Reviewer's report

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

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Reviewer: Samuel Seidu

Reviewer's report:

The reviewers, explore the use of aspirin in primary prevention of cardiovascular disease. Even though the topic has been thoroughly investigated in randomised control trials and meta-analyses, I believe there are still a lot of need for clarification. Hence I believe this is a very important study. In general the article is very well written and the methodology is standard.

Suggestions: to authors: The strength of the review is in the subgroup analyses. The main story of the effect of aspirin and MACE or bleeding, has been clearly answered in various trials, but not the various subgroups. The finding of the interaction with statins to improve benefit is an important finding. In a recent publication by Seidu et al, 2019 in individual patient level data analysis showed no significant evidence of an effect of aspirin on any of the outcomes evaluated; however, aspirin reduced the risk of MACE in non-smokers 0.70 (0.51-0.96) with a NNT of 33 (95% CI 20 to 246) to prevent one MACE. Therefore it will be advisable for the authors to analysis the subgroups of smokers to see if they can corroborate this finding. It may well be the case that aspirin is only beneficial in primary prevention of CVD in the setting of a multifactorial intervention such as in steno-2. This could change the narrative.

Also, I will recommend the authors to double check their calculations of the NNT. From my calculations, it seems the figures they have provided are a tenth of what they should be, (may need to multiply by 10 to get the correct figures. By definition, the NNT is the reciprocal of the Absolute risk reduction. Therefore, for example on page 7 line 44, "The annual ARI was 0.077% and the NNH was 1.295". I think this should be 12.987.

The events prevented/cause in 10,000 (I guess the authors meant 10,000) aspirin treated patients over one year seem confusing and the derivation of these should be explained. How is that different from the NNT supplied?

Minor, I will recommend the authors to read through the manuscript again and correct the grammatical errors. For example Line 38 on page 2 should read "On the contrary", not "In contrary"
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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