Author’s response to reviews

Title: Generalizability of guidelines and physicians’ adherence. Case study on the JNC VI guidelines on hypertension

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PDF covering letter
We would like to thank the reviewer for the extensive and insightful comments to our paper. We do believe that the paper has been much improved after implementing the suggested modifications.

Below you find a point by point response.

1) The guidelines specify who should be considered for treatment… They are derived from systematic review and meta-analysis… to produce more generalisable evidence.
   We do agree on the statement that one of the key points of the guidelines is to define the “target” population, to which the recommendations should be applied. One of the assumptions of the study question was that the target population defined in the guidelines might be different from the population included in the studies upon which the guidelines base their recommendations. The reviewer argue that meta-analyses could overcome this problem by including evidence gathered from different samples. We do not agree on this issue. Meta-analyses are a useful tool to synthesize the evidence¹ and to improve the precision of the estimated measure of a given exposure/outcome association,² but not to improve generalisability. The statement that “a wide range of patients” was covered by the clinical trials is only partially true, since there are categories of people – such as the elderly – who are systematically excluded from clinical trials.³

2) Patients with controlled blood pressure were misclassified.
   This is an objective limitation of our study, and we acknowledge it in the discussion. Although the proportion of people whose high blood pressure was controlled by anti-hypertensive drugs was relatively low (10%), this bias potentially leads to an underestimation of the adherence to guidelines. It should be noted, however, our treatment rates are similar to those found in other studies in different settings.⁴ We reworded the paragraph in the limitations section.

3) Difficult to interpret the data without the underlying numerator and denominator data.
   The omission of the absolute number in the results was due to the sampling strategy of the National Health and Nutrition Evaluation Survey. This was a probability sample, and the proportion reported were obtained using weights that corrected for the different probability of being selected in this study.⁵ Therefore, reporting the actual number of cases would not yield to the correct proportion, while using the weighted number would be misleading for the reader. We corrected the text where necessary according to reviewer’s suggestion.

4) Table 3.
   People with treated hypertension and normal blood pressure values were excluded from the analysis. We clarified this in the first footnote of the table.
5) There is an inconsistency between the categories stated in table 1 and those assigned in the text.
   There was an error in the table, which has been corrected.

6) There is a possible source of bias is that the blood pressure to categorise patients has been measured at a single point in time.
   We added a sentence in the limitation section.

7) The conclusion on the types of drug treatment are difficult to interpret.
   We modified the discussion according to reviewer’s suggestion.

8) Table 3.
   We decided to use only a few inclusion/exclusion criteria. Actually, this was a conservative approach: had we used more criteria, we would have probably found a lower generalisability. The variability in trials’ generalisability was expected, but our point is that it is generally low. We were puzzled by the comment on the fact that VA I enrolled people younger than the population of our study, since we included people as young as 17.

9) It would be helpful to know the reason for exclusion.
   The reason for exclusion varied from study to study. However, the major determinants of the low generalizability of the trials were inclusion criteria (first column of table 1).

10) Methods on page 9. Target organ disease (coronary artery disease, cerebro-vascular diseases, renal failure) were taken into account in assigning the risk category. We apologize for the imprecision in the explanation. We modified the paragraph).

11) Non random sampling. We added a sentence in the methods explaining what NHANES is and how the population was sampled.

12) Statistical analyses. We added a paragraph to the limitation acknowledging the low precision of our estimates. When we reported the finding on the association between generalisability and adherence we made it clear that the confidence intervals were wide.

13) Underestimation of treatment rates. See point 2.

14) We changed the discussion in the section implying that basing treatment decision on risk levels is different than what is recommended by the JNC.

Reference List


(3) Gurwitz JH, Col NF, Avorn J. The exclusion of the elderly and women from clinical trials in acute myocardial infarction. JAMA 1992; 268:1417-1422.
