Interventions for treating overweight or obesity in adults: an overview of systematic reviews (Protocol)

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[Overview of Reviews Protocol]

Interventions for treating overweight or obesity in adults: an overview of systematic reviews

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

Our overall aim is to provide an overview of the efficacy of interventions for obesity or overweight in adults by summarising the evidence from multiple systematic reviews.

BACKGROUND

Description of the condition

Obesity is a multifactorial disorder characterised by an imbalance between intake and daily requirement of nutrients. The causes of obesity are complex and include genetic, psychological, biochemical, environmental, social and economic factors. In clinical practice, overweight and obesity are usually defined by the body mass index (BMI) (IOTF; WHO 2011). Furthermore, obesity can be grouped into three classes, depending on the degree of severity, as shown in the Table 1.

More than one and a half billion adults worldwide are overweight, of which 500 million are obese (WHO 2011). At least one in two people is now overweight or obese in over half of the Organisation for Economic Co-operation and Development (OECD) countries and projections suggest than in some countries more than two out of three people will be obese by 2020 (OECD 2012). In the European Union, the proportion of overweight and obese people in the adult population varied in 2008/09 between 36.9% and

56.7% for women and between 51% and 69.3% for men (EHIS 2009). In Spain, over half of the adult population are overweight and 17% of these are obese (EHIS-S 2009).

People who are overweight are more likely to develop risk factors for cardiovascular disease such as high blood pressure, high levels of triglycerides and low-density lipoprotein (LDL) cholesterol, and low levels of high-density lipoprotein (HDL) cholesterol (NHLBI 2000). Obesity is associated with a large number of health problems (e.g. cardiovascular, endocrine-metabolic, musculoskeletal, respiratory and gastrointestinal diseases as well as certain types of cancer (Guh 2009; NHLBI 2000)). It also has an important impact on individual self esteem and self image, and limits health-related quality of life. Overweight individuals showing one or more obesity-related conditions (e.g. diabetes, hypertension) could have a risk of cardiovascular disease comparable to obese individuals. The specific level of risk associated with a given level of overweight or obesity may vary with race/ethnicity, and also with age, gender and societal conditions (NHLBI 2000).

Description of the interventions

There is a diverse array of interventions available for obesity and being overweight, although the main interventions can be broadly classified into non-pharmacological, pharmacological and surgical. Non-pharmacological 'lifestyle' interventions aim to decrease the nutrient intake and to increase the daily energy requirements through increase in physical activity, such as engaging in exercise (a planned, structured and repetitive physical activity). These interventions can be combined with psychological behavioural interventions to improve adherence to treatment and induce permanent change in the obese or overweight individual. Specific strategies include self monitoring of both eating habits and physical activity, stress management, stimulus control, problem solving, contingency management, cognitive restructuring and social support (NHLBI 2000). These interventions constitute the cornerstone of any weight-reduction programme in overweight and obese individuals, whatever the degree of severity.

Pharmacological interventions include drugs that inhibit appetite and drugs that inhibit absorption. The most widely used drug is orlistat, which can be considered in either obese individuals or in overweight individuals with a BMI of 28.0 or more plus risk factors, in both cases only after dietary, exercise and behavioural approaches have been initiated and evaluated (NICE 2006). The drawbacks of pharmacological treatment are its short-term effect, requiring long-term use, and the possible adverse effects (NICE 2006). There are a number of less commonly used medications approved either for short-term use (appetite suppressants phendimetrazine, diethylpropion and phentermine) or used off-label (such as the antidepressant bupropion, the antidiabetic agent metformin and the antiepileptic drugs topiramate and zonisamide) (NIH 2010). Approval for sibutramine and rimonabant was suspended due to their adverse safety profile (Curioni 2009; James 2010; NICE 2006).

Finally, bariatric surgery interventions encompass restrictive surgery that limits intake (e.g. gastric banding), malabsorptive surgery (e.g. intestinal bypass) and mixed interventions (e.g. gastric bypass, duodenal switch). Bariatric surgery has significant risks of early and late morbidity, and considerable perioperative mortality (Picot 2009). It is usually indicated in patients with grade III obesity or grade II obesity occurring together with another significant disease that could be improved with weight loss (e.g. type 2 diabetes or high blood pressure) and with no maintenance of weight loss for more than six months with other non-surgical measures (NICE 2006).

