Author's response to reviews

Title: The comparative effectiveness of statin therapy in selected chronic diseases compared with the remaining population

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Version: 3 Date: 2 July 2012

Author's response to reviews: see over
Dear Prof Lotufo

Re: 2142139658647609 The comparative effectiveness of statin therapy in selected chronic diseases compared with the remaining population

Thank you very much for your letter of 21st May 2012. We enclose a revised manuscript with major changes highlighted in red. We also include a point-by-point response to the reviewer’s comments and hope that the revised paper is now suitable for publication.

We look forward to hearing from you.

Yours sincerely,

Dr Li Wei on behalf of co-authors
Reviewer's report
Title: The comparative effectiveness of statin therapy in selected chronic diseases compared with the remaining population
Version: 2 Date: 1 May 2012
Reviewer: Gabriel Chodick
Reviewer's report:
The authors have adequately revised their manuscript.
With regard to comment 3 under Minor Essential Revisions, the authors may mention the availability of medical data since as early as 1989 in the text.

Answer: We thank for the reviewer’s comment and mentioned it in the text.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
'I declare that I have no competing interests'

Reviewer's report
Title: The comparative effectiveness of statin therapy in selected chronic diseases compared with the remaining population
Version: 2 Date: 29 April 2012
Reviewer: G. B. John Mancini
Reviewer's report:
This is a revised manuscript and many of the critiques have been addressed.
Major Compulsory Revisions:
In my view, the emphasis in this paper remains problematic, given all the limitations of knowing why both baseline TC and TC in response to statins is heterogeneous. These discussions are of some importance but are eclipsed by the outcome data and the potential, clinical implications or the latter. Moreover, the heterogeneous effects of standardized dose SIMVA may also be affected by the type of lipid abnormality heterogeneity in differing disease states (eg DM often has low LDL/highTG/lowHDL which is not captured by a focus on TC; the dyslipidemia of CKD is also variable, showing for LDL a "J-curve" with respect to severity and, in some analyses, an inverse relationship with LDL.....also factors affecting the authors' primary focus on TC and TC changes). Furthermore, the issue of pleiotropism of statins, particularly in patients with chronic inflammatory diseases and the impact on outcome (not TC) is a very controversial and important area of current debate. Thus, the emphasis and focus in this paper creates a lost opportunity to add some very credible data to the outcome debates.

Answer: We take the reviewer’s comments and added this discussion to the manuscript.

The use of the terms "incident" and "prevalent" as opposed to staying true to the PP and SP terminology was only partly corrected up until page 9 of the paper. In this respect, much of the difficulty in reading the paper also stems perhaps from the excessive end-points. If one were to focus on the APTC end-point as an aggregate of the commonly expected vascular benefits of statins, and the all-cause mortality outcome, as an indication of benefits beyond lipid lowering, then perhaps the paper could be simplified and the most compelling messages regarding clinical implications could be focused.
Answer: We appreciate the reviewer’s comment. However, the present study was a comparison of effectiveness of statin therapy in different disease populations. Therefore the results may not be simple and clear as a single study. We think that providing more information on outcome will help readers to understand the relationship between statins and diseases in detail.

Instead of giving primary focus on the figures pertaining to TC, this paper should give primary focus to figures showing APTC outcomes and all-cause mortality outcomes in PP and SP settings. These figures should indicate which are significant (as has been done by bolding in the current tables...the current tables showing all 5 outcomes could be included in the appendix). These changes in focus could allow the authors to develop a more important discussion and a more mature discussion focused on controversies in outcome benefits, how these results vary from existing (UK) guidelines, where new RCT's are required etc etc In essence, these changes were requested previously but were only partially addressed in this version. These comments are provided humbly and in the spirit of constructive criticism that will most assuredly lead to an article with greater impact among practitioners.

Answer: We have added four forest plots to the manuscript and moved Table 2 to the appendix 2 as the reviewer suggested. However, we prefer to keep the primary outcome of TC change as it stands. This is because TC change was the primary outcome and APTC endpoint was the secondary outcome in the protocol. We feel that to change the primary outcome at publication stage is not scientifically robust. However, we would be happy to be guided by the editor at this matter.

Level of interest: An exceptional article
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.