Reviewer’s report

Title: Deprescribing Preventive Cardiovascular Medication in Patients with Predicted Low Cardiovascular Disease Risk in General Practice - The ECSTATIC Study: A Cluster Randomised Non-inferiority Trial

Version: 0 Date: 06 Nov 2017

Reviewer: Cara Tannenbaum

Reviewer's report:

The authors should be commended for conducting this bold pragmatic, cluster randomized controlled trial on deprescribing antihypertensive and cholesterol-lowering medication for primary prevention in low risk patients. The study answers a critical question about the feasibility and value of stopping (and not starting) medication for primary prevention of cardiac disease in middle aged men and women followed in GP clinics. The authors reasonably conclude that based on the pragmatic nature of the trial, the uptake of such an intervention would be low, and is likely to lead to increased intermediate endpoints of elevated blood pressure and lipid profiles in a significant number of patients who undergo a trial of deprescribing. Although the effect on cardiac risk prediction scores is negligible among those who successfully deprescribe, indicating non-inferiority in this approach compared to usual care, there are no quality of life or cost effectiveness advantages.

Minor suggested edits to improve the clarity of the manuscript:

1) The intro should end after the objective statement on Page 5, line 15. The authors could add a sentence about their hypothesis, but otherwise the rest of the information belongs in the methods section.

2) Page 7 under study design: this is where the information belongs regarding the choice of a cluster RCT design and non-inferiority trial.

3) Move the information on the choice of non-inferiority margin to the methods section under outcomes and/or sample size calculations.

4) Please define your analysis groups in the Methods section under data analysis, and not in the results section. Example: Participants in the intervention group were classified as those who did not attempt deprescribing, those who attempted but failed deprescribing, and those with successful deprescribing. You might want to re-label these three groups as No attempt, failed attempt and successful attempt sub-groups of the intervention arm. For consistency, the
control arm should be referred to as the control arm (not the usual care arm, since the no attempt sub-group in the intervention arm also followed usual care).

5) Under results: please indicate if interviews were conducted with any GPs assigned to the intervention group after the trial to better understand decisions for not attempting deprescribing.

6) Please add a paragraph in the discussion regarding the limitations of such high rates of missing data, the inability to objectively measure drug use via drug claim data (as opposed to self-report) and the difficulties of pragmatic trials for studying the efficacy of an intervention. Future research may include a better understanding of the barriers to attempting deprescribing in the intervention group.

7) The conclusions are sound. I wonder however, if deprescribing might be considered in the absolute lowest risk groups, based on the profile of successful deprescribers.

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

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

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