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**Weight loss for overweight patients with knee or hip osteoarthritis**

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**ABSTRACT**

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To determine the benefits and harms associated with weight loss in overweight individuals with knee or hip osteoarthritis in terms of pain, physical function, quality of life, and safety.

Further we will have an explicit focus on quality of the weight loss intervention (including magnitude and intensity) (Herbert 2005), to see whether there is a dose-response relationship at the trial (i.e. group) level.

**BACKGROUND**

**Description of the condition**

Osteoarthritis (OA) is a chronic disease characterized by joint pain, tenderness, limitation of movement, crepitus, occasional effusion, and variable degrees of local inflammation, but without systemic effects (Brandt 1986). The aetiology of OA is multi-factorial and includes both generalised constitutional factors (e.g. aging, gender and heredity) and local adverse mechanical factors (e.g. trauma and occupational usage) (Dieppe 2005; Felson 2000). Overweight is an important factor in OA since overload to the affected joint...
is one of the risk factors for developing OA or worsening of the symptoms of OA or both (Coggan 2001; Gelber 1999; Oliveria 1999; Sandmark 1999). Further, it has been hypothesized that metabolic derangements (e.g. diabetes, decreased level of endogenous oestrogen, increased high-density lipoprotein (HDL) cholesterol, etc.) may also be a risk factor for developing OA (Sowers 2006). Among the increasing number of elderly people, the average body weight is steadily increasing (Arterburn 2004). In addition, the obesity problem appears across multiple age groups (Flegal 2002), and there is reason to believe that obesity-related OA will increase in both numbers and severity (WHO Technical 2000; WHO Technical 2003). Obesity must therefore be taken seriously also when considering bone and joint diseases (Woolf 2000). The mechanism by which overweight causes osteoarthritis is poorly understood; a contribution from both local increased forces across the joint and systemic factors is likely (Felson 1996).

Description of the intervention

As a consequence of obesity being widely acknowledged as a risk factor for both the incidence and progression of OA (Lementowski 2008), obesity also has a negative influence on disease outcomes such as the need for surgery (Wendelboe 2003). Hence, weight loss, coupled with exercise, is recognized as an important approach in the management of patients living with obesity and OA (Messier 2004). Guidelines from the American College of Rheumatology (Hochberg 2012) and European League Against Rheumatism (Fernandes 2013) recommend the need for weight loss as well as exercise in the management of patients living with overweight or obesity with OA (Bliddal 2014). Several studies support the combination of exercise and weight loss, together with appropriate analgesia, as a cornerstone for these patients (Messier 2000). These studies have highlighted important benefits of combined exercise and diet therapy compared with either exercise or diet alone, including greater improvements in gait, knee pain and physical function (Messier 2000). Although long-term weight loss can be achieved through calorie restriction alone, the addition of exercise is also required in order to significantly improve mobility (an important determinant of disability), self-reported function and pain (Bliddal 2014). In addition, the CAROT study indicated a decrease in lower extremity muscle mass and muscle strength following weight loss in patients living with obesity and knee OA, suggesting that significant weight loss should be followed by an exercise regimen to restore or increase muscle mass in this patient population (Henriksen 2012).

Why it is important to do this review

Given the significant health, social and economic burden of OA, especially in patients living with obesity, it is imperative to advance our knowledge of OA and obesity, and apply this to improving care and outcomes.

Various international guidelines advocate non-pharmacological treatments for OA patients, including weight loss for first-line treatment of patients living with overweight or obesity with OA in the knees and to a large extent also hips. This is a Cochrane review that represents an update of a previous systematic review and meta-analysis on the effects in patients with knee OA (Christensen 2007), which is now expanded to include hip joints as well.

OBJECTIVES

To determine the benefits and harms associated with weight loss in overweight individuals with knee or hip osteoarthritis in terms of pain, physical function, quality of life, and safety.

Further we will have an explicit focus on quality of the weight loss intervention (including magnitude and intensity) (Herbert 2005), to see whether there is a dose-response relationship at the trial (i.e. group) level.

METHODS

Criteria for considering studies for this review

Types of studies
We will consider for inclusion randomised or quasi-randomised controlled trials comparing some form of weight loss intervention. We will include studies reported as full-text, those published as abstract only, and unpublished data. There will be no language restriction.

**Types of participants**
Studies including participants with knee or hip osteoarthritis (OA) as defined by the American College of Rheumatology (ACR) criteria (Altman 1986; Altman 1991) and concomitant overweight (BMI > 25 kg/m²) or obesity (BMI > 30 kg/m²), who (apparently) do not suffer from any concomitant arthritic conditions or any other diseases, which may affect the joints. All degrees of, and both primary and secondary OA, will be considered eligible. Studies including a mixture of different rheumatic patients will only be included if it is possible to extract the data from the OA patients. If possible, the level of disability will be described, and possible gender difference will be considered.

**Types of interventions**
We will consider eligible any intervention where a weight change is reported explicitly. Any weight loss therapeutic regimen aimed at relieving the symptoms of OA, regardless of content, duration, frequency or intensity will be included. The comparator (control) group could be another active (non-weight reducing intervention) or no treatment (including waiting list) group.

**Types of outcome measures**
Primary outcomes
The main outcomes will be pain and physical function, as currently recommended for OA trials (Bellamy 1997), giving preference to the data reported at the longest follow-up while still reporting on all randomised groups; we will also include other major outcomes following the recommendations from Cochrane Musculoskeletal (Ghogomu 2014).
- Pain.
- Physical function.
- Quality of life.
- Radiograph (or appropriate imaging changes).
- Participants who withdraw because of adverse events.
- Serious adverse events (SAEs).
- Number of participants experiencing any adverse event.

If data on more than one pain scale are provided for a trial, we will refer to a previously described hierarchy of pain-related outcomes (Christensen 2015; Juhl 2012; Juni 2006) and extract data on the pain scale that are highest on this list.
2. Pain on walking.
3. Western Ontario and McMaster Universities Arthritis Index (WOMAC) or knee injury and osteoarthritis outcome score (KOOS) / hip disability and osteoarthritis outcome score (HOOS) pain subscores.
4. Composite pain scores other than WOMAC or KOOS/ HOOS.
5. Pain on activities other than walking.
6. Rest pain or pain during the night.
7. WOMAC or KOOS/JOOS global algofunctional score.
8. Lequesne osteoarthritis index global score.
9. Other algofunctional scale.

If data on more than one function scale are provided for a trial, we will extract data according to the following hierarchy.
1. Global disability score.
2. Walking disability.
3. WOMAC or KOOS/HOOS disability subscore.
4. Composite disability scores other than WOMAC and KOOS/HOOS.
5. Disability other than walking.
6. WOMAC or KOOS/HOOS global scale.
7. Lequesne osteoarthritis index global score.
8. Other algofunctional scale.

If radiographic joint structure change is presented more than once in a trial, we will extract data according to the following hierarchy.
1. Minimum joint space width.
2. Median joint space width.
3. Semi-quantitative measurement.

Secondary outcomes
Secondary outcomes will include ‘weight change’ from baseline reported as mean weight loss (in kg or intensity) as change over time. We will apply dose-response efficacy estimates following metaregression analyses, with two subsequent predefined weight change ‘dose measures’ (per cent point weight change as magnitude and per cent point weight change per week as intensity, respectively) as independent variables. This is an important outcome as it will be considered the key explanatory variable of interest (i.e. the mediator of any potential clinical benefit and harm).

**Search methods for identification of studies**

**Electronic searches**
We will search MEDLINE PubMed from 1946, Embase Ovid from 1974, Web of Science Web of Knowledge from 1900, and the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, all until present. Further, we will conduct a search of the US National Institutes of Health...
Search strategy

The following three areas will be combined in the study as medical subject headings/keywords, where existing and with all subheadings, and as free-text in the title or abstract: (1) OA combined with knee or hip, and where possible OA of the knee or hip; (2) weight loss/gain/changes or diet or antiobesity agents or exercise; and (3) controlled studies.

The lists of references of retrieved studies and relevant reviews will be manually checked to add any citations missed by the electronic searches. Abstracts from scientific meetings will be included if enough information is available in the abstract to retrieve relevant data applied. The search strategy is deliberately designed to be broad, thereby ensuring good retrieval, but also creating a high proportion of ‘noise’. The first part of the selection process will be an assessment of title and abstract. Potentially relevant papers at this stage will be retrieved in full-text. If in doubt, a full-text version will be acquired.