Most interventions target the individual but there are other more general approaches that focus also on the individual's environment, such as public health policies or family or workplace interventions. Other interventions with a more holistic approach have been proposed, either complementary therapies targeting weight loss (Cho 2009; Pittler 2004; Pittler 2005) or new proposals focusing on health outcomes rather than weight loss (Bacon 2011).

Adverse effects of the interventions

Very low-calorie diets may be associated with loss of lean muscle mass, increased risk of gout and electrolyte imbalances (Strychar 2006). Adverse effects of approved pharmacological interventions are listed in Table 2 (NIH 2010). Bariatric surgery currently has low 30-day mortality but a risk of complications that cannot be ignored (e.g. anastomotic and staple line leaks, wound infections, pulmonary events, haemorrhage). Morbidity rates are lower after laparoscopic procedures (Dixon 2011).

How the intervention might work

All interventions aim to reduce nutrient intake and increase daily energy requirements in order to induce weight reductions. Even modest weight losses, when maintained over time, have a positive impact on health and can be considered a treatment success. Benefits of weight loss are a decreased risk of development of diabetes, and reductions in LDL cholesterol, total cholesterol and blood pressure (Avenell 2004). Modest weight losses of 5% to 10% of body weight were associated with significant improvements in cardiovascular disease (CVD) risk factors at one year (Wing 2011). For 10 kg weight loss, decreases of 5 mm Hg and 6.0 mm Hg in diastolic and systolic blood pressure, respectively, may be expected (Aucott 2005). Intentional weight loss, irrespective of the amount, was associated with a reduction in all-cause mortality and CVD-, cancer- and diabetes mellitus-related mortality in women with obesity-related illnesses (Avenell 2004). Weight loss may improve psychological measures and health-related quality of life and allow for a more active lifestyle and increased physical activity, which in turn may help with weight loss, weight maintenance or both.

While many interventions have been shown to have a short-term effect in inducing moderate weight loss, only a minority of people are able to maintain their weight loss (Field 2001; Kramer 1989). A weight cycling effect may be observed through the repeated voluntary loss and subsequent regain of body weight in those who repeatedly follow weight loss regimens, mainly diets. Weight cycling is a risk factor for all-cause mortality and cardiovascular mortality (Avenell 2004; Diaz 2005; Rzehak 2007). This renders particular relevance to the assessment of the medium- (one to five years follow-up) and long-term (more than five years follow-up) efficacy of weight loss interventions.

Treatment of overweight or obese individuals with associated co-morbidity is of particular relevance, but recent research has challenged this notion. An obesity paradox has been documented in several trials where overweight and obese individuals with established cardiovascular disease (including cardiac heart disease, heart failure, hypertension and peripheral arterial disease) have a better prognosis compared with non-overweight/non-obese patients (Lavie 2009).

Why it is important to do this overview

To date, many systematic reviews exist which assess the efficacy of interventions for obesity and overweight. It is necessary to identify and summarise the most current evidence to allow better decision-making processes as well as to show the gaps in research that need to be addressed. This project aims to provide an up-to-date overview of the efficacy of the spectrum of interventions for being overweight or obese, completing previous efforts that focused on specific interventions (Picot 2009) or which did not include the most recent research (Avenell 2004; NHLBI 2000; NICE 2006). In particular, it is necessary to assess the medium- and long-term efficacy of interventions, and to identify the interventions most useful for particular subgroups of patients that present co-existing morbidity (e.g. diabetes, cardiac disease).

OBJECTIVES

Our overall aim is to provide an overview of the efficacy of interventions for obesity or overweight in adults by summarising the evidence from multiple systematic reviews.

METHODS

Criteria for considering reviews for inclusion

Types of reviews and studies

We will include systematic reviews of randomised controlled trials (RCTs) evaluating interventions to treat adult obesity or overweight.

A systematic review is characterised by (Higgins 2011):

- a clearly stated set of objectives with pre-defined eligibility criteria for studies;
- an explicit, reproducible methodology;
- a systematic search that attempts to identify all studies that would meet the eligibility criteria;
- an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias;
- a systematic presentation, and synthesis, of the characteristics and findings of the included studies.

