Psychotherapy versus treatment as usual and other control interventions in children and adolescents with overweight and obesity: a protocol for systematic review with meta-analysis and Trial Sequential Analysis

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ABSTRACT
Introduction The prevalence of children with overweight and obesity is increasing worldwide. Multicomponent interventions incorporating diet, physical activity and behavioural change have shown limited improvement to body mass index (BMI). However, the impact of psychotherapy is poorly explored. This systematic review aims to assess the effects of psychotherapeutic approaches for children with all degrees of overweight.

Methods and analysis We will include randomised clinical trials involving children and adolescents between 0 and 18 years with overweight and obesity, irrespective of publication type, year, status or language up to April 2020. Psychotherapy will be compared with no intervention; wait list control; treatment as usual; sham psychotherapy or pharmaceutical placebo. The following databases will be searched: Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, MEDLINE, Embase, PsycINFO, PubMed, Web of Science, CINAHL and LILACS. Primary outcomes will be BMI z-score, quality of life measured by a validated scale and proportion of patients with serious adverse events. Secondary outcomes will be body weight, self-esteem, anxiety, depression and proportion of patients with non-serious adverse events. Exploratory outcomes will be body fat, muscle mass and serious adverse events. Study inclusion, data extraction and bias risk assessments will be conducted independently by at least two authors. We will assess risk of bias according to Cochrane guidelines and the Cochrane Effective Practice and Organisation of Care guidance. We will use meta-analysis and control risks of random errors with Trial Sequential Analysis. The quality of the evidence will be assessed using Grading of Recommendations Assessment, Development and Evaluation Tool. The systematic review will be reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Cochrane guidelines.

Ethics and dissemination As individual patient data will not be included, we do not require ethics approval. This review will be published in a peer review journal. PROSPERO registration number CRD42018086458.

INTRODUCTION
The prevalence of overweight is increasing worldwide both among children and adults irrespective of income.1–3 The rate of overweight in the paediatric population has risen worldwide over the last few decades4 despite significant resources being spent on reversing these trends. This widens health inequality, as the prevalence of children with overweight is higher in areas of social deprivation.5 Recent data from the WHO continues to show an increasing prevalence of children with obesity in Europe.5,6 The International Task Force of Obesity produced age-specific and sex-specific cut-off for the definition of overweight and obesity in children.5 Throughout
this paper, children and adolescents between 0 and 18 years will be referred to as children. Children with all degrees of overweight, including obese and morbidly obese, will be referred to as overweight in the remaining part of the paper.

Overweight has both short-term and long-term consequences on cardiovascular disease, type 2 diabetes, metabolic syndrome and cancer, resulting in a significant burden on health services across the world. The severity of these comorbidities typically increases with the severity of overweight. Mental health sequelae such as poor self-esteem, anxiety and depression may result in bullying, discrimination, long-term socioeconomic disadvantages and is often coupled with difficult family circumstances.

As such, psychological variables such as quality of life, self-esteem, life events, parental attitudes, eating disorders and anxiety need to be addressed in the long-term treatment of overweight and obesity. Psycho-education, cognitive behavioural therapy, solution-based therapy, including systemic therapy, and psychodynamic counselling are used.

Psychotherapeutic interventions

Psychotherapy is widely used in the management of children with overweight. It may support the child to change and maintain more weight-friendly habits while also potentially improving body image, self-esteem and social adaptation. Several types of psychotherapy are used in the treatment of children with overweight. Solution-focused brief therapy might be an effective modality for weight management in children through helping them to use their inner resources. Motivational interviewing appears to be a beneficial communication tool for initiating and maintaining healthy habits and weight reduction through self-help or self-determination. Family therapy is a form of systemic therapy, widely used to treat children with overweight, often as part of multicomponent programmes. Cognitive-behavioural therapy is a very widely used form of psychotherapy that has been used to treat children with overweight. Group psychotherapy is an alternative to individual programmes for supporting weight loss in teenagers. Interpersonal therapy is most commonly used to treat low mood, depression and disordered eating with studies showing indications of its efficacy in decreasing the weight gain in teenage girls with overweight. Finally, psycho-dynamic therapy emphasises the systematic study of the psychological drivers that underlie human behaviour, feelings and emotions associated with weight gain. Psychotherapeutic approaches thus seek to support the child and their parents towards a healthier weight in the child.