See Appendix 1 for the search strategies which will be applied in the chosen bibliographic databases.

Searching other resources

We will check reference lists of all primary studies and review articles on the subject for additional references. Further, we will search for errata or retractions from included studies published in full-text on PubMed (www.ncbi.nlm.nih.gov/pubmed) and report the date this was done within the review.

Data collection and analysis

Selection of studies

Two review authors (Julie Bolvig (JB), Hans Lund (HL)) will independently screen titles and abstracts for inclusion of all the potential studies we identify as a result of the search. Among the potentially eligible findings, we will retrieve the full-text study reports/publication and two review authors (JB, HL) will independently screen the full-text and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult a third person (Robin Christensen (RC) or Henning Bliddal (HB)). We will identify and exclude duplicates and collate multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and ‘Characteristics of excluded studies’ table via Covidence (Covidence 2016).

Assessment of risk of bias in included studies

Two review authors (RC, JB) will independently assess risk of bias for each included study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will resolve any disagreements by discussion or by involving another author (HL, JAS) or both. We will assess the risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

Data extraction and management

We will use a data collection form for study characteristics and outcome data which has been piloted on at least one study in the review. Two review authors (RC, JB) will extract study characteristics from included studies. Uncertainty or disagreement will be resolved by discussion with HB, SL and Arne Vernon Astrup (AA) depending on the topic. We will extract the following study characteristics.

1. Methods: study design, total duration of study, details of any ‘run in’ period, number of study centres and location, study setting, withdrawals, and date of study.
2. Participants: number, mean age, age range, sex, disease duration, severity of condition, diagnostic criteria, inclusion and exclusion criteria.
3. Interventions: intervention, comparison, concomitant medications, and excluded medications.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Characteristics of the design of the trial as outlined below in the ‘Assessment of risk of bias in included trials’ section.
6. Notes: funding for trial, and notable declarations of interest of trial authors.

Two review authors (RC, JB) will independently extract outcome data from included studies. The number of events and number of participants per treatment group for dichotomous outcomes, and means and standard deviations and number of participants per treatment group for continuous outcomes will be extracted. We will note in the ‘Characteristics of included studies’ table if outcome data were not reported in a usable way and when data were transformed or estimated from a graph. We will resolve disagreements by consensus or by involving a third person (HB, Marc C Hochberg (MCH), Jasvinder A Singh (JAS) or SL) or both.
We will grade each potential source of bias as high, low or unclear and provide a quote from the study report together with a justification for our judgement in the ‘Risk of bias’ table. We will summarise the risk of bias judgements across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be different than for a patient-reported pain scale). As well, we will consider the impact of missing data by key outcomes. Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the ‘Risk of bias’ table.

We will present the figures generated by the risk of bias tool to provide summary assessments of the risk of bias.

### Assessment of bias in conducting the systematic review

We will conduct the review according to this published protocol and report any deviations from it in the ‘Differences between protocol and review’ section of the systematic review.

### Measures of treatment effect

We will summarise continuous outcomes using standardised mean differences (SMD) with 95% confidence intervals (95% CI), with the differences in mean change from baseline values across treatment groups divided by the pooled standard deviation (SD). According to Cochrane standards, Review Manager software (RevMan 2014) will apply the Hedges’ bias-correction by default to adjust for small sample bias (Hedges 1981). If differences in mean change are unavailable, we will use differences in mean values at the end of the treatment (da Costa 2013). If some of the required data are unavailable, we will use various customized approximations (Reichenbach 2007).

As originally suggested by J Cohen (Cohen 1988), an SMD of -0.20 will be considered a small clinical difference between the intervention and comparator groups, whereas an SMD of -0.50 a moderate difference, and -0.80 a large difference (Bliddal 2009). When SMDs are used as the summary measure with corresponding 95% CI, these will be back-translated to a typical visual analogue scale (VAS) (e.g. 0 to 10 for pain and function (Bliddal 2009)) by multiplying the SMD by a typical among-person standard deviation (e.g. the standard deviation of the control group at baseline from the most representative trial) according to chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions (Sihunemann 2011b).

