Reviewer's report

Title: Do Prescription Stimulants Increase the Risk of Adverse Cardiovascular Events?: A Systematic Review

Version: 4 Date: 2 March 2012

Reviewer: Sanne A. E. Peters

Reviewer's report:

The authors have made major changes based on the reviewers’ comments. Issues and suggestions with regard to the current version of the paper are described below:

Abstract
The abstract requires some textual revision as sentences are not smoothly written and as the results section includes references which is unusual for abstracts. Also, the conclusion does not reflect the result from the study but is rather a recommendation for future studies. Which conclusions can be drawn from the present investigation?

Introduction
The revised introduction, although still lengthy, is much more to the point than it was before. However, a key issue which is not clearly described is why stimulants are used at all. In the end of the introduction section, there is a hidden sentence saying that they are you to promote weight loss, but a clear rationale for the use of stimulants is required in the beginning of the introduction section.

Methods
The authors describe that ‘Studies were assessed for bias at both the study and outcome levels. Catchment, comparison groups, exposure and outcome ascertainment, statistical power and methodologies were assessed.’ How was this done? There exist widely used checklists to assess the quality of observational studies. Was any of these used? Please check the Cochrane collaboration for their current recommendations.

Results
The results section is very lengthy. It is strongly recommended to just describe the results of each separate study without describing the limitations of each study very extensively. This may be done in the discussion section, or a table may be included describing the strengths and limitations of each study separately. Such overview would be much easier to interpret than the current lengthy description. Such table could be combined with a quality appraisal of each study as suggested above.

The last sentence of the results section: ‘Neither report by Habel and colleagues included data on individuals 65 years or older, who might be expected to be
those at highest potential risk of adverse cardiac events. ‘ should be moved to the discussion section and some references should be provided to support this hypothesis.

The authors provided sufficient additional references to further explain the potential mechanism through which stimulants may elevate cardiovascular disease risk. However, not being an expert in the field, it is still difficult to understand the mechanisms through which stimulants act based on the description provided by the authors. As the paper is lengthy, it may be beneficial to make two papers out of it. One describing evidence on the potential mechanisms through which stimulants may increase cardiovascular disease risk followed by a paper describing the actual evidence on this issue. Such approach would probably result in two papers both having a clear message and would avoid multiple messages and aims which the current paper has.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests