Author’s response to reviews

Title: Prevalence and comorbidity of attention deficit hyperactivity disorder in Spain: a study protocol for extending a systematic review with updated meta-analysis of observational studies

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Author’s response to reviews:

Madrid, 4 January 2019

Alexandra Maria Bodnaruc
Associate Editor
Systematic Reviews

Dear Editor,

We thank you for having recently shared peer review on our protocol manuscript entitled: “(SYSR-D-18-00366) Prevalence and comorbidity of attention deficit hyperactivity disorder in Spain: a study protocol for extending a systematic review with updated meta-analysis of observational studies” for publication in Systematic Reviews.

Along with this letter you will find a summary of our point-by-point responses to deal with reviewers’ (minor) comments. We have uploaded the revised manuscript and shown modifications using yellow highlighting to facilitate verification.

We thank you for your interest in our work and we look forward to hearing from you.
Sincerely yours,

Ferrán Catalá-López, on behalf of the rest of coauthors

Reviewer 1: Darren William Roddy

This protocol aims to investigate the epidemiology of ADHD through metaanalysis of pooled prevalence data in Spain.

Overall the protocol looks comprehensive, and considering this research team has already published a previous metaanalysis of ADHD in Spain in 2012 (BMC Psychiatry 12(1):168), the protocol quite rightly follows most of the methods outlined in that previous paper. This protocol aims to expand this by including a) studies since 2013 b) adult ADHD, and c) comorbidities. This is a worthwhile effort.

The actual protocol looks fine.

Authors’ response:

Thank you very much for your kind comments and for your time to review our manuscript.

A few minor points to improve the paper...

Why are you doing this now - apart from newer data extraction techniques and new studies in other countries - e.g. more emphasis on comorbidities in the literature maybe? Changes in diagnostic criteria since 2012?, better ADHD awareness in Spain?

Authors’ response:

Thank you for your comments. In the introduction section (p. 3), we report the following reasons for conducting an update extending our previous systematic review: “In 2011, members of our review team conducted a meta-analysis of ADHD prevalence in Spain from 14 observational studies and more than 13,000 children and adolescent participants (...). The 2011 review results drew attention in particular to ADHD among children and adolescents, but did not include aspects such as comorbidity or adult population. In addition, overall findings were limited by clinical and methodological heterogeneity. In recent years, several (new) epidemiological studies have been conducted in different geographical locations and population groups. In addition, methods have advanced quickly, planning data extraction and analyses, and understanding of the review process have become more sophisticated. Therefore, we consider it timely to update and expand on our previous systematic review and meta-analysis with much more detailed analysis of relevant data.”
In addition, in methods section (p. 4), we acknowledge the following: “This study protocol is part of an ongoing evidence synthesis project on the descriptive epidemiology and surveillance of neurodevelopmental disorders (such as autism spectrum disorder).”

Where does Spain sit in the ADHD prevalence continuum (6.8% in your previous metanalysis seemed on the high end; what explanation was there for this? - better services in Spain compared to other countries maybe?

Authors’ response:

Thank you for this comment. In the introduction section (p.3), we acknowledge the following: “Recent prevalence estimates suggest that ADHD affects about 3–7% of young people worldwide [18-23], producing considerable impact on health services and the community [18,24,25]. However, prevalence estimates of ADHD within and between countries often vary widely [19,20,26], and reports of increases in prevalence further fuel the controversy [19].”

In our previous review, we discussed some of these topics, and concluded: “Our findings suggest that the prevalence of ADHD among children and adolescents in Spain is consistent with previous studies conducted in other countries and regions”. Further explanations together with most up-to-date ADHD estimates will be provided in the final manuscript with final results.

What specific co-morbidities are expected? Can you reference other studies that look at comorbidities in ADHD in other countries, as a guide for what comorbidities you may be looking for? Are these comorbidities expected to differ between childhood and adult ADHD?

Authors’ response:

Thank you for this comment. As per our protocol (methods section, p.5), secondary outcomes will be the prevalence of any comorbidity, indicating the existence of any distinct additional (physical or mental) condition in association with ADHD (e.g. according to main DSM-IV or ICD-10 categories of diagnoses).

Therefore, all (physical or mental) comorbidities reported in individual studies are potentially eligible for the analysis, irrespective of age or sex.

In references 5 and 6, we report references to other studies that look at comorbidities in other countries. Please, see:


There is some evidence that adult ADHD is more like ADD. Will you also be including ADD in your analysis (children and adults)?

