not serious	none	9589	13787	**HR 1.60** (1.30 to 1.97)	⨁⨁◯◯ LOW	CRITICAL
Surgical site infection (wound infection) at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	very serious [c]	serious [d]	none	2461	1105	**OR 1.01** (0.32 to 3.19)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **HR:** Hazard Ratio; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to prognostic variable indirectness

c. Downgraded by 2 increments due to population and prognostic variable indirectness

d. Downgraded as 95% CI around the effect size crosses null line

Table 67: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are of healthy weight	Relative (95% CI)		
Surgical site infection (wound infection) at >3 months (follow up: 5 years)											
1	cohort study	very serious [a]	not serious	very serious [b]	serious [c]	none	1635	1105	**OR 1.76** (0.56 to 5.53)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 2 increments due to population and prognostic variable indirectness

c. Downgraded as 95% CI around the effect size crosses null line

Table 68: Clinical evidence profile: joint replacement for people who have obesity I compared to people who are overweight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are overweight	Relative (95% CI)		
Mortality at ≤3 months (follow up: 30 days)											

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity I	joint replacement for people who are overweight	Relative (95% CI)		
1	cohort study	very serious [a]	not serious	serious [b]	serious [c]	none	7450	13787	**HR 1.50** (0.87 to 2.59)	⨁◯◯◯ VERY LOW	CRITICAL
Mortality at >3 months (follow up: 5 years)											
1	cohort study	very serious [a]	not serious	not serious	serious [c]	none	482	786	**HR 0.89** (0.65 to 1.22)	⨁◯◯◯ VERY LOW	CRITICAL
Mortality at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	not serious	serious [c]	none	7450	13787	**HR 1.10** (0.87 to 1.39)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **HR:** Hazard Ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments due to prognostic variable indirectness

c. Downgraded as 95% CI around the effect size crosses null line

Table 69: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are of healthy weight	Relative (95% CI)		
Surgical site infection (wound infection) at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	very serious [b]	serious [c]	none	559	1105	**OR 0.83** (0.17 to 4.05)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 2 increments due to population and prognostic variable indirectness

c. Downgraded as 95% CI around the effect size crosses null line

Table 70: Clinical evidence profile: joint replacement for people who have obesity II compared to people who are overweight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are overweight	Relative (95% CI)		
Mortality at ≤3 months (follow up: 30 days)											
1	cohort study	very serious [a]	not serious	not serious	serious [b]	none	3295	13787	**HR 1.90** (0.90 to 4.01)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity II	joint replacement for people who are overweight	Relative (95% CI)		
Mortality at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	not serious	not serious	none	3295	13787	**HR 1.40** (1.01 to 1.94)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **HR:** Hazard Ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded as 95% CI around the effect size crosses null line

Table 71: Clinical evidence profile: joint replacement for people who have obesity III compared to people who are of healthy weight with mixed osteoarthritis (hip and knee osteoarthritis)

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	joint replacement for people who have obesity III	joint replacement for people who are of healthy weight	Relative (95% CI)		
Surgical site infection (wound infection) at >3 months (follow up: 1 years)											
1	cohort study	very serious [a]	not serious	very serious [b]	not serious	none	193	1105	**OR 1.40** (1.01 to 1.94)	⨁◯◯◯ VERY LOW	IMPORTANT

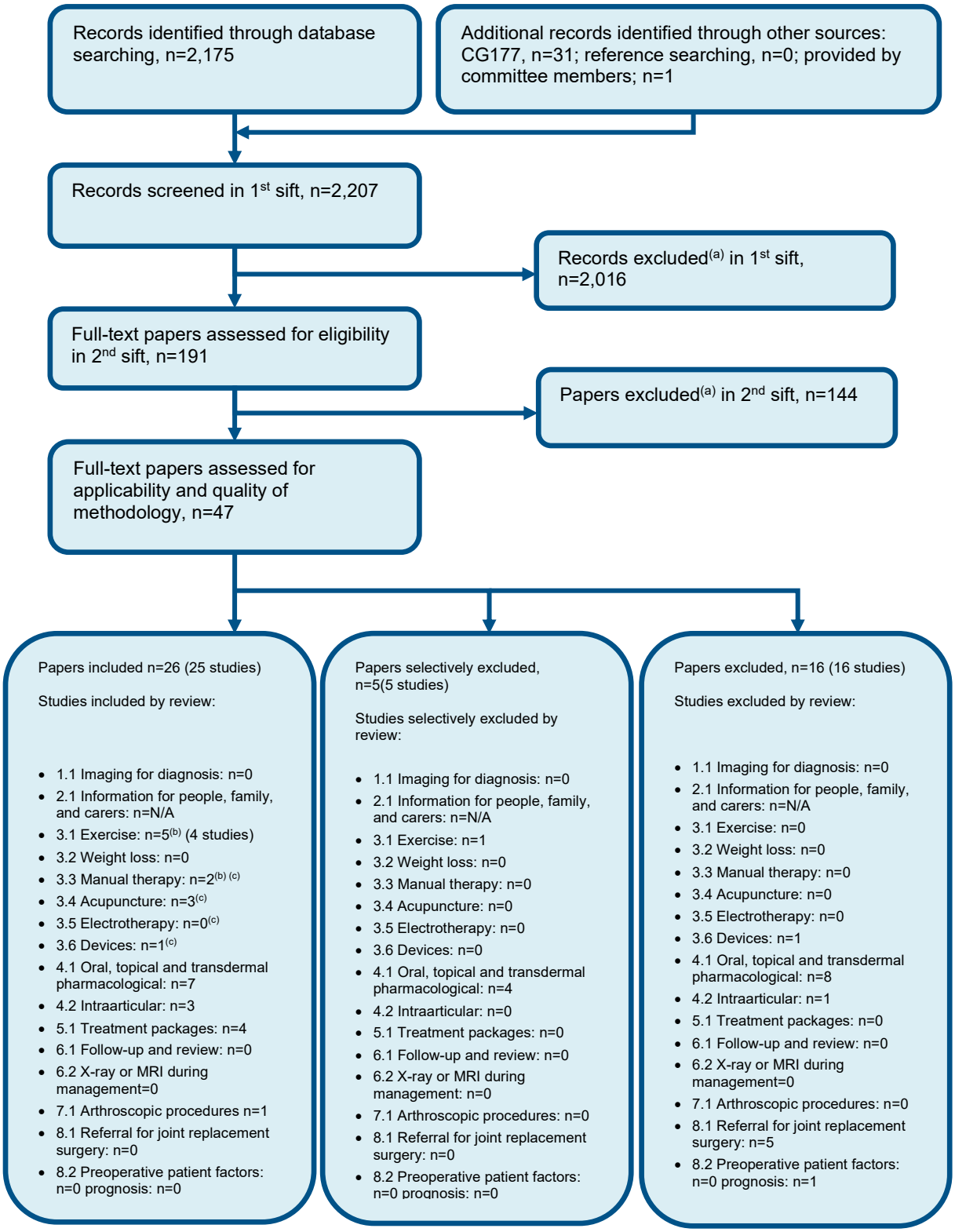
CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 2 increments due to population and prognostic variable indirectness

Appendix G – Economic evidence study selection



(a) Non-relevant population, intervention, comparison, design or setting; non-English language.
(b) Two articles identified were applicable to Q3.1 and Q3.3, for the purposes of this diagram they have been included under Q3.1 only.
(c) One article identified was applicable to Q3.3, Q3.4, Q3.5 and Q3.6, for the purposes of this diagram it has been included under Q3.3 only.

Appendix H – Economic evidence tables

There were no health economic studies found in the review.

Appendix I – Health economic model

No original economic modelling was undertaken.

Appendix J – Excluded studies

Clinical studies

Table 72: Studies excluded from the clinical review

Study	Exclusion reason
Agarwal 2021[1]	Wrong comparison (different BMI categories were used to those in the protocol)
Agarwala 2020[3]	Does not adjust for all important confounders in a multivariate analysis
Agarwal 2021[2]	Wrong comparison (compared people who were obese with people who were not obese)
Ahmed 2016[4]	Wrong study type (cross-sectional study)
Al-Amiry 2019[5]	Wrong prognostic factor (not BMI)
Amin 2006[7]	Does not adjust for all important confounders in a multivariate analysis
Amin 2006[6]	Does not adjust for all important confounders in a multivariate analysis
Anakwenze 2017[8]	Wrong comparison (Reports results as risk from increase with every 5 kg/m2 increase in BMI, which was not a valid comparison included in the protocol)
Andrew 2008[9]	Does not adjust for all important confounders in a multivariate analysis
Ang 2017[10]	Wrong prognostic factor (not BMI)
Aranda Villalobos 2013[11]	Does not adjust for all important confounders in a multivariate analysis
Baker 2013[13]	No usable outcomes (only reports outcomes comparing BMI categories not included in the protocol)
Baker 2009[12]	Wrong comparison (BMI categories not included in the protocol)
Basdelioglu 2021[15]	Does not adjust for all important confounders in a multivariate analysis
Bin Abd Razak 2013[16]	Does not adjust for all important confounders in a multivariate analysis
Bonnefoy-Mazure 2017[17]	Does not adjust for all important confounders in a multivariate analysis
Bottle 2019[19]	Does not adjust for all important confounders in a multivariate analysis
Boyce 2019[20]	Wrong comparison (BMI categories not included in the protocol)
Bradley 2014[21]	No relevant outcomes
Brown 2018[22]	Wrong prognostic factor (not BMI)
Burn 2019[23]	Wrong comparison (BMI categories not included in the protocol)
Busato 2008[24]	No relevant outcomes
Cavaignac 2013[25]	Wrong prognostic factor (not BMI)
Chalmers 2014[26]	Does not adjust for all important confounders in a multivariate analysis
Chan 1996[27]	Does not adjust for all important confounders in a multivariate analysis
Charles-Lozoya 2020[28]	Not in English
Chaudhry 2019[29]	Wrong comparison (BMI categories not included in the protocol)

Study	Exclusion reason
Chee 2010[30]	Does not adjust for all important confounders in a multivariate analysis
Chen 2021[31]	Cost-effectiveness study not relevant for clinical review
Clement 2020[32]	No relevant outcomes
Clement 2019[33]	No relevant outcomes
Cleveland Clinic 2020[34]	Does not adjust for all important confounders in a multivariate analysis
Connelly 2020[36]	Wrong comparison (BMI categories not included in the protocol)
Crawford 2020[37]	Does not adjust for all important confounders in a multivariate analysis
Cunningham 2018[38]	Wrong comparison (BMI categories not included in the protocol)
Dall 2009[40]	No relevant outcomes
Davidovitch 2020[41]	Does not adjust for all important confounders in a multivariate analysis
Davis 2011[42]	Wrong prognostic factor (not BMI)
Deshmukh 2002[43]	No relevant outcomes
Dowsey 2010[44]	Does not adjust for all important confounders in a multivariate analysis
Dowsey 2010[45]	Does not adjust for all important confounders in a multivariate analysis
Flugsrud 2007[47]	Does not adjust for all important confounders in a multivariate analysis
Foran 2004[48]	Does not adjust for all important confounders in a multivariate analysis
Foreman 2020[49]	Does not adjust for all important confounders in a multivariate analysis
Gadinsky 2011[50]	No usable outcomes (outcomes reported in graph form only)
Gaillard 2017[51]	Does not adjust for all important confounders in a multivariate analysis
Giesinger 2018[53]	Does not adjust for all important confounders in a multivariate analysis
Giesinger 2021[54]	Does not adjust for all important confounders in a multivariate analysis
Gill 2021[55]	Wrong comparison (compares different techniques for shoulder arthroplasty)
Goh 2015[56]	Does not adjust for all important confounders in a multivariate analysis
Gould 2020[57]	Narrative review only
Gould 2021[58]	Wrong comparison (BMI categories not included in the protocol)
Gould 2021[59]	Systematic review (inadequate/unclear quality assessment); references checked
Gross 2012[60]	No usable outcomes (outcomes reported in graph form only)
Guo 2020[61]	Wrong comparison (BMI categories not included in the protocol)
Gupta 2021[62]	Wrong population (discusses people who have had a fracture rather than specifically people who have osteoarthritis)
Haebich 2020[65]	No usable outcomes (outcomes reported in graph form only)
Hailer 2021[66]	Wrong comparison (BMI categories not included in the protocol)

