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ARTICLE DETAILS

| TITLE (PROVISIONAL) | Prevalence of Obesity in Attention-Deficit/Hyperactivity Disorder: Study Protocol for a Systematic Review and Meta-Analysis |
|---------------------|----------------------------------------------------------------------------------------------------------------|
| AUTHORS             | Cortese, S; Moreira Maia, Carlos; Rohde, Luis; Morcillo-Penalver, Carmen; Faraone, Stephen |

GENERAL COMMENTS

The present article describes a protocol of a systematic review and meta-analysis aimed at assessing the prevalence of obesity/overweight in individuals with vs. those without ADHD. The article is clearly written and the methods are fully described with sufficient details.

In my opinion this systematic review, if completed successfully, may represent a substantial contribution in the field. I have no major points to raise. However, the authors might want to consider the following minor points.

(1) The “study type” section (page 7) is not 100% clear to me, as it reports that “case series without control group… will be excluded”. As reported, this sentence may induce to think that other types of studies without control group will be included, which is not true, as later in the text (last line of page 7) it is reported that a comparison group of participants without a diagnosis of ADHD must be present. My suggestion is to report clearly in the “study type” section that studies without a control group will be excluded, if this is the case.

(2) I wonder what the impact of excluding studies without a control group (i.e. studies without a comparison group of participants without a diagnosis of ADHD) might be: I’m not an expert of these studies but I would expect several epidemiological studies calculating the prevalence of obesity in ADHD without a control group. The authors might want to reason on whether this exclusion criterion might systematically exclude a relevant proportion of prevalence studies. One possible approach would be to include these studies which may contribute to a meta-analysis of point prevalence rates, which would give a summary estimate of prevalence of obesity in ADHD; a second meta-analysis might then be carried out including studies with control group in order to assess if the prevalence is significantly higher in individuals with ADHD compared to those without.

(3) The last two lines of page 14 report that “Meta-analyses of both unadjusted and, where available, adjusted odds ratios (by the study authors, to control for confounding variables) will be carried out..."
using random-effects models”. I would suggest rephrasing this sentence to make it clear that, if available, adjusted risk estimates will be extracted and analysed. This is of paramount relevance as the included studies are observational in design. A related issue is whether the authors would consider to add a sentence on other measures, such as for example RR or HR, that original studies might have used to express this association? Would the authors lump together OR with RR and HR? I guess it may depend on how frequent or rare the outcome variable is. 

(4) A very interesting protocol.

REVIEWER
Carol Curtin
University of Massachusetts Medical School
USA

REVIEW RETURNED
20-Jan-2014

GENERAL COMMENTS
Thank you for the opportunity to review this manuscript. This paper proposes a protocol for conducting a systematic review/meta-analysis to assess the prevalence of overweight & obesity in children and adults with ADHD. This is an important topic and a quantitative approach (via metaanalysis) to the issue would be helpful in resolving some of the conflicting extant literature. The manuscript is well-written and clear, but I am uncertain as to the utility of a paper that describes a proposed method, especially when the method does not seem to depart significantly from methods typically undertaken in such endeavors. The approach described herein should be included in the paper that is eventually published from this endeavor; however, as a stand-alone paper, it almost reads like a grant proposal. Thus, in its current form it does not seem to add substantially to a body of knowledge. I do, however, very much look forward to reading about the study that the authors propose to undertake, and believe that it will make an important contribution to the field.

VERSION 1 – AUTHOR RESPONSE

Reply to Reviewer # 1

The present article describes a protocol of a systematic review and meta-analysis aimed at assessing the prevalence of obesity/overweight in individuals with vs. those without ADHD. The article is clearly written and the methods are fully described with sufficient details. 

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We thank the Reviewer for this note and we agree with this remark. We have replaced “All original,
peer-reviewed studies, independently from the design will be considered. However, cases series without control group and studies with less than ten subjects per arm will be excluded (due to low statistical power)” with “All original, peer-reviewed studies with a control group, independently from the design (excluding case series and case studies), will be considered”.

(2) I wonder what the impact of excluding studies without a control group (i.e. studies without a comparison group of participants without a diagnosis of ADHD) might be: I’m not an expert of these studies but I would expect several epidemiological studies calculating the prevalence of obesity in ADHD without a control group. The authors might want to reason on whether this exclusion criterion might systematically exclude a relevant proportion of prevalence studies. One possible approach would be to include these studies which may contribute to a meta-analysis of point prevalence rates, which would give a summary estimate of prevalence of obesity in ADHD; a second meta-analysis might then be carried out including studies with control group in order to assess if the prevalence is significantly higher in individuals with ADHD compared to those without.

The Reviewer raises a very relevant issue. In our view, given the high heterogeneity in the prevalence of obesity according to country/geographical region, pooling the point prevalence rates would be poorly informative and its clinical as well as public health implications would not be clear. We think that pooling odds ratios from each study comparing obesity rates in ADHD vs controls, which, thus, takes country/geographic location into account, is more relevant in terms of public health implications. We have added: “We will exclude studies without control group since, given the high heterogeneity in the prevalence of obesity according to country/geographical region, pooling the point prevalence rates of obesity without a comparison to a control group would be poorly informative and its clinical as well as public health implications would not be clear.”

(3) The last two lines of page 14 report that “Meta-analyses of both unadjusted and, where available, adjusted odds ratios (by the study authors, to control for confounding variables) will be carried out using random-effects models”. I would suggest rephrasing this sentence to make it clear that, if available, adjusted risk estimates will be extracted and analysed. This is of paramount relevance as the included studies are observational in design. A related issue is whether the authors would consider to add a sentence on other measures, such as for example RR or HR, that original studies might have used to express this association? Would the authors lump together OR with RR and HR? I guess it may depend on how frequent or rare the outcome variable is.

We thank the Reviewer for these thoughtful recommendations. We have added : “If available, adjusted risk estimates will be extracted and analysed.” (pag 15).

Regarding RR and HR, the consensus of the authors was that we will run parallel analyses should these be available, although, based on a scope search, we expect that ORs will be the only reported measure in most papers. We have added “If available, RR and HR will be extracted and addressed in parallel analyses” (pag 15).

(4) A very interesting protocol.

We thank the Reviewer for this positive comment.

Reply to Reviewer #2

Thank you for the opportunity to review this manuscript. This paper proposes a protocol for conducting a systematic review/meta-analysis to assess the prevalence of overweight & obesity in children and adults with ADHD. This is an important topic and a quantitative approach (via metanalysis) to the issue would be helpful in resolving some of the conflicting extant literature. The
manuscript is well-written and clear, but I am uncertain as to the utility of a paper that describes a proposed method, especially when the method does not seem to depart significantly from methods typically undertaken in such endeavors. The approach described herein should be included in the paper that is eventually published from this endeavor; however, as a stand-alone paper, it almost reads like a grant proposal. Thus, in its current form it does not seem to add substantially to a body of knowledge. I do, however, very much look forward to reading about the study that the authors propose to undertake, and believe that it will make an important contribution to the field.

We appreciate the Reviewer's interest in the topic of our proposed meta-analysis. We felt that it is important to publish the protocol of our meta-analysis as recommended by the authoritative Cochrane Group, according to which “Publishing protocols is a crucial element …to help avoid unplanned duplication of reviews and minimise the risk of bias by making the production of reviews transparent.” (Cochrane Handbook, Chapter 1). We are pleased that important journals, such as BMJ Open, encourage the submission of protocols of planned meta-analyses.