Author's response to reviews

Title: Revisiting the J shaped curve, exploring the association between cardiovascular risk factors and concurrent depressive symptoms in patients with cardiometabolic disease: Findings from a large cross-sectional study.

Authors:

Bhautesh Dinesh Jani (bhautesh.jani@glasgow.ac.uk)
Jonathan Cavanagh (jonathan.cavanagh@glasgow.ac.uk)
Sarah Barry (sarah.barry@glasgow.ac.uk)
Geoff Der (geoff.der@glasgow.ac.uk)
Naveed Sattar (naveed.sattar@glasgow.ac.uk)
Frances S Mair (frances.mair@glasgow.ac.uk)

Version: 5
Date: 4 September 2014

Author's response to reviews: see over
Dear Editor,

Thank you for considering the aforementioned manuscript for publication in *BMC Cardiovascular Disorders*. We would like to take up the offer of submitting a revised version of the manuscript. We would like to thank the member of the editorial board again for his useful comments on the revised manuscript.

"I think that, overall, the authors have been very responsive to the feedback provided. A few minor things may still need to be addressed:

? Perhaps the authors could just leave the title as descriptive as possible, by taking out the following "Revisiting the J shaped curve, exploring?"

Authors’ Response: Our preference would be to retain the title as: "Revisiting the J shaped curve, exploring the association between cardiovascular risk factors and concurrent depressive symptoms in patients with cardiometabolic disease: Findings from a large cross-sectional study." This is because we have indeed demonstrated that there is a J shaped curve, and there is a substantial literature on this topic. If we remove this from the title it will make it harder for researchers to identify our paper as one that looks at this phenomenon or for others conducting systematic literature review about the J-shaped curve phenomenon to identify a paper like ours that would be highly relevant to such a review. However, we would not want this to be a barrier to publication and will permit amendment if this is deemed essential.

? I am not particularly in favor of using the subtitles in the discussion as these do not add anything additional to the discussion, but are just referring to the essential ingredients of a discussion.

Authors’ Response: We have removed subtitles from the discussion section as suggested.

? Related to this prior comment, the limitations of a study usually are being described in the last but one paragraph, prior to the conclusion.

Authors’ Response: We have restructured the discussion section as suggested; the limitations are described prior to the conclusion section now.

? On page 16-17, the 2nd explanation provided for the extreme lower end values observed for cholesterol needs to be tempered. You can just simply state that the nature of this relationship will require further investigation to see whether the lower cholesterol values are a marker of another disease process (e.g. liver disease, malnutrition, leukemia,?), that may make patients also more vulnerable to experiencing depressive symptoms or whether it could be attributed to a potential side-effect of aggressive lipid management. Appropriate references for each of these 2 possibilities should also be added.

Authors’ Response: Thank you for your comments. We have made the following changes to the discussion section where we discuss the implication of our findings.

Changes to Manuscript (Discussion>4th Paragraph>Page 16): There are two potential implications of our findings. Firstly, if the association between extreme values of these risk factors with depressive symptoms in those with cardiometabolic disease is supported by prospective studies, then this
relationship could be used to identify those at “high risk” of depression. This would then offer a mechanism for targeting of depression screening in those with cardiometabolic disease. Secondly, these results need to be replicated using other datasets and also prospectively to further explain the nature and direction of the observed association between depressive symptoms and cardiovascular risk factor values. Such further investigation is necessary in order to determine whether the lower cardiovascular risk factors are merely markers of other disease processes (for example, low total cholesterol levels associated with malnutrition, liver diseases and haematological diseases) [44–46] that may make patients more vulnerable to experiencing depressive symptoms or whether it could be attributed to a potential side-effect of aggressive cardiovascular risk factor management [47–50].

The same applies for the conclusion. No implications should be provided for the way we are treating patients in terms of their lipid management based upon this study. Instead, we should encourage further research clarifying the nature of the observed associations.

Authors’ Response: Thank you for your comments. We have reworded the conclusion section and this does not have any reference to the way we are treating patients for lipid management.

Changes to Manuscript (Conclusion>Page19): In a general practice sample of patients with CHD, stroke, or diabetes, depressive symptoms were found to have a strong curvilinear association with SBP, BMI, and HbA1c; and a weaker curvilinear association with total cholesterol and DBP. Further investigation of these relationships is urgently needed to clarify the nature of these associations, in order to determine whether they have potentially important implications for clinical practice in relation to either risk stratification for depression or our approach to secondary prevention in individuals with cardiometabolic disease.

We look forward to hearing your decision on our revised manuscript in due course.

Yours sincerely