Study	Exclusion reason
Hakim 2020[67]	Does not adjust for all important confounders in a multivariate analysis
Hanly 2017[68]	Does not adjust for all important confounders in a multivariate analysis
Harbourne 2019[69]	Wrong comparison (BMI categories not included in the protocol)
Harmelink 2017[70]	Paper unavailable
Hartford 2016[71]	Does not adjust for all important confounders in a multivariate analysis
Hawker 2021[72]	No relevant outcomes
Hoogeboom 2015[73]	Wrong comparison (BMI categories not included in the protocol)
Hussain 2019[74]	Wrong comparison (BMI categories not included in the protocol)
Jain 2003[75]	Wrong comparison (BMI categories not included in the protocol)
Jameson 2014[76]	Wrong BMI categories, use of a subgroup system that is not relevant to this review, outcomes not relevant
Jarvenpaa 2010[79]	Duplicate reference
Jarvenpaa 2010[79]	Does not adjust for all important confounders in a multivariate analysis
Jarvenpaa 2013[80]	Does not adjust for all important confounders in a multivariate analysis
Jeschke 2016[81]	Wrong comparison (BMI categories not included in the protocol)
Judge 2012[82]	Wrong comparison (Reports results as risk from increase with every 5 kg/m2 increase in BMI, which was not a valid comparison included in the protocol)
Judge 2012[84]	Does not adjust for all important confounders in a multivariate analysis
Kadum 2021[85]	Does not adjust for all important confounders in a multivariate analysis
Katakam 2021[87]	Paper unavailable
Katakam 2021[86]	Wrong comparison (BMI categories not included in the protocol)
Katakam 2021[88]	Does not adjust for all important confounders in a multivariate analysis
Kerkhoffs 2012[89]	Wrong comparison (BMI categories not included in the protocol)
Kessler 2007[90]	No usable outcomes (only reports outcomes for BMI as a whole, not for the categories in the protocol)
Kester 2018[91]	Wrong prognostic factor (not BMI)
Keulen 2021[92]	Wrong prognostic variable (compares different techniques of hip and knee replacement)
Kuipers 2010[93]	Wrong prognostic factor (not BMI)
Ledford 2016[94]	Wrong prognostic factor (not BMI)
Lenguerrand 2018[95]	No usable outcomes (reports incidences, where it is unclear if a multivariate analysis was used on the values)
Li 2020[96]	Does not adjust for all important confounders in a multivariate analysis
Li 2020[97]	Does not adjust for all important confounders in a multivariate analysis
Liao 2015[100]	Does not adjust for all important confounders in a multivariate analysis
Liljensoe 2019[102]	Reports outcomes in an inappropriate way (continuous outcomes reported in dichotomous form)

Study	Exclusion reason
Liljensoe 2013[101]	No usable outcomes (does not use BMI in the analysis when producing outcomes)
Lizaur-Utrilla 2015[103]	Wrong comparison (BMI categories not included in the protocol)
Lowik 2019[104]	Does not adjust for all important confounders in a multivariate analysis
Lozano 2012[105]	Does not adjust for all important confounders in a multivariate analysis
Lubbeke 2007[106]	Wrong comparison (BMI categories not included in the protocol)
Luger 2021[107]	Does not adjust for all important confounders in a multivariate analysis
Mackie 2015[108]	No usable outcomes (reported regression coefficients only)
Mak 2020[109]	Wrong prognostic factor (not BMI)
Malik 2019[110]	Wrong comparison (BMI categories not included in the protocol)
Malinzak 2009[111]	Does not adjust for all important confounders in a multivariate analysis
Martinez-Cano 2020[112]	Does not adjust for all important confounders in a multivariate analysis
McHugh 2013[113]	No usable outcomes (reported coefficients only)
Mellion 2021[114]	Narrative review only
Minarro 2016[115]	Wrong comparison (BMI categories not included in the protocol)
Mohammad 2021[116]	Wrong prognostic factor (not BMI)
Molloy 2019[117]	Does not adjust for all important confounders in a multivariate analysis
Mouchti 2018[118]	Wrong comparison (BMI categories not included in the protocol)
Mulhall 2007[120]	No usable outcomes (reported regression coefficients only)
Murray 2013[121]	Does not adjust for all important confounders in a multivariate analysis
Musbahi 2020[122]	Wrong comparison (compared people who were obese to people who were not obese)
Nettrour 2020[124]	Does not adjust for all important confounders in a multivariate analysis
Nielsen 2017[126]	Wrong comparison (BMI categories not included in the protocol)
Oak 2017[127]	Wrong prognostic factor (not BMI)
Oberbek 2015[128]	Does not adjust for all important confounders in a multivariate analysis
Ogur 2021[129]	Does not adjust for all important confounders in a multivariate analysis
Pan 2017[130]	Wrong comparison (BMI categories not included in the protocol)
Patel 2008[131]	Does not adjust for all important confounders in a multivariate analysis
Paterson 2017[133]	Does not adjust for all important confounders in a multivariate analysis
Paterson 2020[132]	Does not adjust for all important confounders in a multivariate analysis
Perka 2000[134]	Wrong study type (case control study)
Peters 2021[136]	Wrong comparison (BMI categories not included in the protocol)
Pozzobon 2018[138]	Wrong comparison (BMI categories not included in the protocol)

