Reviewer's report

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

Version: 2 Date: 11 November 2011

Reviewer: Pim Langendijk

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Review report by PNJ Langendijk
On: Do prescription stimulants increase the risk of cardiovascular events? A systematic review
Authors: Arthur Westover & Ethan Halm.

Is the question posed by the authors well defined? Yes, relevant question and well defined
2. Are the methods appropriate and well described? Yes, appropriate description of methods and well described. Authors do also state clearly the limitations of their work.
3. Are the data sound? Yes
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes
6. Are limitations of the work clearly stated? Yes, see also answer 2.
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes, because they systematically review the literature on this topic they should come across all the relevant work that addresses this problem. In reading the manuscript I clearly get the impression the authors did concordingly so, but because of this methodology they do not address unpublished data. That is fine with me.
8. Do the title and abstract accurately convey what has been found? Yes
9. Is the writing acceptable? Yes

Remarks of reviewer

• I have no serious remarks on methods, results and interpretation by the authors. The work seems sound and to the point. The only remark I can make as a non-US /North American resident that the authors do address the topic mainly on the US continent, use US data and literature. In Europe this topic is also increasingly addressed, but has not yet gained as much attention as in the US. This can be due to differences between US and European society and health care organisation.
This topic is relevant since stimulants like amphetamines and amphetamine-like-drugs (like methylphenidate) have become routinely prescribed in ADHD or other attention disorders (such as ADD). From the history and data of similar drugs used in obesity and weight loss we can anticipate cardiovascular risks, especially since adults are prescribed these drugs in increasing amounts. Pharmacological knowledge hypothesizes that routinely using these types of drugs will have drawbacks. For instance the amphetamine class of drugs increases heart rate and this will have effects on life expectancy and increases risk on cardiac arrhythmias. This report gives a good insight in what has been published in the literature on this topic. It’s methodology is thorough and the interpretation of data is good and descriptive.

Publication of this work increases our understanding on what has been published in this field. The author’s conclusion, namely that the question of the presence of and magnitude of an association between prescription stimulant use and adverse cardiovascular outcomes remain unanswered, is of value. To my understanding this is mainly because the data reviewed are usually not strong enough to detect adverse cardiovascular outcomes. This on itself is a valuable contribution to our knowledge, since mainly anecdotal and authority based reports have warned prescribers and users (parents) for these risks.

Apparently, the incidence of adverse cardiovascular outcomes are too low to be detected in large databases. This is also a valuable contribution to existing knowledge

Leiden, November 11, 2011
Pim Langendijk

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