Systematic reviews on interventions

The effects of interventions for children with overweight have been analysed recently in Cochrane reviews. Quality of life was included in only two of these reviews, showing no effects in children after the end of intervention. A moderate improvement of health-related quality of life in the intervention groups was seen in older children (p=0.01), but the evidence was uncertain. In preschool children, multicomponent interventions showed reductions in body mass index (BMI) (p<0.00001) and improvements in some markers of quality of life.

Overall, systematic reviews have not shown that structured interventions in children with overweight are associated with an increased risk of depression or anxiety and may result in a mild reduction in symptoms. Similarly, a very recent systematic review demonstrated that paediatric obesity treatment improves self-esteem and body image in the short and medium term. These findings may underpin improvements in other psychological outcomes. However, a 5-year follow-up study in adolescents with morbid obesity who underwent bariatric surgery demonstrated no significant improvement in self-esteem. Potentially, a small proportion of participants may be at risk of developing worsening pathology, which clinicians should monitor, while treatment of weight concerns should be considered within treatment plans for young people with depression and obesity. Identification of these young people and provision of additional support may improve treatment outcomes while benefits to psychological well-being following treatment should be considered when assessing treatment success.

While previous reviews have commented upon the significant risk of bias in many studies, none of the earlier reviews have consistently assessed the risk of bias, the risk of random errors, or assessed the overall evidence certainty with Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Objective

The objective of this systematic review will be to assess the benefits and harms of psychotherapy versus no intervention in children with all degrees of overweight (including all levels of obesity); wait list control; treatment as usual; sham psychotherapy or pharmaceutical placebo. Benefits will include a reduction of BMI z-score or body weight and quality of life while harms will include developing eating disorders.

METHODS AND ANALYSIS

This systematic review protocol has been developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guidelines (online supplemental additional file 1). We will assess the beneficial and harmful effects of psychotherapy for in children with overweight taking risks of bias (systematic errors), risks of play of chance (random errors), type of psychotherapy and control interventions and GRADE assessments into consideration.
Criteria for considering studies for this review

Types of studies
Randomised clinical trials irrespective of language, publication status, publication type or publication year will be searched for and include benefits and harms. We will follow Population, Intervention, Control and Outcomes (PICO) criteria as per the Cochrane Handbook for Systematic Reviews of Interventions for inclusion and exclusion criteria. Eligible studies which are not published in English will be translated using Google translate. Authors will be contacted if necessary, for an English translation or for any clarification of their data. Data on harms from quasi-randomised studies, controlled clinical studies and other observational studies if retrieved from our searches for randomised clinical trials will be included. Such data will be described narratively as adverse events are rarely reported in randomised clinical trials while such observational studies may provide information on rare or late occurring adverse events.

Types of participants
All children who are overweight (including all levels of obesity) up to 18 years of age. We will also include randomised controlled clinical trials which include children and young adults below the age of 21 years. Children with associated co-morbidities, either physical or psychological secondary to overweight and obesity will be included.

Types of interventions
As the experimental intervention, we will include any type of solution-focused brief therapy, family therapy, cognitive behavioural therapy, interpersonal therapy or psycho-dynamic therapy as described in our introduction with the intention to treat children with overweight. The therapy can be delivered, face-to-face, either individually, delivered to parents only or in groups, in any setting. The control intervention can be no intervention; wait list control; treatment as usual; sham psychotherapy or pharmaceutical placebo.

There is no restriction as to who delivers the treatment or treatment duration. We will accept any co-intervention providing that they are planned to be delivered in similar fashion in both the experimental group and the control group.

Types of outcomes
We will assess all outcomes at baseline and then at two time points:

- End of intervention, as defined by trialist (our primary time point of interest).
- Maximum follow up.

Primary outcomes
1. BMI z-score (kg/m²).
2. Quality of life: as measured by a scale that has been validated for use in the target population.
3. Proportion of participants with one or more serious adverse events; that is, any untoward medical occurrence that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity.

Secondary outcomes
1. Body weight measured in kg.
2. Self-esteem.
3. Anxiety.
4. Depression.
5. Proportion of participants with at least one non-serious adverse event.

Exploratory outcomes
1. Body fat (%) measured by bioimpedance or dual energy X-ray absorptiometry.
2. Muscle mass (kg) via bioimpedance or dual energy X-ray absorptiometry.
3. Individual serious adverse events and individual adverse events not considered serious.