Study	Exclusion reason
Pritchett 1991[139]	Does not adjust for all important confounders in a multivariate analysis
Pua 2015[140]	Wrong prognostic factor (not BMI)
Purcell 2021[141]	Does not adjust for all important confounders in a multivariate analysis
Rajgopal 2008[143]	Does not adjust for all important confounders in a multivariate analysis
Rajgopal 2013[142]	Does not adjust for all important confounders in a multivariate analysis
Rassir 2020[144]	Reports participants from the same joint registry (Danish Arthroplasty Register) as another study, but includes less participants (more narrow follow up period)
Razzaki 2020[145]	Wrong prognostic factor (not BMI)
Reeves 2021[146]	No relevant outcomes
Russo 2015[147]	Does not adjust for all important confounders in a multivariate analysis
Sadr Azodi 2006[148]	Does not adjust for all important confounders in a multivariate analysis
Sayed-Noor 2019[149]	No usable outcomes (reports outcomes in graphical form only)
Scully 2020[150]	No usable outcomes (reports adjusted outcomes in graphical form only)
Seth 2021[151]	Wrong prognostic factor (not BMI)
Seyfettinoglu 2021[152]	Not in English language
Shadyab 2018[153]	Does not adjust for all important confounders in a multivariate analysis
Sharma 2018[154]	Wrong comparison (BMI categories not included in the protocol)
Sharma 1996[155]	Wrong prognostic factor (not BMI)
Sharrock 1993[156]	Wrong prognostic factor (not BMI)
Singh 2011[162]	No relevant outcomes
Singh 2009[161]	No relevant outcomes
Singh 2010[163]	No relevant outcomes
Singh 2012[157]	Wrong comparison (BMI categories not included in the protocol)
Sniderman 2021[158]	Wrong study type (computer learning model)
Spicer 2001[159]	No relevant outcomes
Steinhaus 2020[160]	Does not adjust for all important confounders in a multivariate analysis
Stevens 2013[165]	Wrong comparison (BMI categories not included in the protocol)
Stevens-Lapslay 2019[168]	No relevant outcomes
Sveikata 2016[170]	Does not adjust for all important confounders in a multivariate analysis
Tai 2014[164]	Does not adjust for all important confounders in a multivariate analysis
Tanaka 2020[171]	No usable outcomes (only reports beta coefficients)
Tishelman 2022[166]	Does not adjust for all important confounders in a multivariate analysis
Tohidi 2018[167]	Wrong comparison (BMI categories not included in the protocol)
Tohidi 2019[168]	Wrong comparison (BMI categories not included in the protocol)
Tolk 2020[169]	Wrong study type (cross-sectional study)

Study	Exclusion reason
Torres-Claramunt 2016[170]	Does not adjust for all important confounders in a multivariate analysis
Trela-Larsen 2020[171]	Does not adjust for all important confounders in a multivariate analysis
van der List 2016[172]	Wrong comparison (BMI categories not included in the protocol)
Vincent 2009[173]	Does not adjust for all important confounders in a multivariate analysis
Wagner 2016[174]	>20% of people had indications other than osteoarthritis
Wang 2010[176]	Wrong prognostic factor (not BMI)
Ward 2015[177]	Does not adjust for all important confounders in a multivariate analysis
Waterman 2015[178]	Wrong prognostic factor (not BMI)
Watts 2015[179]	Does not adjust for all important confounders in a multivariate analysis
Wilfong 2020[180]	Does not adjust for all important confounders in a multivariate analysis
Woo 2017[181]	Does not adjust for all important confounders in a multivariate analysis
Xu 2019[184]	No usable outcomes (reports beta coefficients only)
Xu 2018[183]	No usable outcomes (reports beta coefficients only)
Xu 2019[182]	Does not adjust for all important confounders in a multivariate analysis
Yoo 2018[185]	Does not adjust for all important confounders in a multivariate analysis

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2005 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 73: Studies excluded from the health economic review

Reference	Reason for exclusion
Ponnusamy 2018[137]	Excluded as rated not applicable. Though the authors were based in Canada, US resource use and costs were applied and judged unlikely to be applicable to current UK NHS context. In addition, the utility after failed surgery is higher than the utility preoperatively, which may bias in favour of surgery. Surgical mortality rate is assumed the same regardless of BMI group.