Reviewer’s report

Title: Aspirin for primary prevention of cardiovascular disease: a meta-analysis with a particular focus on subgroups

Version: 0 Date: 30 May 2019

Reviewer: Safi Khan

Reviewer's report:

I read meta-analysis of Gelbenegger and colleagues with great interest. While, over all this is a well written and well conducted analysis, I have certain concerns:

1. Recently two quality Meta analyses, Zhen SL et al (JAMA 2019) and Mahmoud et al (EHJ 2019) have shed light on this topic with similar conclusions. I am not sure if this current report will add any novel information to the prior well performed meta analyses.

2. The new ACC/AHA primary prevention guidelines have restricted the role of aspirin in very limited population. The ESC guidelines were already against the use of this medication. Therefore, findings of this meta-analysis are unlikely to challenge these recommendations.

3. Using PubMed only for search is an insufficient strategy. Authors should have searched at least two search engines to avoid publication bias.

4. Results should be reported in accordance with primary outcome followed by secondary outcomes. This pattern should be consistent in abstract and throughout the manuscript.

5. Authors did not define all-cause mortality and cardiovascular mortality as secondary outcomes. All outcome measures should be clearly reported. In my opinion, mortality is the most robust endpoint and should be primary outcome instead of MACE as later is a composite endpoint.

6. The concept of net clinical benefit is informative and strong point of this paper. That said, the conclusions drawn using this information don’t add any further information to the literature.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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