We will express binary outcomes as risk ratios (RR) with 95% CI. However, according to the recommendations in the Cochrane Handbook for Systematic Reviews of Interventions, we will apply the Peto odds ratio when the outcome is a rare event (approximately less than 10%). In the ‘Effects of interventions’ results section and the comments column of the ‘Summary of findings’ table, we will provide the absolute per cent difference, the relative per cent change from baseline, and the number needed to treat (NNT) (the NNT will be provided only when the outcome shows a statistically significant difference).

For dichotomous outcomes, such as the number of participants who withdraw because of adverse events and SAEs, the number needed to treat will be calculated from the control group event rate and the relative risk using the Visual Rx NNT calculator (Cates 2008). For continuous outcomes, the absolute benefit will be calculated as the improvement in the intervention group minus the improvement in the control group, in the original units. The relative per cent change for dichotomous data will be calculated as the risk ratio - 1 and expressed as a percentage. For continuous outcomes, the relative difference in the change from baseline will be calculated as the absolute benefit divided by the baseline mean of the control group.

### Unit of analysis issues

The unit of analysis will be the participants; we will not include single-joint assessments. Where multiple trial arms are reported in a single study, we will include only the relevant arms. If two comparisons (e.g. intervention A versus comparator and intervention B versus comparator) are combined in the same meta-analysis, we will halve the control group to avoid double-counting.

### Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as abstract only or when data are not available for all participants). Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis. Any assumptions and imputations to handle missing data will be clearly described and the effect of imputation will be explored by sensitivity analyses.

For dichotomous outcomes (e.g. number of withdrawals due to adverse events), the withdrawal rate will be calculated using the number of patients randomised in the group as the denominator. For continuous outcomes (e.g. mean change in pain score), we will calculate the SMD based on the number of participants analysed and reported at that particular time point. If the number of participants analysed is not presented for each time point, the number of randomised participants in each group at baseline will be used. Where possible, missing standard deviations will be computed from other statistics such as standard errors, confidence intervals or P values, according to the methods recommended in the Cochrane Handbook for Systematic Reviews of Interventions. If standard deviations cannot be calculated, they will be imputed (e.g. from other studies in the meta-analysis).
**Assessment of heterogeneity**

Clinical and methodological diversity will be assessed in terms of participants, interventions, outcomes and study characteristics for the included studies to determine whether a meta-analysis is appropriate. This will be conducted by observing these data from the data extraction tables. Statistical heterogeneity will be assessed by visual inspection of the forest plot to assess for obvious differences in result between the studies, supported by use of the $I^2$ and Chi² statistics (Higgins 2003).

As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011), the interpretation of an $I^2$ value of 0% to 40% might 'not be important'; 30% to 60% may represent 'moderate' heterogeneity; 50% to 90% may represent 'substantial' heterogeneity; and 75% to 100% represents 'considerable' heterogeneity. As noted in the *Cochrane Handbook for Systematic Reviews of Interventions*, we will keep in mind that the importance of $I^2$ depends on (i) magnitude and direction of effects and (ii) strength of evidence for heterogeneity.

The Chi² test will be loosely interpreted as a $P$ value ≤ 0.10 indicating evidence of statistical heterogeneity. If we identify substantial heterogeneity we will report it and investigate possible causes.

**Assessment of reporting biases**

We will create and examine a funnel plot to explore possible small study biases. In interpreting funnel plots, we will examine the different possible reasons for funnel plot asymmetry as outlined in section 10.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* and relate this to the results of the review. If we are able to pool more than 10 trials, we will undertake formal statistical tests to investigate funnel plot asymmetry, and will follow the recommendations in section 10.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Sterne 2011).

To assess outcome reporting bias, we will check trial protocols against published reports. For studies published after 1st July 2005, we will screen the Clinical Trial Register at the World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch) for the a priori trial protocol. We will evaluate whether selective reporting of outcomes is present.

**Data synthesis**

We will undertake meta-analyses only where this is meaningful (i.e. if the treatments, participants and the underlying clinical (PICO) question are similar enough for pooling to make sense). Independent of any apparent statistical heterogeneity, we will use a standard inverse variance random-effects model per default for meta-analysis (DerSimonian 1986), whereas a fixed-effect analysis will be applied for the purpose of sensitivity. We prespecify a number of stratified and metaregression analyses, stratifying the pain and function outcomes from the individual studies according to trial characteristics and continuous variables at study level.

