Author’s response to reviews

Title: Primary care patient willingness for genetic testing for salt-sensitive hypertension: a cross sectional study

Authors:

Masanobu Okayama (okayama@jichi.ac.jp)
Taro Takeshima (taro-tksm@jichi.ac.jp)
Ryusuke Ae (shirouae@jichi.ac.jp)
Masanori Harada (masa.harada@mac.com)
Eiji Kajii (kajieiji@jichi.ac.jp)

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Author’s response to reviews: see over
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Dear Prof Abdulbari Bener:
Deputy Section Editor
BMC Family Practice

Thank you for your email of September 25, 2013, regarding our manuscript, “Primary care patient willingness for genetic testing for salt-sensitive hypertension: a cross sectional study” (MS: 1332797415104617), and the valuable comments of the two reviewers. I attach here our revised manuscript as well as a point-by-point response to the reviewer’s comments described below. We have highlighted all changes in red color. We feel that the revised manuscript is a suitable response to the comments, and is significantly improved over the initial submission. We trust that it is now suitable for publication in BMC Family Practice. Thank you in advance for your kind consideration of this paper.

Sincerely,

Masanobu Okayama M.D., Ph.D.
Division of Community and Family Medicine
Center for Community Medicine, Jichi Medical University
3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan
E-mail: okayama@jichi.ac.jp
Responses to the reviewer’s comments;
Referee 1;
Comment 1:
Hypertension is a prevalent and potent risk factor for future cardiovascular disease (CVD) (1), and control of hypertension in the general population, despite recent improvements, remains at about 50%. The link between sodium intake and blood pressure is strong (2), particularly in the subset of patients whose hypertension is “salt-sensitive.” Although there are many sources for the shortfall in blood pressure control, patients’ awareness, attitudes and behaviors contribute significantly.

In an effort to assist in identifying individuals who would benefit from future therapies, Okayama et al sought to determine the willingness of patients to undergo genetic testing for salt-sensitivity in a primary care population. The study design was cross-sectional and employed a questionnaire for self-reporting by outpatients. They found that half their patients would chose genetic testing, which was a function of age>50 years (y), educational level, family history of hypertension, and concern or “worry” about high blood pressure.

The authors note the “promise of personalized medicine, with the potential to enhance human health through more effective prevention” and suggest that “primary care physicians should provide patients with advice on genetic testing, as well as address their anxieties and concerns related to developing hypertension.”

Response 1:
I appreciate you kindly reviewing our manuscript and providing the constructive remarks. I would like you to confirm the changes highlighted in the red color.

Comment 2:
Major revisions
The broader subject of this paper—identification and personalization of patients at high risk for intensive therapy—is highly relevant. The purpose and methods in this study are clearly stated. The paper would be enhanced if the discussion were expanded to put the findings in perspective. True, the promise of personalized medicine is early identification of high-risk individuals prior in order to target therapy and prevent clinical expression of disease. A cogent, specific, and directed statement about the significance of the findings leading to the conclusion would be welcome.

In this case, will identification of 50%, or even 100%, of patients who are salt-sensitive
actually lead to such therapy, given the current practice milieu? What are the barriers? Will improved motivation among positive patients translate into clinically meaningful, cost-effective, changes in outcomes? The bridges from raised awareness to actual changes in behavior, for instance, especially with respect to physician guideline compliance, or patient adherence, are vast and not easily crossed. While no one is able to predict the future, what do currently available data suggest about the answers to these questions?

Response 2:
I appreciate the reviewer's constructive comments. In accordance with the comments, I add the following sentences (paragraph) in the Discussion:

Behavioral modification is more efficient in preventing hypertension in people younger than 50 than in people over 50. However, the findings in the present study indicate that people over 50 years old are more willing than their younger counterparts to undergo genetic testing for salt-sensitive hypertension. Although the positive effects of knowing one’s genetic risk profile on making positive behavioral changes has been established, this benefit can, of course, not be achieved without first undergoing genetic testing. Therefore, improved motivation among patients to know more about their genetic risk of salt-sensitive hypertension can translate into clinically meaningful, cost-effective changes in outcomes for hypertensive patients. More positive changes can be made by finding ways to encourage patients younger than 50 years old to agree to undergo genetic testing for their risk of salt-sensitive hypertension.

Comment 3:
In the section concerning limitations, a comment about self-reported data and the patient population might be considered. Self-reporting may introduce considerable error in data presentation. Patients who are highly educated perform differently with respect to reporting and healthy behaviors.

Response 3:
In accordance to the reviewer’s comment, I inserted the following sentences into the section concerning the study limitations:

Third, this study used self-report data, and self-reporting frequently results in considerable error in data presentation. In addition, patients who were highly
educated may perform different healthy behaviors from those they reported. These methodological weaknesses might have influenced findings regarding the relationships between salt preference, current lifestyle behaviors, and the willingness to undergo genetic testing.

Comment 4:
Hypertension is also prevalent among patients younger than age 50—how will the greater willingness of older patients to have genetic testing influence the significance of the findings?  
Response 4:  
I agree with the reviewer’s comment. According to it, I revised the manuscript. Please see the changes in the Response 1.

Comment 5:  
How generalizable are the reported data to other populations? A comment might be warranted in the limitations section about the cultural, dietary, and genetic differences that might diminish or reinforce the applicability of results to Western and other countries. Would the relative heterogeneity, for instance, of the United States population be a factor?  
Response 5:  
In accordance to the reviewer’s comment, I inserted the following sentences into the section concerning the study limitations:  
Fourth, although study findings were consistent with those obtained previously in samples using patients of different nationalities, the participants in this study were all Japanese, and cultural, dietary, and genetic differences might have diminished or reinforced the applicability of the findings in this study to other countries.

Comment 6:  
The advice primary care physicians should give to patients with hypertension and about genetic testing might be more specific, rather than general.  
Response 6:  
I agree on the reviewer’s comment. I add the following sentence at the bottom of the Conclusion:
For example, when discussing the results of genetic testing, primary care physicians should be specific, rather than general.

**Referee 2:**

**Comment 1:**

Overall comments: The study aims to determine the proportion of patients willing to undergo genetic testing for salt-sensitive hypertension and its related factors at primary care setting. The study is not novel however the findings of this study might be of interest for primary care physicians and researchers working the respective area. The sample size is sufficiently large and statistical methods are adequate however the manuscript is poorly written and needs substantial revisions by an English language expert. Also, conclusion of the paper is vague and not inline with the main findings of this study. The paper can be accepted as a short communication provided the authors agree to format the manuscript according to the guidelines for a short communication.

**Response 1:**

I appreciate you kindly reviewing our manuscript and providing the remarks. In the basis of the comments of the Referee 1, we revise our manuscript especially with attention to the discussion. We would like you to confirm the changes highlighted in red color in the revised manuscript. According to the information on the journal web site, BMC Family Practice doesn’t have a category, “short communication”. I believe the revised manuscript become acceptable for you to be published as the original article.