Author's response to reviews

Title: Epidemiological and economic burden of metabolic syndrome and its consequences in patients with hypertension in Germany, Spain and Italy; a prevalence-based model.

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

Thank you for sending us the reviewers comments on our paper entitled ‘Epidemiological and economic burden of metabolic syndrome and its consequences in patients with hypertension in Germany, Spain and Italy; a prevalence-based model’.

We have made some changes to the manuscript (highlighted in yellow) corresponding to the reviewers comments and below have given a point by point response to the issues raised.

**Reviewer 1**

*Comment 1*: Introduction: In this section, the rationale behind the conduction of the study on hypertensive patients with metabolic syndrome should be mentioned in greater detail. The specific reason as to why it is more important to study the epidemiologic and economic burden of MS in patients with hypertension should be stated considering that the other MS components like the lipid parameters and the glucose levels have a more direct role on the development of CVD. For instance the relative risks of other MS components in leading to diabetes and CVD could be compared with that of the relative risk of hypertension.

*Our response to comment 1*: We have outlined our rationale for assessing the epidemiology and economic impact of metabolic syndrome in patients with hypertension in the introduction by highlighting how when several risk factors cluster together in a patient with hypertension it doubles the risk of CVD and triples the risk of diabetes. We have now stressed this point further by adding the following sentence:

‘As there are 16 different conceivable combinations of risk factors that could be diagnosed as MetS not all can be weighted equally in terms of their impact on risk and for some combinations this increase in risk is controversial. However, what is known for sure is that the coexistence of hypertension disproportionately increases the risk of cardiovascular disease[1].’
Comment 2: Methods: As this study assesses the Epidemiological burden of MS in hypertensive patients, the actual criteria of 135/85 mmHg could have been used. Modifying it to 140/90 mmHg could have underestimated the actual prevalence of MS.

Our response to comment 2: We accept that using a higher threshold may have underestimated the actual prevalence of MS. However this higher threshold was used because all epidemiological publications and databases used to develop the model defined hypertension as blood pressure of $\geq 140/90$ mm Hg and second, because current European and U.S. guidelines use this definition as the treatment threshold for antihypertensive medication[2,3].

Comment 3: Only two references are provided for the prevalence of type 2 diabetes in the hypertensive population and costs (Ref. 30, 45). Is the prevalence mentioned in these references consistent with that of the other prevalence studies done on the same population?

Our response to comment 3: We purposefully kept the methods of this paper relatively short to allow for detailed reporting on the consequences of metabolic syndrome and their costs and to provide a more detailed discussion of the public health implications of the study. The rationale for the prevalence data chosen has been outlined previously in our methods paper of the model[4]. In this previous methods paper we reported:

‘The prevalence of type 2 diabetes estimated in our study (10% to 18%) was also compared to other studies in hypertension subjects and again comparable estimates were noted (7-17%) [5-10].’

Comment 4: It is mentioned in the methods section that “MS was indicated by the hypertensive individual having at least two other ATP III criteria”. But the ATPIII criterion classifies MS based on the presence of any three of the 5 risk factors. What about the MS patients who are not hypertensive? How is this discrepancy accounted for?

Our response to comment 4: Our paper is about the epidemiological and economic burden of metabolic syndrome and its consequences in patients with hypertension. Therefore our patient cohort in the model all had hypertension and our interest lay is assessing the prevalence of metabolic syndrome in this population and its associated cost. Given that all patients had hypertension (1 risk factor), then the requirement for classification of MetS indicated an additional two other risk factors.
Comment 5. As this study is being done in a population with MS, prescription of Lipid lowering drugs like statins, fibrates and other drugs like aspirin that could also bring down the blood pressure of patients (even if not directly) would be common. Considering that this study captures the cost of only antihypertensive medication how was the effect of other drugs on lowering of BP and their implication on the costs associated captured. If the authors consider the probability of such an impact to be nil or minimal, proper justification should be provided for the same.

Response to comment 5: We accept that in patients with hypertension and metabolic syndrome a proportion of those patients may be receiving other medication. Such medications in those patients with CVD were taken into account. These are detailed in the methods paper[4].

Comment 6. Results: Table 2 mentions only the number of events per 1000. The forecasted rise in the annual costs in percentages should be included in the table which would provide a better perception to the readers. Similarly in Table 1 also, the forecasted rise in the year 2020 should be expressed in percentages.

Response to comment 6: We felt that adding percentages to the tables would make them too busy, hence impeding interpretation. We have therefore put percentage increases into the text and referred to the table. For example:

‘By 2020, keeping costs set at 2008 prices, these annual costs of hypertension with MetS were forecast to rise by 59%, 179%, 157% in Germany, Spain and Italy respectively (table 2).’

Comment 7. Figure 3. The given title is “Prevalence of MetS in patients with hypertension; 2008 and 2020” but the figure shows the prevalence of individual components of MS in patients with hypertension. This should be corrected.

Our response to comment 7: This has been corrected to:

‘Prevalence of individual components of MetS in patients with hypertension; 2008 and 2020.’

Comment 8: Results: what about the costs associated with the consumption of special diet (low sodium, high saturated fat). Were they considered negligible or was the data not captured?
Response to comment 8: These data were considered beyond the scope of our evaluation and were not included in the epidemiological model.


Our response to comment 9: This has been corrected.

Comment 10. The discussion is too lengthy and can be shortened.

Our response to comment 10: As mentioned previously we purposefully kept the methods of this paper relatively short to allow for detailed reporting on the consequences of metabolic syndrome and their costs and to provide a more detailed discussion of the public health implications of the study. We therefore feel that shortening the discussion would detract from some of the policy implications being made in the paper.

Reviewer 2:

Comment 1: I have gone through the article and found it scientifically stimulating. The contents of the article are contemporary and will help the cardiologists in treating patients of metabolic syndrome. I strongly recommend early publication of this article.

We thank both reviewers for their comments and look forward to hearing from you about the outcome of our manuscript.

Yours faithfully,

Sue Langham, on behalf of all authors.


