

11 February 2014

Dr. Jin-Lei Wang,
Director,
Baishideng Publishing Group Co., Limited.

Dear Dr. Wang,

Thank you for your comments on our previous manuscript, which was submitted as an invited topic highlight article (ID 02474367) to contribute the special issue celebrating the 6th anniversary of the *World Journal of Cardiology*.

Please find enclosed the edited manuscript in Word format (file name: 8233-Revised Manuscript.doc).

Title: Hypertension and medical expenditure in the Japanese population: review of prospective studies

Author: Koshi Nakamura, Tomonori Okamura, Katsuyuki Miura, Akira Okayama

Name of Journal: World Journal of Cardiology

ESPS Manuscript NO: 8233

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

#Editor

Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. For those references that have not been indexed by PubMed, a printed copy of the first page of the full reference should be submitted.

PMID (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>)

DOI (<http://www.crossref.org/SimpleTextQuery/>) (Please begin with DOI: 10.**)

We have added the PubMed citation numbers and DOI citation to the reference list and also listed all the authors.

Two references (References 3 and 19) have not been indexed by PubMed.

We are sending a printed copy of the first page of Reference 19.

We are not sending any printed copy of Reference 3, because this is a book written in Japanese.

<References>

#Reviewer No. 00608224

In this neatly written and soundly discussed manuscript by Nakamura and colleagues, the authors reviewed several articles published on prospective cohort studies that measured medical expenditure attributable to hypertension in community-dwelling populations in Japan. They convincingly demonstrated that medical expenditure was increased in relation to the degree of hypertension and that other concomitant cardiovascular risk factors like diabetes or smoking further increase these costs. As an another important finding the authors underpin Rose's theory that a large number of people exposed to a small risk may generate more cases than a small number exposed to high risk. These findings support current strategies to shift the entire population towards lower blood pressure levels.

Specific comments

The medical expenditures in the text as well as in the figures differ in both, currency and buying power. Therefore the authors should transfer all expenditures to US-\$ and correct them for their buying power, e.g. by using the Inflation Calculator of the US Bureau of Labor Statistics (http://www.bls.gov/data/inflation_calculator.htm).

Thank you for your suggestion. Although we acknowledge that the revision you recommend would help readers understand the results of the selected articles, we have

not carried out this revision. This is because our paper is a review paper and not an original research paper. We considered it was important to extract valuable information from the articles, and to provide it exactly without any modification. Otherwise, the publishers who retain the copyright of the article may complain of our modification of the results of the articles. As an alternative, we have listed the crude arithmetic mean and adjusted geometric mean for each of the categories and other necessary information in Figures 1a,b, 3a,b, and 4 a,b and also in the main text so that readers are able to transfer these values to US dollars and correct them for buying power.

<Line 168 on page 8>, <Line 203 on page 9>, <Line 309 on page 14>, <Figures 1a,b, 3a,b, and 4a,b>

#Reviewer No. 00608229

This is a well-conducted study presented as an elegant manuscript that highlights important aspects of the relationship between hypertension status and medical expenditure.

Several minor concerns need to be addressed.

1. The description of the medical insurance system of Japan in the Introduction section should be shortened.

Although we acknowledge the need to shorten the manuscript, we still consider that it is necessary to provide detailed information on the medical insurance system of Japan in order to understand the articles cited in the manuscript. Therefore, we have removed substantial parts of the description of the medical insurance system in Japan from the Introduction section of the revised manuscript, and inserted these sections as an Appendix at the end of the main text.

<Line 111 on page 5>, <Line 486 on page 21>

2. I wonder if the addition of the term “expenses” to the systematic search on Medline would yield more relevant results.

In accordance with this suggestion, we carried out an updated systematic search on Medline for relevant articles published between January 1966 and January 2014 using the text word “expense” in addition to the medical subject headings terms and text words we had used previously. This new search strategy identified further seven articles other than the 156 articles we had identified previously. However, none of the additional seven articles were considered as relevant to our study. We have therefore only revised the Search strategy and selection section in response to your suggestion.

<Line 123, 128, 130 and 143 on page 6>

3. Adjustment for confounding factors should be clarified with respect to the statistical method used.

For the Osaki NHI cohort study, we have described detailed information on adjustment for confounding factors in the statistical methods in the main text of the revised manuscript.

We had already provided relevant information in the Figure legends for the Shiga NHI cohort study and the latest large study.

The Ibaraki NHI cohort study did not use any statistical tests to adjust for confounding factors.

<Line 203 on page 9>

4. It would be useful for the readers if the authors provided a cumulative direct comparison between the pre-to-mild hypertension status and the more severe hypertension status in regard to medical expenditure, in order to put emphasis to the point they make in the Conclusions section. Otherwise, the whole concept could be considered as a self-fulfilling prophecy.

Thank you for your suggestion. Unfortunately, we did not find any such information in the selected articles and therefore could not address this suggestion. Because our paper is a review paper and not an original research paper we can only provide information included in the articles.

5. References 1-6 could be updated and merged to two references in total.

We have updated References 1-6 and merged to two references in total in order to shorten the manuscript. In addition, we merged several other references to decrease the number of references.

<Line 99 on page 5>

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

Sincerely yours,

A handwritten signature in black ink, reading "Koshi Nakamura". The signature is written in a cursive, flowing style.

Koshi Nakamura, MD, PhD

Department of Epidemiology and Public Health

Kanazawa Medical University