Search methods for identification of studies

Electronic searches
Searches will include literature up to April 2020. We will search the following databases: The Cochrane Library, MEDLINE, Excerpta Medica database (Embase), PsycINFO, Web of Science (SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC), CINAHL and LILACS. Examples of keywords used in the search strategy will include: obesity, overweight, psychotherapy, BMI, weight gain, weight loss, hyperphagia and systematic review. Controlled descriptors will be included using MeSH. A preliminary search strategy for MEDLINE is enclosed as online supplemental additional file 2.

Searching other resources
We will search for trials or ongoing studies on the following resources:

- ClinicalTrials.gov (http://www.clinicaltrials.gov).
- Google Scholar (https://scholar.google.com/).
- European Medicine Agency (http://www.ema.europa.eu/ema/).
- United States Food and Drug Administration (http://www.fda.gov).
- Medicines and Healthcare Products Regulatory Agency (https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency).
- The WHO International Clinical Trials Registry Platform (ICTRP) Search Portal (http://www.who.int/).
- Global Obesity Forum (previously International Association for the Study of Obesity) (http://www.iaso.org).
- European Association for the Study of Obesity (http://easo.org).

Keywords used in the search strategy

- Obesity.
- Overweight.
- Psychotherapy.
Data collection and analysis
Selection of studies
We will perform the review following the recommenda-
tions in the Cochrane Handbook for Systematic Reviews
of Interventions.69 The meta-analyses will be performed
using Review Manager and Trial Sequential Analysis
programme.67 68

At least two authors will independently screen titles and
abstracts using software Covidence,69. They will retrieve
all identified and relevant full-text publications after
which two authors will independently screen the full
text and identify and record reasons for exclusion of the
ineligible studies. Disagreement will be resolved through
discussion or by consulting a with a third author. Trial
selection will be displayed in an adapted flow diagram
as per the PRISMA statement. At least two authors will
extract data. Disagreement will be resolved by discussing
with a third author. We will assess duplicate publications
and companion papers of a trial together.

Data extraction and management
Data extraction will be performed by at least two authors
independently using software Covidence,69 who will both
compare the extracted data for primary, secondary and
exploratory outcomes. Disagreements will be resolved by
a third author. We will use Review Manager software to
extract data.64 For outcome data not reported in a usable
manner, we will present this in a table outlining the
characteristics of these studies using the following head-
ing: Methods, Participants, Interventions, Outcomes
and Notes described in chapter 4 (section 4.6.1) of the
Cochrane Handbook for Systematic Reviews of Interventions.66
Two review authors will independently transfer data into
the Covidence. Disagreements will be resolved through
discussion or by consulting a third author.

Assessment of risk of bias in included studies
The risk of bias of every included trial will be evaluated
independently by at least two authors. In case of any
disagreement, discrepancies will be discussed with a third
author and resolved by consensus. Risk of bias will be
assessed using Cochrane’s ‘Risk of bias’ assessment tool
and the Cochrane Effective Practice and Organisation of
Care Group’s guidance.70 71 We will evaluate the method-
ology in respect of:
► Random sequence generation.
► Allocation concealment.
► Blinding of participants and treatment providers.
► Blinding of outcome assessment.
► Incomplete outcome data.
► Selective outcome reporting.
► Other risks of bias.
► Overall risk of bias.

Classification of the trials will follow criteria defined in
online supplemental additional file 2.

Meta-analysis
Data will be meta-analysed using RevMan V.5 statistical
software.72 We will use STATA statistical software (STATA
2015) in case of zero event trials, where RevMan V.5 zero
event handling is insufficient.73 74

We will assess our intervention effects with random-
effects model meta-analyses and fixed-effect model meta-
analyses75–77 using the more conservative point estimate
of the two.78 Three primary outcomes will be examined
with p≤0.025 being statistically significant.78 An eight-
step procedure will be used to assess if the thresholds for
significance are crossed.78 Five secondary outcomes will
be examined with p≤0.017 being statistically significant.78
Analysis of the exploratory outcomes will be considered
hypothesis generating only. We will measure effect size
using standardised mean differences using CIs of 95%.
Analysis of all included studies will be compared with
a subgroup analysis comparing trials at low risk of bias
to trials at high risk of bias. If the results do not differ,
primary conclusions will be based on the overall analysis.
If the results differ, primary conclusions will be based on
trials at low risk of bias. A table describing the types of
serious adverse events in each trial will be provided.

Trial Sequential Analysis
Traditional meta-analysis runs the risk of random errors
due to sparse data and repetitive testing of accumulating
data when updating reviews. In order to control the risks
of type I errors and type II errors,57 58 79 Trial Sequential
Analysis will be conducted on the outcomes. In order to
do so, we will calculate the required information size (that
is the number of participants needed in a meta-analysis to
detect or reject a certain intervention effect).79

For continuous outcomes, we will in the Trial Sequen-
tial Analysis use the observed SD, a mean difference of
the observed SD/2, an alpha of 2.5% for our three
primary outcomes and an alpha of 1.67% for our five
secondary outcomes, and a beta of 10%.80 For dichot-
omous outcomes, we will use the proportion of partici-
pants with an outcome in the control group, a relative risk
reduction of 20%, and an alpha of 2.5% for our primary
outcomes and an alpha of 1.67% for secondary outcomes,
and a beta of 10%.80 We will calculate risk ratios with 95% CI
for dichotomous outcomes.

Subgroup analysis
In order to investigate and compare different trials and
interventions subgroup analysis will be performed on the
following:
► Trials at high risk of bias trials compared to trials at
low risk of bias trials.
Trial stratified according to experimental interventions.

Trials stratified according to weight status: overweight, obese or morbidly obese at the point of entry into the trial.5

Trials stratified according to the duration of intervention, the number of in person sessions and length of sessions in hours.81

Trials stratified if treatment fidelity was assessed or not.82

Trials stratified according to the control interventions.

Complexity: trials with participants with no co-morbidities compared to trials with participants pre-existing co-morbidities.

Trials in which the experimental intervention was evaluated by either the parents or the child after the treatment sessions had been delivered compared to trials in which the experimental intervention was not evaluated by either the parents or the child after the treatment sessions had been delivered.

We will use the formal test for subgroup interactions in Review Manager.72

Sensitivity analysis

To assess the potential impact of the missing data for dichotomous outcomes, we will perform the following sensitivity analyses.

‘Best–worst case’ scenario: we will assume that all participants lost to follow-up in the experimental group had no serious adverse events, including not developing any psychiatric disease such as an eating disorder.

‘Worst–best case’ scenario: we will assume that all participants lost to follow-up in the experimental group, had a serious adverse event, for instance, developing a psychiatric disease such as an eating disorder.46

Statistical heterogeneity will be assessed by visual inspection of the forest plots and I² statistic values.78 Underlying reasons behind statistical heterogeneity in meta-analyses will be investigated by assessing trial characteristics.

Summary of findings table

A summary of findings table using each of the prespecified primary outcomes will be presented using GRADE considerations for studies contributing data to the meta-analyses for the prespecified outcomes.78 83–96 Methods and recommendations described in chapter 8 (section 8.5) and chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions60 using GRADEpro software will be used.

DISCUSSION

This protocol intends to outline a rigorous, methodical approach to developing a systematic review to provide evidence on the potential effects of psychotherapy as an intervention for children with overweight. The protocol has been registered on PROSPERO and through peer review and publication aims to reduce the risk of bias in the future systematic review.

Currently, there is no comprehensive systematic review of psychotherapeutic interventions in the treatment of children with overweight to inform clinical practice. Previous systematic reviews in this population have considered behavioural interventions for lifestyle behaviour change as a mediating factor for weight loss initiation and maintenance.44 45 We will also be able to assess the different types of psychotherapeutic interventions as well as their individual comparison groups (no intervention; wait list control; treatment as usual; sham psychotherapy; or pharmaceutical placebo). This review will also highlight any gaps in the evidence base of such interventions which will help to shape the development and optimisation of future interventions.

ETHICS AND DISSEMINATION

No ethical approval required. Dissemination of results will be published in peer reviewed journals.

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Acknowledgements The authors would like to thank Sarah Louise Klingenberg, Information Specialist at the Copenhagen Trial Unit, Centre for Clinical Intervention Research for her guidance and assistance on developing search methods and keywords for search strategies.

Contributors IL, RR, LC, CG, JCJ and JL wrote the first draft of the protocol. RR, IL, JCJ, CG, LC and JL have revised the protocol. All authors critically reviewed and approved the manuscript. IL is the guarantor of the review.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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