Authors’ response:

Thank you. Attention-deficit disorder (ADD) and attention-deficit hyperactivity disorder (ADHD) are indeed the same condition. ADHD has had several name changes in the last three decades. ADHD is now the “official name” of this disorder. However, many people still use the term ADD, which was the formal name from 1980 to 1987.

There have been subtle changes in the diagnostic criteria from DSM IV to V for ADHD. Are these expected to alter the prevalence of ADHD? Also, one very minor point, you mention just DSM IV in the data collection section, but then include DSM V in the data analysis section. By the way, I like the analysis by "most recent diagnostic system" angle.

Overall however, this protocol seems fairly comprehensive.

Authors’ response:

Thank you so much for this comment. We have revised the manuscript including “DSM-V”, and “ICD-11” (as suggested).

Reviewer 2: Ram Bajpai

Authors have well written the protocol however, following minor points should be addressed to improve the quality of their manuscript:

Authors’ response:

Thank you so much for your comment.

1. There is no mention of searching unpublished research or the grey literature e.g., government reports, that also contributing to potential missing out on relevant and important data to include.

Authors’ response:

Thank you for this comment. In methods section (p.4), we report we will search unpublished research or the grey literature, as follows: “(…) The secondary source of potentially relevant material will be a search of the grey or difficult to locate literature, including two dissertation databases (TESEO – Base de datos de Tesis Doctorales [Spanish Data Base of Doctoral Thesis Dissertations] and ProQuest Dissertations and Theses Database), Google Scholar and conference abstracts from selected national or local symposia on mental health, neurology and paediatrics. We will perform hand-searching of the reference lists of included studies, relevant reviews, national clinical practice guidelines or other relevant documents. Content experts and authors who are prolific in the field will be contacted.”
We have edited the manuscript to include: “official documents and government reports”.

2. Authors have mentioned that in case of missing outcome data, the primary study authors will be contacted. However, it is not clear that what mode of contact will be used and how many times.

Authors’ response:

Thank you for this comment. We have revised our manuscript to clarify this point, as suggested:

“Authors of primary publications (e.g. corresponding authors) will be contacted by email for data clarifications or missing outcome data, as necessary. First, authors will be sent an email requesting their missing outcome data or data clarifications. Second, we will send three email reminders at 2-, 6-, 10-week intervals after the initial email. In cases where the identified studies do not report authors’ email addresses or include non-working email addresses, we will search authors’ publications, PubMed, and profiles that are publicly available (e.g. ORCID, ResearchGate and Google Scholar), to find contact information.”

3. In case of using non-validated tools, it may be considered as other risk of bias while assessing RoB. It may also be considered for in subgroup analysis (i.e., validated vs. non-validated) of substantial number of studies are available.

Authors’ response:

Thank you for this suggestion. As per our protocol (methods section, p.6): “(t)he risk of bias in individual studies will be evaluated using a methodological quality critical appraisal checklist proposed by the Joanna Briggs Institute (JBI) systematic review methods manual [37,38]. This tool for observational studies reporting prevalence data considers: sample representativeness, recruitment appropriateness, sample size, description of subjects and setting, coverage of data analysis, ascertainment and measurement of the condition, thoroughness of reporting statistical analysis, and identification and accountability of potential confounding factors/subgroups (see Additional file 3).” We pre-planned a subgroup analysis considering risk of bias (see p.7).

4. Authors should also report about publication bias separately in a subheading. Here, you can describe about funnel (of course, if number of studies allowed to do so) plot and its asymmetry tests.

Authors’ response:

Thank you for this comment. We have included a subheading “Meta-bias” in methods p.7 (as per PRISMA-P checklist):
Meta-bias

Small study effects (or “publication bias” across studies) will be assessed by inspection of the funnel plots for asymmetry and with Egger’s test [49] and Begg’s test [50], with the results considered to indicate potential small study effects when P values < 0.10.

5. There is no mention about the influence and outlier analysis in protocol. A priori statement may be useful if applicable during the analysis.

Authors’ response:

Thank you for this comment. We did not plan (a priori) to conduct an influence or outlier analysis. However, as we discuss in p.8: “Any amendments made to this protocol when conducting the study will be outlined and reported in the final manuscript.”

6. It also desirable to mention about the agreement analysis (such as kappa statistic) between the two reviewers who mainly involved in the data collection.

Authors’ response:

Thank you for this suggestion. We will consider this in our manuscript reporting the final findings.

7. Line 240-241, forest plots are also used to demonstrate the effect sizes (individual or pooled). So, need to correct this sentence.

Authors’ response:

Thank you for this comment. We have revised the manuscript, accordingly.