

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	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
AUTHORS	Rashid, Rajeeb; Condon, Laura; Gluud, Christian; Jakobsen, Janus; Lindschou, Jane; Lissau, Inge

VERSION 1 – REVIEW

REVIEWER	Serena Broccoli Local Health Authority of Reggio Emilia, Italy
REVIEW RETURNED	18-Dec-2019

GENERAL COMMENTS	<p>It was my pleasure to review this well-written protocol. Treatment of overweight and obesity in children is a topic that is of great interest. Below are my suggestions and questions that I hope will help to clarify some issue.</p> <p>ABSTRACT</p> <ol style="list-style-type: none"> 1) Are there date limits for the search? What are they? 2) You should specify also in the abstract what you mean for "overweight" but I encourage you to follow the suggestion at point 8). 3) Can you better explain what you mean with "body weight"? variation in body weight? 4) I suggest changing "quality of life" in "quality of life measured by a validated scale". 5) "We will assess risk of bias through eight domains": not clear. <p>STRENGTHS AND LIMITATIONS</p> <ol style="list-style-type: none"> 6) Add a point to explain the strengths to publish a systematic review protocol. 7) "A comprehensive search strategy will be used with a large number of databases searched": This point is needless as you previously declared that you are following Cochrane methodology. <p>MAIN TEXT</p> <ol style="list-style-type: none"> 8) I found it confusing to use the term overweight for overweight and obese children. Moreover, I suggest considering them separately in the analysis. They are completely different conditions and I suspect that the same intervention could affect them differently. 9) "Systematic reviews on interventions": this paragraph is mainly concentrated on the effect of intervention (psychotherapy in general?) on quality of life. What about all other outcomes? I suggest reorganizing the paragraph by intervention and outcome.
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	<p>10) Line 125: "In this systematic review, 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 control interventions, and GRADE assessments into consideration." This sentence should be written in methods section, not in introduction.</p> <p>11) "Criteria for Considering Studies for this Review": I strongly recommend using PICO strategy for defining inclusion and exclusion criteria of the studies (The Cochrane Collaboration. Chapter 5: Defining the review question and developing criteria for including studies. In: Higgins JPT, Green S, eds. Cochrane handbook of systematic reviews. Version 5.0.1: The Cochrane Collaboration, 2008.).</p> <p>12) I suppose that all outcomes (primary and secondary) are measured as variation from end of the study and baseline. Is this correct? Please, make it clearer.</p> <p>13) Justify why you consider body weight measure as primary outcome. In a pediatric population it is strongly recommended to use standardized measures (BMI z-score) to define weight conditions. This is a strong limit of the protocol. In my opinion you should exclude studies that use variation in body weight in kg to investigate the effect of intervention. Weight in children must grow up, even if they are overweight.</p> <p>14) "Exploratory outcomes": contextualize in introduction.</p> <p>15) "Electronic searches": are there date limits for the search? What are they?</p> <p>16) "Keywords used in the search strategy": please specify if you use also controlled descriptor (such as MeSH term) or not, and if not why.</p> <p>17) "Data extraction and management": specify which variables you will collect.</p> <p>18) Line 246: Add reference for "Review Manager software"</p> <p>19) Line 247: You cited the 'Characteristics of included studies' table. Describe better.</p> <p>20) "Meta-analysis": Clarify how do you measure effect size by outcome variable (RR? Standardized mean difference? Other?)</p> <p>21) "Subgroup analysis": age? sex? overweight/obesity...?</p> <p>22) "Discussion": Add a paragraph that justify the publication of the study protocol and discuss limits.</p>
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REVIEWER	Andrew Hill University of Leeds, UK
REVIEW RETURNED	24-Jan-2020