Types of participants

Adults (aged 18 years or older) with obesity or overweight as defined by the World Health Organization (WHO) (WHO 2011). We will exclude systematic reviews on obese or overweight adults presenting specific conditions or co-morbidities (e.g. pregnant women, people with diabetes) if the intervention primarily focuses on the comorbidity.

We will only include systematic reviews evaluating children and adults if separate results are available for adults.

Types of interventions

We will include systematic reviews evaluating any intervention or combination of interventions which is designed to treat obesity or overweight in adults. These interventions will be compared with either control interventions (such as standard or usual care, placebo) or with another type of intervention aimed at treatment of obesity or overweight.

Interventions will be broadly grouped as follows.

- 'Lifestyle' interventions (e.g. diet, exercise, physical activity, any combination of these interventions).
- Psychological interventions (e.g. behavioural therapy, transtheoretical model of change).
- Pharmacological interventions.
- Surgical interventions.
- Complimentary therapies (e.g. acupuncture, green tea).
- Community and family interventions (e.g. workplace interventions, public health or policy interventions).

Types of outcomes

Primary outcomes

- Weight loss (e.g. body weight, body mass index (BMI), waist circumference).
- Obesity-related comorbidity (e.g. cardiovascular events, incidence of diabetes mellitus, incidence of hypertension).

- Adverse effects.

Secondary outcomes

- Health-related quality of life (measured using a validated instrument).
- All-cause mortality.
- Costs.

Search methods for identification of reviews

We will search the following sources from inception to the present.

- *The Cochrane Library*
- MEDLINE
- EMBASE
- PsycINFO

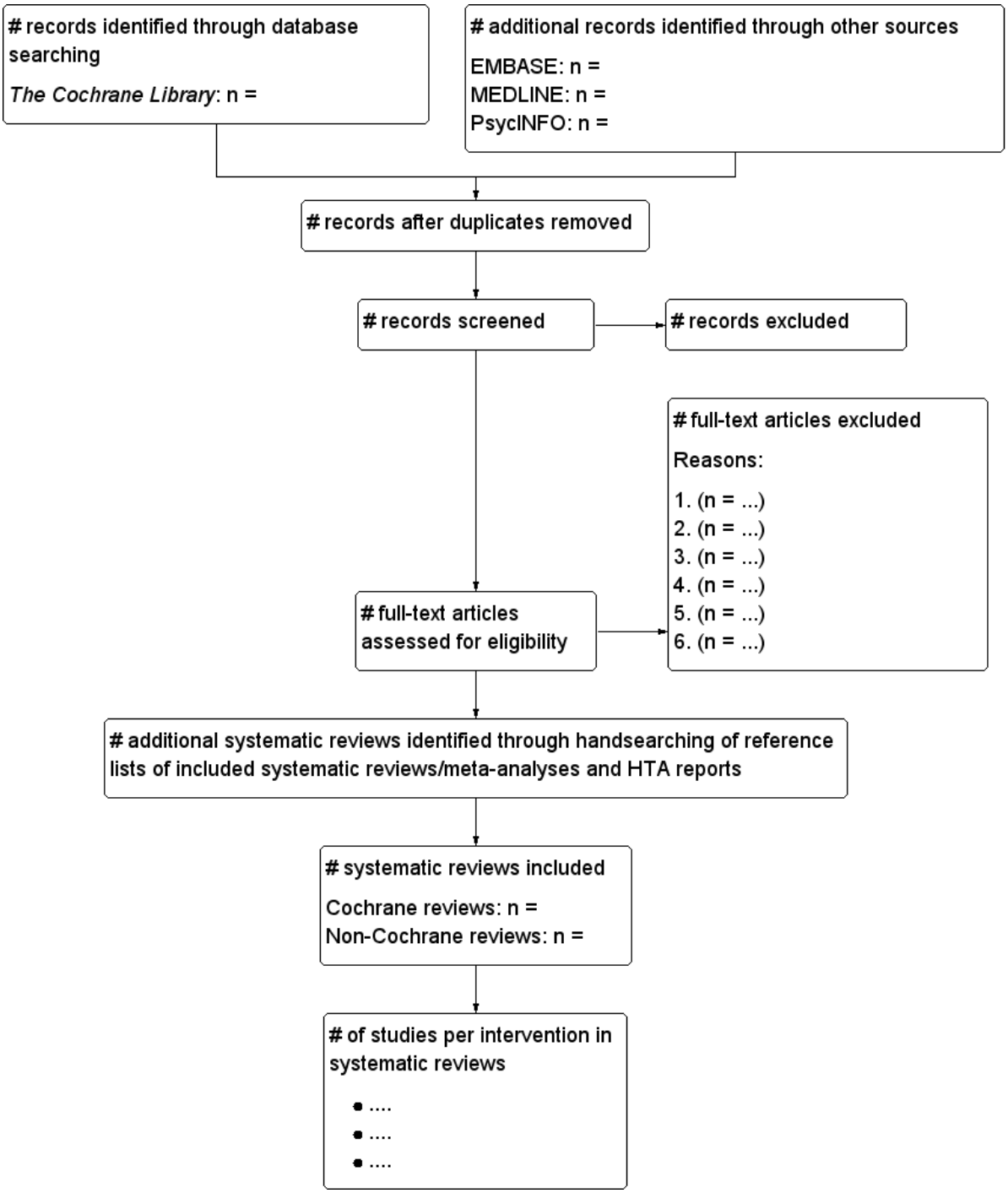
For detailed search strategies see Appendix 1. Searches will not be older than six months at the moment the final review draft is checked into the Cochrane Information and Management System for editorial approval). We will use PubMed's 'My NCBI' (National Center for Biotechnology Information) email alert service for identification of newly published systematic reviews using a basic search strategy (see Appendix 1).