Metaregression will be restricted to investigation of suspected differences between trials, which vary substantially across trials. Therefore, all the trial-level features collected are considered potential covariates of exploratory value.

**'Summary of findings' table (SoF)**

We will create a 'Summary of findings' table using the following outcomes.

1. Pain.
2. Physical function.
3. Quality of life.
4. Radiograph (or appropriate imaging changes).
5. Patients who withdraw because of adverse events.
6. Serious adverse events.
7. Number of participants experiencing any adverse event.

If pain and function outcomes are reported at several time points, we will use the time point reported as being 'the primary endpoint', and then subsequently stratify the analyses according to time points. The overall quality of the evidence will be evaluated using GRADE. We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies which contribute data to the meta-analyses for the prespecified outcomes (Higgins 2011; Schünemann 2011a).

We will justify all decisions to down- or upgrade the quality of studies using footnotes and we will make comments to aid reader's understanding of the review where necessary.

In the comments column of the 'Summary of findings' table, we will provide the absolute per cent difference, the relative per cent change from baseline, and the NNT (the NNT will be provided only when the outcome shows a statistically significant difference). For dichotomous outcomes, such as serious adverse events, the NNT will be calculated from the control group event rate and the relative risk using the Visual Rx NNT calculator (Cates 2008). The NNT for continuous measures will be calculated using the Wells calculator.

For dichotomous outcomes, the absolute risk difference will be calculated using the risk difference statistic in Review Manager (RevMan 2014) and the result expressed as a percentage. For continuous outcomes, the absolute benefit will be calculated as the improvement in the intervention group minus the improvement in the control group (mean difference), in the original units, and expressed as a percentage.

The relative per cent change for dichotomous data will be calculated as the risk ratio - 1 and expressed as a percentage. For continuous outcomes, the relative difference in the change from baseline will be calculated as the absolute benefit divided by the baseline mean of the control group, expressed as a percentage.

**Subgroup analysis and investigation of heterogeneity**
We will perform stratified analyses of the primary outcomes, pain and function, accompanied by interaction tests according to the following trial characteristics: type of comparator group (sham versus no intervention); trial duration (short term < 16 weeks versus intermediate versus long term > 1 year); concomitant use of exercise (yes versus no); use of analgesics as cointervention (yes versus no); analysis in accordance with the intention-to-treat principle (yes versus no or unclear); publication type (full journal article versus other type or unpublished material); concealment of allocation (adequate versus inadequate or unclear); blinding of participants (adequate versus inadequate or unclear); and blinding of therapists (adequate versus inadequate or unclear).

We will use the formal test for subgroup interactions in Review Manager (RevMan 2014) and will use caution in the interpretation of subgroup analyses as advised in section 9.6 of the Cochrane Handbook for Systematic Reviews of Interventions. The magnitude of the effects will be compared between the subgroups by means of assessing the overlap of the confidence intervals of the summary estimated. Non-overlap of the confidence intervals indicates statistical significance.

We will perform metaregression analyses to explore the expected dose-response phenomena. Restricted maximum likelihood (REML)-based (i.e. random-effects) metaregression analysis (Thompson 2002) will be applied in order to answer the specific question raised by the secondary hypothesis - whether the absolute magnitude and intensity (magnitude over time) of weight loss is associated with the quantitative changes in pain and function (Christensen 2007).

**Sensitivity analysis**

As it should be anticipated that estimation of treatment effects in meta-analyses differs depending on the strategy used, there is need for systematic sensitivity analyses (Dechartres 2014).

**Interpreting results and reaching conclusions**

We will follow the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions, chapter 12 (Schünemann 2011b), for interpreting results and will be aware of distinguishing a lack of evidence of effect from a lack of effect. We will base our conclusions only on findings from the quantitative or narrative synthesis of included studies for this review. We will avoid making recommendations for practice and our implications for research will suggest priorities for future research and outline what the remaining uncertainties are in the area.

**Acknowledgements**

The authors are indebted to the database consultant Christian Cato Holm, and to the staff of the Interlibrary Loan Department, Copenhagen University Library.

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The Parker Institute at Bispebjerg and Frederiksberg Hospital is supported by a core grant from the Oak Foundation (OCAY-13-309).

**References**

**Additional references**

Altman 1986


Altman 1991


Arterburn 2004


Bellamy 1997


Bliddal 2006


Bliddal 2009

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Bliddal 2014

Brandt 1986

Cates 2008 [Computer program]

Christensen 2007

Christensen 2015

Coggon 2001

Cohen 1988

Covidence 2016 [Computer program]

da Costa 2013

Dechartres 2014

Deeks 2011

DerSimonian 1986

Dieppe 2005

Felson 1992

Felson 1996

Felson 2000

Felson 2004

Fernandes 2013

Flegal 2002

Gelber 1999

Ghogomu 2014

Hedges 1981

Henriksen 2012

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Herbert 2005

Higgins 2003

Higgins 2011

Hochberg 2012

Juhl 2012

Juni 2006

Lementowski 2008

Marks 2002

Messier 2000

Messier 2004

Mikesky 2000

Oliveria 1999

Reichenbach 2007

RevMan 2014 [Computer program]

Roddy 2005

Røgind 1998

Sandmark 1999

Schünemann 2011a

Schünemann 2011b

Sowers 2006

Sterne 2011
Appendix 1. Elements of search strategy

The search strategies in the bibliographic databases will contain the following elements.

(1) Osteoarthritis/osteoarthrosis combined with knee or hip, as well as, where possible, osteoarthritis of the knee or hip, all both as keywords with all subheadings, where existent, and as TI/AB.

AND

(2) body weight OR weight change* OR weight loss OR weight reduction OR weight gain OR anti obesity OR antiobesity OR diet* OR exercise, all Ti/Ab.

AND

(3) Controlled OR randomized OR randomised, all TI/AB

There will be no restriction on language, but a restriction to ‘human’.

Specified search strategies

The reason for including both osteoarthritis and the more specific knee or hip osteoarthritis is that one loses some relevant references if only the more specific term is used.

Embase via Ovid from 1974

((Exp osteoarthritis/ OR osteoarthr*/ TI OR osteoarthr*/AB OR degenerative arthritis/TI OR degenerative arthritis/AB OR osteoarthritis/TI OR osteoarthritis/AB) AND (knee/TI OR knee/AB OR hip/TI OR hip/AB)) OR Exp knee osteoarthritis/ OR Exp hip osteoarthritis/

AND

body weight OR weight change* OR weight loss OR weight reduction OR slimming OR weight gain OR anti obesity OR antiobesity OR diet*OR exercise, all TI/AB.

AND

(controlled OR randomised OR randomized) TI/AB

Limitation: human.
MEDLINE via PubMed from 1945

((osteoarthritis [Mesh Terms] OR osteoarthr* TI/AB OR degenerative arthritis) AND (hip TI/AB OR Knee TI/AB)) OR knee osteoarthritis [Mesh Terms] OR hip osteoarthritis [Mesh Terms] AND (body weight OR weight change* OR weight loss OR weight reduction OR slimming OR weight gain OR anti obesity OR antiobesity OR diet* OR exercise, all TI/AB)

AND

controlled OR randomised OR randomized) TI/AB

Limitation: human.

Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library

Similar search to the MEDLINE search, except the limitation to 'human'.

Web of Science via Web of Knowledge from 1900

((osteoarthr* OR degenerative arthritis) AND (hip OR Knee))

AND

(body weight OR weight change* OR weight loss OR weight reduction OR slimming OR weight gain OR anti-obesity OR antiobesity OR diet* OR exercise)

AND

controlled OR randomised OR randomized)

AND

human

US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (apps.who.int/trialsearch)

Osteoarthritis OR degenerative arthritis

AND

weight change or weight loss or anti-obesity OR antiobesity OR slimming

CONTRIBUTIONS OF AUTHORS

Content: All authors

Methodology: RC, JB, HL, EMB, and HB

Statistics: RC and JB.

DECLARATIONS OF INTEREST

Robin Christensen: none known.

Julie Bolvig: none known.

Hans Lund: none known.

Else Marie Bartels: none known.

Arne Vernon Astrup: none known.

Marc C Hochberg: none known.

Jasvinder A Singh: none known.

Stefan Lohmander: none known.

Henning Bliddal: none known.
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• Copenhagen University Library, Denmark.

External sources
• No sources of support supplied

NOTES
This protocol is based on the protocol template provided by Cochrane Musculoskeletal.