GENERAL COMMENTS	<p>Just a few issues to consider:</p> <ol style="list-style-type: none"> 1. "psychotherapy used in the treatment of children with overweight" appears several times. But it's not clear what the purpose of this treatment is. Will the authors distinguish interventions that are used to reduce weight from those whose primary intention is to address psychological distress or comorbidity? Given that body weight is a primary outcome then should the search be restricted to psychotherapeutic interventions directed at weight loss? Should not reporting body weight be a study exclusion criterion? 2. P.4. Brief therapy describes its duration rather than content (c.f. low intensity). It feels at odds with the other therapy types listed. 3. P.6. The study objective includes "assess the benefits and harms." It would be more accurate to state that the review will assess effects on body weight and quality of life.
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	<p>4. P.8. Do the authors mean self-esteem rather than "self-efficacy"? Relatively few studies examine self-efficacy.</p> <p>5. Do the authors intend the sub-group analyses to include comparison of different types of psychotherapy (as listed in the introduction), by age, by gender, by extent of overweight etc.?</p>
REVIEWER	Meghan M JaKa HealthPartners Institute, USA
REVIEW RETURNED	07-Feb-2020
GENERAL COMMENTS	<p>This is a very through, well-written and carefully designed protocol of great importance to the field. The primary critique is a lack of description related to how and if the elements of psychotherapy within interventions will be evaluated or analyzed (eg, behavior change techniques). Some additional considerations are provided below:</p> <ul style="list-style-type: none"> • Appreciate the authors' inclusion of quality of life and adverse events as a primary outcome. However it is notable that intermediate outcomes, behaviors and determinants are largely not included. This should be justified. Further, the authors note 'self-efficacy' as an outcome, but this is more commonly characterized as a psycho social-determinant of behavior and authors should specify for what behavior self-efficacy is related to. It is also of note that authors include depression and anxiety as target outcomes rather than potential moderators of treatment effectiveness. A case can be made for this, but authors should discuss whether or not they will test these as potential moderators as well. • Authors should provide a more robust description of how treatment fidelity will be assessed and whether and how it will be included in analyses. • Other points of critical importance to the field are the types of behavior change strategies used within these psychotherapy applications using standardized language. Authors should specify whether or not they will track and use this in describing the interventions and analyzing their impact. • The authors used appropriate, respectful terminology to describe study participants in the title and methods, but not done consistently in the abstract or introduction. It is also unusual and slightly confusing to readers to include children with obesity in the nomenclature of children with overweight. Clarity would be improved by stating children with overweight or obesity throughout. • State that multi-component interventions have been successful at addressing overweight abstract, but that is an overstatement of the success of interventions across the field particularly for obesity prevention efforts. • Specify in the abstract that this is also a meta-analysis • Interesting that selection of body weight as the primary outcome, but the abstract discusses the effectiveness of programs on BMI. This should be justified or aligned. • Authors note that it likely that many papers will not provide sufficient details without communication with corresponding authors. An a priori description of the planned methods for outreach would improve this manuscript. • Authors should specify why additional a secondary analyses such as whether treatment effects differ by weight status were not included

	<ul style="list-style-type: none"> • Many of the psychological variables mentioned could be put in social, environmental context (eg, use of psycho-social terminology when appropriate). • Some details in the abstract do not match the body of the manuscript (eg use of Google Scholar as a database, following PRISMA and/or Cochrane guidance)
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VERSION 1 – AUTHOR RESPONSE

Reply to Reviewer: 1

Reviewer Name: Serena Broccoli

Institution and Country: Local Health Authority of Reggio Emilia, Italy

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below

It was my pleasure to review this well-written protocol. Treatment of overweight and obesity in children is a topic that is of great interest. Below are my suggestions and questions that I hope will help to clarify some issue.

Reply: We are happy that the reviewer liked our protocol and found the topic of great interest. Thank you.

ABSTRACT

1) Are there date limits for the search? What are they?

Reply: Thank you for your comments. Our search will be up to April 2020. Line 36

2) You should specify also in the abstract what you mean for "overweight" but I encourage you to follow the suggestion at point 8).

Reply: Thank you for your comments. Due to word limitations in the abstract, we have sought to define our use of the term "overweight" within the introduction. We thus include the terms overweight and obesity in the abstract. Line 35

We aim to maintain Coles et al's definition of all degrees of overweight and obesity (ref.8) but use the "defined" terminology to improve the reading flow of the paper. Line 80

3) Can you better explain what you mean with "body weight"? variation in body weight?

Reply: Thank you for your comments. Within the paper we have changed our primary outcome to BMI z-score, moving body weight - change in body weight during intervention – to secondary outcomes. Line 40, Line 193

4) I suggest changing "quality of life" in "quality of life measured by a validated scale".

Reply: We have accepted and changed the manuscript as requested. Line 40

5) "We will assess risk of bias through eight domains": not clear.

Reply: We have accepted and changed the manuscript as requested. Line 45

STRENGTHS AND LIMITATIONS

6) Add a point to explain the strengths to publish a systematic review protocol.

Reply: We have accepted and changed the manuscript as requested. Line 57

7) "A comprehensive search strategy will be used with a large number of databases searched": This point is needless as you previously declared that you are following Cochrane methodology.

Reply: We have accepted and changed the manuscript as requested. Line 57

MAIN TEXT

8) I found it confusing to use the term overweight for overweight and obese children. Moreover, I

suggest considering them separately in the analysis. They are completely different conditions and I suspect that the same intervention could affect them differently.

Reply: Many thanks for your comments. We have defined the term overweight for overweight and obese children within the abstract and the introduction. We accept with your suggestion and have added a subgroup analyses as regards degree of overweight. We will perform subgroup analyses according to whether the participant at entry to the trial are overweight, obese, or morbidly obese. Line 80, Line 328

9) "Systematic reviews on interventions": this paragraph is mainly concentrated on the effect of intervention (psychotherapy in general?) on quality of life. What about all other outcomes? I suggest reorganizing the paragraph by intervention and outcome.

Reply: Thank-you for your comments. We have expanded the paragraph to also include Self-esteem, anxiety, and depression and have included the following references (46-48). Line 124.

- Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of Pediatric Obesity Treatment, Including a Dietary Component, With Change in Depression and Anxiety: A Systematic Review and Meta-analysis. *JAMA pediatrics*. 2019:e192841.
- Gow ML, Tee MSY, Garnett SP, Baur LA, Aldwell K, Thomas S, et al. Pediatric obesity treatment, self-esteem, and body image: A systematic review with meta-analysis. *Pediatric obesity*. 2020;15(3):e12600.
- Jarvholm K, Bruze G, Peltonen M, Marcus C, Flodmark CE, Henfridsson P, et al. 5-year mental health and eating pattern outcomes following bariatric surgery in adolescents: a prospective cohort study. *The Lancet Child & adolescent health*. 2020;4(3):210-9.

10) Line 125: "In this systematic review, 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 control interventions, and GRADE assessments into consideration." This sentence should be written in methods section, not in introduction.

Reply: We have accepted and changed the manuscript as requested. Line 151

11) "Criteria for Considering Studies for this Review": I strongly recommend using PICO strategy for defining inclusion and exclusion criteria of the studies (The Cochrane Collaboration. Chapter 5: Defining the review question and developing criteria for including studies. In: Higgins JPT, Green S, eds. *Cochrane handbook of systematic reviews*. Version 5.0.1: The Cochrane Collaboration, 2008.).

Reply: Thank you for our comments. We accept your comments and have changed the manuscript to highlight the use of PICO criteria as per Cochrane Handbook of Systematic Reviews. Line 159

12) I suppose that all outcomes (primary and secondary) are measured as variation from end of the study and baseline. Is this correct? Please, make it clearer.

Reply: Yes, many thanks for the clarification. We have changed the manuscript as recommended. We will compare outcomes at the stipulated times between the two groups according to the Cochrane Handbook. Line 187

13) Justify why you consider body weight measure as primary outcome. In a pediatric population it is strongly recommended to use standardized measures (BMI z-score) to define weight conditions. This is a strong limit of the protocol. In my opinion you should exclude studies that use variation in body weight in kg to investigate the effect of intervention. Weight in children must grow up, even if they are overweight.

Reply: Thank-you for your valuable comments. We have changed the manuscript as requested with BMI z-score becoming a primary outcome and body weight becoming a secondary outcome. Line 193, Line 201

14) "Exploratory outcomes": contextualize in introduction.