If we detect additional relevant key words during any of the electronic or other searches we will modify the electronic search strategies to incorporate these terms and document the changes. We will place no restrictions on the language of publication when searching the electronic databases or reviewing reference lists in identified studies.

We will send the results of electronic searches to the Cochrane Metabolic and Endocrine Disorders Group for databases which are not available at the editorial office.

We will try to identify other potentially eligible systematic reviews by searching the reference lists of retrieved systematic reviews, meta-analyses and health technology assessment reports. We will present the results of the screening in a flow chart (Figure 1).

Figure 1. Systematic review selection flow chart



Data collection and analysis

Selection of reviews

Two overview authors (MR, RP) working independently will screen the search results, and differences will be resolved by discussion or by consultation with a third party to reach consensus.
The inclusion of reviews in the overview will prioritise Cochrane reviews and for any topic where a Cochrane review exists, we will only consider high-quality, more up-to-date reviews identified from other sourcesas sources of complementary information. For topics where no Cochrane review is available, we will consider the inclusion of systematic reviews identified from other sources. In those cases, we will select for each topic the more up-to-date and highest-quality review available.
Cochrane reviews are prioritised over other sources because they are, on average, of higher quality than systematic reviews from other sources (Moher 2007). Cochrane reviews are also regularly updated to reflect the state of the evidence, whereas reviews from other sources typically are not. It is to be expected that in future updates of this overview, as more Cochrane reviews become available, they will replace the other reviews included and ultimately the overview may include only Cochrane reviews. The reason for including reviews from other sources is to avoid gaps in the evidence for a number of relevant topics where Cochrane reviews are planned but not yet published (Aponte 2008; Nkansah 2007).
We have adapted the selection of reviews procedure from the methodology used in Ryan 2011. We will follow a two-step selection procedure. In the first step, we will screen the *Cochrane Database of Systematic Reviews* (CDSR) to identify Cochrane reviews that fulfil the inclusion criteria.
In the second step, we will identify high-relevance non-Cochrane systematic reviews in MEDLINE, EMBASE, Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment database and PsycINFO.
High-relevance non-Cochrane reviews will be screened and included in this overview if:

- the review focus on an intervention not reviewed by a Cochrane review, or the review is more current than an existing Cochrane review dealing with the same interventions;
- the review is rated as high-quality and has no serious methodological flaws according to the results of the AMSTAR instrument (a measurement tool for the 'assessment of multiple systematic reviews') (Shea 2007). If we identify two or more non-Cochrane reviews with similar scope, we will include the most recent higher-quality review in this overview. For the purposes of this overview, we will consider high-quality reviews to be those that fulfil all of a selection of AMSTAR criteria: duplicate study selection and data extraction, comprehensive searching of the literature, provision of a list of included studies, provision of characteristics of included studies, assessment of methodological quality of included studies and appropriate methods for combining results of studies.

