Reviewer’s report

Title: Predictors for major cardiovascular outcomes in stable ischaemic heart disease (PREMAC): Statistical analysis plan for data originating from the CLARICOR (clarithromycin for patients with stable coronary heart disease) trial

Version: 0 Date: 26 Oct 2016

Reviewer: Bilal Majed

Reviewer's report:

This is an interesting paper which aims to investigate new predictors for several cardio-vascular events in a future publication. Paper writing is clear-cut and concise presenting a database yielded from a previous clinical trial. The authors exposed planned selection strategy to test new predictors’ reliability and efficiency.

Authors may consider following remarks regarding mainly methods issues:

- it would be important to report and clarify pathophysiological mechanisms and/or prior findings related to selected new predictors

- since more than 10 predictors will be tested in time-to-event analyses using 5 endpoints, p-values threshold should be corrected to the value of $0.001 = 0.05/ (12*5)$ due to multiple testing

- additional tools to C-index can be used to assess discrimination ability such as net reclassification improvement (NRI); Kerr KF, Wang Z, Janes H, McClelland RL, Psaty BM, Pepe MS. Net reclassification indices for evaluating risk prediction instruments: a critical review. Epidemiology. 2014 Jan;25(1):114-21. doi:0.1097/EDE.0000000000000018. Review. PubMed PMID: 24240655; PubMed Central PMCID: PMC3918180.

- Statistical analyses should be stratified using sex, as in main CVD risk equations, which may also be used in the present study depending on the outcome of interest (Wong ND. Epidemiological studies of CHD and the evolution of preventive cardiology. Nat Rev Cardiol. 2014 May;11(5):276-89. doi: 10.1038/nrcardio.2014.26. Review. PubMed PMID: 24663092.)

- In sensitivity analyses, tough authors planned to use cox models given the data (time-to-event), competing risks cases in related to death events should be considered (depending on the outcome of interest).
Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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