Reply: We have accepted and changed the manuscript as requested. Line 43

15) "Electronic searches": are there date limits for the search? What are they?

Reply: Many thanks for your comments. Our searches will be up until April 2020. Line 215

16) "Keywords used in the search strategy": please specify if you use also controlled descriptor (such as MeSH term) or not, and if not why.

Reply: We have accepted and changed the manuscript as requested. Line 220

17) "Data extraction and management": specify which variables you will collect.

Reply: Thank you for your comments. We have accepted and changed the manuscript with data extracted for primary, secondary, and explanatory outcomes. Line 265

18) Line 246: Add reference for "Review Manager software"

Reply: We have accepted and added the reference as requested. Line 267

19) Line 247: You cited the 'Characteristics of included studies' table. Describe better.

Reply: Thank-you for your comments. We have clarified the characteristics that we will use in the table using the following headings Methods, Participants, Interventions, Outcomes and Notes as per Cochrane Handbook for Systematic Reviews of Interventions, Chapter 4.6.1 (ref 66). Line 269

20) "Meta-analysis": Clarify how do you measure effect size by outcome variable (RR? Standardized mean difference? Other?)

Reply: Thank-you for your comments. Standardized mean difference is described in the paragraph on meta-analysis. Line 301

21) "Subgroup analysis": age? sex? overweight/obesity...,?

Reply: Thank you for your comments. We have added subgroup analysis for trials stratified according to weight status: overweight, obese, or morbidly obese at the entry to the trial. Our aim through subgroup analysis is to investigate and compare different trials and interventions as per Cochrane Handbook for Systematic Reviews of Interventions, Chapter 9.6.2 . Line 328

22) "Discussion": Add a paragraph that justify the publication of the study protocol and discuss limits.

Reply: We have accepted and added the reference as requested. Line 364

Reviewer: 2

Reviewer Name: Professor Andrew Hill

Institution and Country: University of Leeds, UK

Please state any competing interests or state 'None declared': None.

Please leave your comments for the authors below

Just a few issues to consider:

1. "psychotherapy used in the treatment of children with overweight" appears several times. But it's not clear what the purpose of this treatment is. Will the authors distinguish interventions that are used to reduce weight from those whose primary intention is to address psychological distress or comorbidity? Given that body weight is a primary outcome then should the search be restricted to psychotherapeutic interventions directed at weight loss? Should not reporting body weight be a study exclusion criterion?

Reply: Thank you for your comments. The focus on the intervention effect of psychotherapy will be on all degrees of overweight in children. We include all studies with this aim. We will not exclude studies, who did not use body weight as a primary or secondary outcome. We will report these as trials with missing data. Otherwise, how shall we be able to evaluate the potential risks of outcome reporting bias?

2. P.4. Brief therapy describes its duration rather than content (c.f. low intensity). It feels at odds with the other therapy types listed.

Reply: Thank you for your comments. We accept the need for further clarification. We now refer to brief therapy as solution-focused (brief) therapy, which is a goal-directed collaborative

approach to psychotherapeutic change. This is conducted through direct observations of the child's responses to constructed questions. Line 100, Line 176

3. P.6. The study objective includes "assess the benefits and harms." It would be more accurate to state that the review will assess effects on body weight and quality of life.

Reply: Thank you for your comments. We assess "benefits and harms" as per Cochrane recommendation. Benefits will include a reduction of BMI z-score or body weight whilst harms would include developing eating disorders. The protocol has been developed according to Cochrane Handbook guidelines. Line 142

4. P.8. Do the authors mean self-esteem rather than "self-efficacy"? Relatively few studies examine self-efficacy.

Reply: Thank you for your comments. We agree and accept the use self-esteem rather than self-efficacy and have changed this within the manuscript. Line 42, 91, 202

5. Do the authors intend the sub-group analyses to include comparison of different types of psychotherapy (as listed in the introduction), by age, by gender, by extent of overweight etc.?