We will classify the results of the search strategy depending on the interventions studied in the review. In each intervention category, we will pre-select those non-Cochrane reviews that are more current than the existing Cochrane review. We will assess these pre-selected reviews with regards to their relevance. If there is no Cochrane review assessing a specific intervention, we will select the most recent higher-quality review.
Two investigators (MR and either LM, MJM or RP) working independently will perform the selection and assessment of reviews, and differences will be resolved by discussion or by consultation with a third party to reach consensus.

Data extraction and management

For reviews that fulfil the inclusion criteria, two overview authors (MR and either LM, MJM, RP) will independently abstract key characteristics of the review using standard data extraction templates, with any disagreements to be resolved by discussion (for details see Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7; Appendix 8; Appendix 9) or if required by a third party. We will provide a figure of 'Summary of interventions and controls within included reviews' (Figure 2).

Figure 2. Summary of interventions and controls within included systematic reviews

	NUMBER OF STUDIES (NUMBER OF PARTICIPANTS)									
Interventions										
No treatment										
Placebo										
Regular care										
Method 1										
Method 2										
Method 3										
Method 4										
Method 5										
Method 6										
Method 7										
Controls	No treatment	Placebo	Regular care	Method 1	Method 2	Method 3	Method 4	Method 5	Method 6	Method 7

We will send an email to all authors of included systematic reviews to enquire whether they are willing to answer questions regarding their publications. The results of this survey will be published in Appendix 10. Thereafter, we will seek relevant missing information on the publication from the corresponding author(s) of the article, if required.

Assessment of methodological quality of included reviews

We will assess the methodological quality of included systematic reviews using the AMSTAR instrument (Shea 2007). AMSTAR assesses the degree to which review methods avoided bias by evaluating the methods against 11 distinct criteria (Appendix 11), including the following.

1. Use of an 'a priori' design.
2. Duplicate study selection and data extraction.
3. Comprehensive searching of the literature.
4. Use of publication status as an exclusion criterion.
5. Provision of (included and excluded) studies.
6. Provision of characteristics of included studies.
7. Assessment of methodological quality of included studies.
8. Appropriate use of quality of included studies in formulating conclusions.
9. Appropriate methods for combining results of studies.
10. Assessment of publication bias.
11. Conflict of interest stated (both review and included studies).

We will rate each AMSTAR item as yes (clearly done), no (clearly not done), cannot answer or not applicable, based on the published review report.

Data synthesis

We will generate descriptive summaries about the efficacy of the diverse interventions, broadly grouped into: lifestyle interventions; complementary therapies; psychological interventions; pharmacological interventions; surgical interventions; community and family interventions.

If possible, we will assess results at short-, medium- and long-term (up to one year, one to five years, five years and more).

Subgroup analyses and sensitivity analyses

If there is enough information in the included systematic reviews, we will carry out subgroup analyses based on comorbidity.

- Diabetic participants versus non-diabetic participants.
- Hypertensive participants versus non-hypertensive participants.
- Cardiac disease versus other cardiovascular diseases.

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* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Classification weight/obesity

Classification	BMI (kg/m^2)	Class
Normal weight	18.5 to 24.9	-
Overweight	25 to 29.9	-
Obesity		
Mild	30 to 34.9	I
Moderate	35 to 39.9	II
Extreme	40 or more	III

Table 2. Adverse effects of pharmacological interventions

Drug name	Drug type	Common adverse effects
Phentermine	Appetite suppressant	Increased blood pressure and heart rate, sleeplessness, nervousness
Diethylpropion	Appetite suppressant	Dizziness, headache, sleeplessness, nervousness
Phendimetrazine	Appetite suppressant	Sleeplessness, nervousness
Orlistat	Lipase inhibitor	Gastrointestinal adverse effects (cramping, diarrhoea, oily spotting), rare cases of severe liver injury reported
Bupropion	Depression treatment	Dry mouth, insomnia
Topiramate	Seizure treatment	Numbness of skin, change in taste
Zonisamide	Seizure treatment	Drowsiness, dry mouth, dizziness, headache, nausea
Metformin	Diabetes treatment	Weakness, dizziness, metallic taste, nausea

Table extracted from NIH 2010.

APPENDICES

Appendix 1. Search strategies

Search terms and databases
Unless otherwise stated, search terms are free-text terms. Abbreviations: '$': stands for any character; '?': substitutes one or no character; adj: adjacent (i.e. number of words within range of search term); exp: exploded MeSH; MeSH: medical subject heading (MEDLINE medical index term); pt: publication type; sh: MeSH; tw: text word
The Cochrane Library
#1 MeSH descriptor Obesity explode all trees #2 MeSH descriptor Body mass index explode all trees #3 MeSH descriptor Skinfold thickness explode all trees #4 MeSH descriptor Waist-hip ratio explode all trees #5 MeSH descriptor Abdominal fat explode all trees #6 MeSH descriptor Overweight explode all trees

(*Continued*)

#7 (overweight* in All Text or (over in All Text and weight* in All Text))
#8 (fat in All Text and overload in All Text and syndrom* in All Text)
#9 (adipos* in All Text or obes* in All Text)
#10 ((body in All Text and mass in All Text and ind* in All Text) or (waist-hip in All Text and ratio* in All Text))
#11 (skinfold in All Text and thickness* in All Text)
#12 (abdominal in All Text and fat* in All Text)
#13 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12)

MEDLINE

I. Obesity/overweight
1 exp Obesity/ or exp Obesity, morbid/
2 exp Overweight/
3 (overweight$ or over weight$).tw,ot.
4 obes$.tw,ot.
5 1 or 2 or 3 or 4
II. Meta-analysis/health technology assessment report/systematic review
1 Meta-analysis.pt.
2 exp Technology Assessment, Biomedical/
3 exp Meta-analysis/
4 exp Meta-analysis as topic/
5 hta.tw,ot.
6 (health technology adj6 assessment$).tw,ot.
7 (meta analy$ or metaanaly$ or meta?analy$).tw,ot.
8 (search* adj10 (medical databas*or medline or pubmed or embase or cochrane or cinahl or psycinfo or psyclit or healthstar or biosis or current content*)).tw,ot
9 (systematic adj3 review*).tw,ot.
10 or/1-9
11 (comment or editorial or historical-article).pt.
12 10 not 11
I and II

EMBASE

I. Obesity/overweight
1 exp morbid obesity/ or exp obesity/
2 exp Overweight/
3 (overweight$ or over weight$).tw.
4 obes$.tw.
5 1 or 2 or 3 or 4
II. Meta-analysis/health technology assessment report/systematic review
1 exp "systematic review"/
2 meta analysis/
3 systematic review*.ti,ab.
4 Meta?nalys$.ti,ab.
5 Meta analys$.ti,ab.
6 Cochrane.ti,ab.
7 (MEDLINE and CENTRAL).ti,ab.
8 1 or 2 or 3 or 4 or 5 or 6 or 7
I and II

(*Continued*)

DARE
#1 MeSH descriptor: [Obesity, Morbid] explode all trees #2 MeSH descriptor: [Obesity] explode all trees #3 MeSH descriptor: [Overweight] explode all trees #4 overweight #5 over weight* #6 obes* #7 #1 or #2 or #3 or #4 or #5 or #6 Select references in "Other Reviews" and "Technology Assessments"
PsycINFO
1 exp Obesity/ 2 exp Overweight/ 3 (overweight$ or over weight$).tw. 4 obes$.tw. 5 1 or 2 or 3 or 4 6 *"Literature Review"/ 7 exp Meta Analysis/ 8 systematic review*.ti,ab. 9 Meta?nalys$.ti,ab. 10 Meta analys$.ti,ab. 11 Cochrane.ti,ab. 12 (MEDLINE and CENTRAL).ti,ab. 13 6 or 7 or 8 or 9 or 10 or 11 or 12 14 5 and 13
'My NCBI' alert service
("obesity"[MeSH Terms] OR "obesity"[All Fields]) OR ("overweight"[MeSH Terms] OR "overweight"[All Fields]) AND systematic[sb]

Appendix 2. Taxonomy of interventions and reviews mapped to intervention categories

Short description of intervention (no. of reviews)	Definition	Examples of interventions	Reviews mapped to this category
Intervention 1 ()			
Footnotes			

Appendix 3. Characteristics of included systematic reviews (I)

Characteristic Review ID	Date of search	Objectives	Inclusion criteria for 'Types of participants'	Interventions	Comparison interventions
Review 1					
Footnotes					

Appendix 4. Characteristics of included systematic reviews (II)

Characteristic Review ID	Settings	No. studies included (no. participants)	Outcomes reported (+)[a]	Summary of findings	Review limitations
Review 1					
Footnotes [a] "+" denotes that data were reported					

Appendix 5. Characteristics of excluded reviews

Characteristic Review ID	Short description of review	Reason for exclusion
Review 1		
Footnotes		

Appendix 6. Quality of evidence in Cochrane systematic reviews

Characteristic Review ID	Sequence generation assessed (% studies with low risk of bias)	Allocation concealment assessed (% studies with low risk of bias)	Blinding of participants and personnel assessed (% studies with low risk of bias)	Blinding of outcome assessors assessed (% studies with low risk of bias)	Incomplete outcome data assessed (% studies with low risk of bias)	Selective outcome reporting assessed (% studies with low risk of bias)	Other potential threats to validity assessed (% studies with low risk of bias)
Review 1							

(*Continued*)

Footnotes
[a] "+" denotes that data were reported

Appendix 7. AMSTAR ratings for each systematic review (I)

AMSTAR criterion Review ID	A priori design	Duplicate selection and extraction	Comprehensive literature research	Status of publication used as inclusion criterion	List of included/excluded studies provided
Review 1					

Footnotes
c/a: cannot answer; n: no; n/a: not applicable; y: yes

Appendix 8. AMSTAR ratings for each systematic review (II)

AMSTAR criterion Review ID	Study characteristics provided	Quality assessed and documented	Quality impacted conclusions	Appropriate methods for combining findings	Publication bias assessed	Conflict of interest stated
Review 1						

Footnotes
c/a: cannot answer; n: no; n/a: not applicable; y: yes

Appendix 9. Results by individual review

Characteristic Review ID	Intervention(s) and comparison(s)	Outcomes (P/S/NR)[a]	No. studies included (no. participants in included studies)	Results
Review 1				

Footnotes
[a] (P): primary outcome(s) of review; (S): secondary outcomes of review; (NR): not reported
CI: confidence interval; OR: odds ratio; RR: risk ratio

Appendix 10. Survey of authors providing information on included systematic reviews

Characteristic Review ID	Review author contacted	Review author replied	Review author asked for additional information	Review author provided data
Study 1	Y			

Footnotes
N: no; Y: yes

Appendix 11. AMSTAR measurement tool to assess the methodological quality of systematic reviews

AMSTAR[a] question	Operationalisation
1. Was an 'a priori' design provided?	The research question and inclusion criteria should be established before the conduct of the review
2. Was there duplicate study selection and data extraction?	There should be at least two independent data extractors and a consensus procedure for disagreements should be in place
3. Was a comprehensive literature search performed?	At least two electronic sources should be searched. The report must include years and databases used (e.g. CENTRAL, EMBASE and MEDLINE). Key words and/or MeSH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialised registers or experts in the particular field of study, and by reviewing the references in the studies found
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc
5. Was a list of studies (included and excluded) provided?	A list of included and excluded studies should be provided.
6. Were the characteristics of the included studies provided?	In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed, e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity or other diseases, should be reported
7. Was the scientific quality of the included studies assessed and documented?	'A priori' methods of assessment should be provided (e.g. for effectiveness studies if the author(s) chose to include only randomised, double-blind, placebo-controlled studies, or alloca-

(*Continued*)

	tion concealment as inclusion criteria); for other types of studies alternative items will be relevant
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	The results of the methodological rigour and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations
9. Were the methods used to combine the findings of studies appropriate?	For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi^2 test for homogeneity, I^2 statistic). If heterogeneity exists a random-effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?)
10. Was the likelihood of publication bias assessed?	An assessment of publication bias should include a combination of graphical aids (e.g. funnel plot, other available tests) and/or statistical tests (e.g. Egger regression test)
11. Was the conflict of interest stated?	Potential sources of support should be clearly acknowledged in both the systematic review and the included studies

Footnotes
[a] AMSTAR (a measurement tool for the 'assessment of multiple systematic reviews') operationalisation as published in Shea 2007. Possible answers to questions include 'Yes', 'No', 'Cannot answer' and 'Not applicable'

CONTRIBUTIONS OF AUTHORS

Marta Roqué i Figuls (MR): protocol draft, acquiring trial copies, trial selection, data extraction, data analysis, data interpretation, review draft and future review update.

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