Reply: We will perform the subgroup analyses as describe in the updated section "subgroup analyses". This will include trials stratified for experimental intervention which refer to different types of psychotherapy as well as for different weight groups, overweight, obese, and morbidly obese. We have not included age or sex in the analysis as to our knowledge there is no evidence that age or sex affect the effects of different types of psychotherapy. Line 323

Reviewer: 3

Reviewer Name: Meghan M JaKa

Institution and Country: HealthPartners Institute, USA

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

This is a very through, well-written and carefully designed protocol of great importance to the field.

The primary critique is a lack of description related to how and if the elements of psychotherapy within interventions will be evaluated or analyzed (eg, behavior change techniques).

Reply: We thank the reviewer for these very positive and stimulating comments. We will deal with the primary critique below.

Some additional considerations are provided below:

1 Appreciate the authors' inclusion of quality of life and adverse events as a primary outcome. However it is notable that intermediate outcomes, behaviors and determinants are largely not included. This should be justified. Further, the authors note 'self-efficacy' as an outcome, but this is more commonly characterized as a psycho social-determinant of behavior and authors should specify for what behavior self-efficacy is related to. It is also of note that authors include depression and anxiety as target outcomes rather than potential moderators of treatment effectiveness. A case can be made for this, but authors should discuss whether or not they will test these as potential moderators as well. A case can be made for this, but authors should discuss whether or not they will test these as potential moderators as well.

Reply: Thank you for your comments. The aim for this protocol for a systematic review explore the efficacy of psychotherapeutic interventions on children with overweight/obesity rather than lifestyle. Previous reviews explore the effect of different lifestyle including diet and physical activity which is not the goal of our review. Oude Luttikhuis et al. – Cochrane Systematic Review 2019 on "Interventions for treating obesity in children" looked at lifestyle interventions in treating children but found no significant changes. Therefore, they are not included.

We have referenced systematic reviews by Colquitt, Al-Khudairy and Mead (ref 43-45) describing quality of life. Line 117

We have now changed self-efficacy to self-esteem as suggested by yourself and other reviewers. Moreover, we have expanded on systematic reviews on anxiety and depression as outcomes (ref 46-48). Line 124

We agree that it does make sense to include moderators of treatment effectiveness as duration of intervention, the number of in person sessions, and length of session in hours. We include these variable in the assessment of different kinds of psychotherapy and have included this reference (82): Heerman WJ, JaKa MM, Berge JM, Trapl ES, Sommer EC, Samuels LR, et al. The dose of behavioral interventions to prevent and treat childhood obesity: a systematic review and meta-regression. The international journal of behavioral nutrition and physical activity. 2017;14(1):157. Line 330

Of course, depression and anxiety etc. can be effect modifiers during the trial. However, that is why we are looking at randomised clinical trials assuming that the severity of anxiety and depression will be equally distributed in the compared groups. According to The Cochrane Handbook we use include these variables as secondary outcomes. Moreover, if one need to assess their impact on treatment effects one need to assess these variables on a regular basis during the trials and this calls for another design. We are primarily interested in pragmatic trials assessing the effects of psychotherapy and not in exploratory trials assessing the effects of modifiers. The simple explanation is that we need to establish treatment benefits before it really becomes interesting to examine modifiers of these benefits.

2 Authors should provide a more robust description of how treatment fidelity will be assessed and whether and how it will be included in analyses.

Reply: Many thanks for this constructive suggestion. We will include treatment fidelity and have included a further subgroup analysis to assess if treatment fidelity is included in the assessment of the intervention and will include this paper in the revised version.

We have referenced this within the revised paper (Reference 83) Line 332

- JaKa MM, Haapala JL, Trapl ES, Kunin-Batson AS, Olson-Bullis BA, Heerman WJ, et al. Reporting of treatment fidelity in behavioural paediatric obesity intervention trials: a systematic review. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2016;17(12):1287-300.

We accept the importance of knowing what is going on in the 'black box' in intervention of paediatric obesity.

3 Other points of critical importance to the field are the types of behavior change strategies used within these psychotherapy applications using standardized language. Authors should specify whether or not they will track and use this in describing the interventions and analyzing their impact.

Reply: We have not planned to analyse specific behaviour change strategies but rather compared the effects of different psychotherapeutic approaches as mentioned above. This review is focused on different modes of psychotherapy rather than on behaviour change strategies. Again, we are primarily interested in pragmatic trials assessing the effects of psychotherapy and not in exploratory trials assessing the effects of modifiers. The simple explanation is that we need to establish treatment benefits before it really becomes interesting to examine modifiers of these benefits.

4 The authors used appropriate, respectful terminology to describe study participants in the title and methods, but not done consistently in the abstract or introduction. It is also unusual and slightly confusing to readers to include children with obesity in the nomenclature of children with overweight. Clarity would be improved by stating children with overweight or obesity throughout.

Reply: Thank you for your comments. We have sought to define our use of the term "overweight" within the introduction. We aim to maintain Coles et al.'s definition of all degrees of overweight and obesity (ref.8) but use the "defined" terminology to improve the reading flow of the paper. We have attempted to provide a consistent respectful tone throughout the paper. Line 80

5 State that multi-component interventions have been successful at addressing overweight abstract, but that is an overstatement of the success of interventions across the field particularly for obesity prevention efforts.

Reply: Thank you for your comments. We have adjusted the language as suggested. Line 30, Line 120

6 Specify in the abstract that this is also a meta-analysis

Reply: Thank you for your comments. We have changed the title to include meta-analysis. Line 3

7 Interesting that selection of body weight as the primary outcome, but the abstract discusses the effectiveness of programs on BMI. This should be justified or aligned.

Reply: Thank you for your comments. We have now adjusted the primary outcome from body weight to BMI z-score which we believe is more in keeping with measurements in children and in keeping with the effectiveness of interventions on BMI. Line 193

8 Authors note that it likely that many papers will not provide sufficient details without communication with corresponding authors. An a priori description of the planned methods for outreach would improve this manuscript.

Reply: Thank you for your comments. We have included a description of our planned methods for outreach. Line 162

9 Authors should specify why additional a secondary analyses such as whether treatment effects differ by weight status were not included

Reply: Thank you for your comments. We have clarified secondary analysis based on weight status - overweight, obese, and morbidly obese. Line 328

10 Many of the psychological variables mentioned could be put in social, environmental context (eg, use of psycho-social terminology when appropriate).

Reply: The different intervention and modifiers can likely be put in a variety of social and environmental and social frames, but we are not sure this will help the readers.

11 Some details in the abstract do not match the body of the manuscript (eg use of Google Scholar as a database, following PRISMA and/or Cochrane guidance)

Reply: Thank you for your comments. Due to limitations in the abstract word count we have highlighted additional resources searched in the main body of the text. Line 223

VERSION 2 – REVIEW

REVIEWER	Serena Broccoli Local Health Authority of Reggio Emilia, Italy
REVIEW RETURNED	28-May-2020
GENERAL COMMENTS	Thank to the authors, the updated manuscript is much improved on the previous version. I have no other comments.
REVIEWER	Andrew Hill University of Leeds, UK
REVIEW RETURNED	01-May-2020
GENERAL COMMENTS	Please use person first language throughout the paper: children with obesity rather than obese children

VERSION 2 – AUTHOR RESPONSE

Reply To Reviewer: 1

Reviewer Name: Serena Broccoli

Institution and Country: Local Health Authority of Reggio Emilia, Italy

Please state any competing interests or state 'None declared':

none declared

Please leave your comments for the authors below.

Thanks to the authors, the updated manuscript is much improved on the previous version. I have no other comments. best regard, Serena

Reply: We are grateful for your previous suggestions which we feel greatly improved the manuscript. We are glad that our changes have met with your approval.

Reply to Reviewer: 2

Reviewer Name: Andrew Hill

Institution and Country: University of Leeds, UK

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below:

Please use person first language throughout the paper: children with obesity rather than obese children

Reply: Thank you for your comments. We have adjusted the manuscript to ensure the terms such as “children with obesity/overweight” rather than “obese/overweight children” are used throughout.