Author's response to reviews

Title: Causes of death and associated risk factors among climacteric women from Southern Brazil: a population based-study

Authors:

Verônica Colpani (vecolpani@gmail.com)
Karen Oppermann (karenoppermann@gmail.com)
Poli Mara Spritzer (spritzer@ufrgs.br)

Version: 2
Date: 20 December 2013

Author's response to reviews: see over
May 22, 2013

Natalie Pafitis
Executive Editor, BMC Public Health

Dear Dr. Pafitis,

Thank you very much for your e-mail dated 27 Nov 2013 and for the careful review of our manuscript. We have examined all the reviews and extensively revised the paper according to the suggestions made. A highlighted version of the paper was uploaded with the same manuscript number.

We look forward to hearing from you concerning the status of this submission. In the meantime, please feel free to contact us if you require any further information.

Sincerely,

Karen Oppermann
Corresponding author

Medical School of Universidade de Passo Fundo
Rua Teixeira Soares 885/704, CEP 99010-081
Passo Fundo, RS, Brazil
Phone: +55 51 3359 8027 / Fax: +55 51 3359 8777
E-mail: karenoppermann@gmail.com
Reviewer's report 1
Title: Causes of death and associated risk factors among climacteric women from Southern Brazil: a population based-study Version: 1 Date: 10 October 2013
Reviewer: Julien Dumurgier
Reviewer's report:

This study aimed to investigate the causes of death in a cohort of pre, peri, and post-menopausal women in the South of Brazil. The authors concluded that cardiovascular disease was the main cause of mortality.

Major comment:

The authors concluded that menopausal status is associated with a major probability of death. Maybe could they verify if the age of menopause play a role in this relationship (we may hypothethyze that a younger age at time of the menopause would be associated with an increased risk of death).

Age at menopause was available since the second follow-up, in 2001 and did not differ between survivors and non-survivors groups (47.52 ± 6.33 versus 45.53±4.99 years, p=0.116, respectively). This information was included in the Results section.

Level of interest: An article whose findings are important to those with closely related research interests. Quality of written English: Acceptable. Statistical review: Yes, and I have assessed the statistics in my report.
Reviewer's report
Title: Causes of death and associated risk factors among climacteric women from Southern Brazil: a population based-study
Version:1 Date:30 October 2013
Reviewer: Gastón Perman
Reviewer's report:
Dear authors,
Thank you for submitting your work to an open access journal. It is also a pleasure to read a Latin American study. I think you have a neat paper. Congratulations on that. Nevertheless, there are major compulsory revisions needed:
- It is very important to improve the description of the selection process (sampling better described, as well as recruitment; what happened to the two sampled women in each lot?;

   The Study population sub-section was rewritten in order to clarify these points.

- A flow diagram would be important.

   A Figure 1 was included to the manuscript.

- In addition, did women that did not accept to participate at the beginning differ in any important characteristics from the original cohort? The same applies to those lost to follow up, and the additional 119 women included.

   Only 4 women refused to participate at the beginning of the study and we don’t have information regarding these women. Concerning the 59 losses on the second follow-up and the 358 cohort participants, no statistical differences were found on age, age of menarche, blood pressure, BMI, climacteric symptoms, and educational level between these groups. This information was added to the Population Study subsection.

- You must discuss the implications of the low number of included persons and of events detected. Some of the 95%CI are enormous. This is the weakest point in your study. After you argue in favor of how representative of the reference population your
cohort is (previous point), you must deal with how valid the results are. What conclusions can you make about causes of deaths out of 17 deaths?

The low number of deaths may be related to the relatively young and healthy status of this population in the baseline. In addition, when data were adjusted for age and smoking, 95%CI values became lower, showing the influence of age on the other risk factors for all cause mortality. Our results should be viewed as hypothesis generating and will require further evaluation in other studies. Equally, longer follow-up of these women is needed to better understand the influence of risk factors on the cardiovascular mortality in the Brazilian women population. A sentence was included in the Discussion section, addressing this issue.

-You must state clearly what variables were included in the multivariate model, in the text and in the table. Age and smoking status data must be reported.

A sentence was included in Statistical Analysis sub-section detailing that the multivariate model was adjusted for age and smoking. A paragraph in the Results section and the title and footnote of Table 4 were also rewritten in order to state these points.

-The multivariate model is probably underpowered to detect important associations (few events for the number of variables included). You mentioned it very briefly. Please, discuss this a little further.

As already cited, when data were adjusted for age and smoking, important associations of mortality with diabetes, alcohol intake and abdominal obesity could be found. The three last paragraphs of the Discussion section were rewritten addressing this issue.

-Hysterectomy, included in the model as an independent variable is actually (I guess), a proxy variable of cancer. These women had (supposedly) uterine cancer, had a hysterectomy, and died anyway. So, cancer is the risk factor for death, not hysterectomy per se. Linking this with my previous observations: hysterectomy’s HR is 11.8 (95%CI 3.6-121.4!!!). And if you had not had two deaths from uterine cancer, the HR of hysterectomy would have been 1. You must dedicate an entire page to discuss all these issues.
Actually, the group of women, called “hysterectomy”, was those with intact ovaries, in which menopausal status was impossible to classify because of the absence of menses. The main reasons for hysterectomy without bilateral oophorectomy are benign causes rather than uterine cancer. Among the 7 non-survivors who had previous hysterectomy, only 2 of them could be associated to cancer as death cause. The others 5 were submitted to hysterectomy due benign causes, not directly related to death. A new paragraph was inserted in the Discussion section addressing these issues and two new references were included to the manuscript:


- In the discussion section, you mention that “postmenopausal status, (...) were associated with increased risk of mortality”, although you results are borderline. Please be precise in your descriptions. Moreover, HR confidence interval is 0.963-40.143. It needs further discussion. Same problem.

  We agree with the Reviewer concern and have removed the postmenopause HR as significant finding in the Abstract and Results section. In addition, a paragraph was added to the Discussion section in order to clarify this point.

- You mention that you used “pretested” questionnaires. Were they validated? In Brazil or at least in Portuguese? If not, please discuss implications.

  The questionnaires applied in this research were previously validated in Brazil, as reported in previous publications [references 21,22, 62]. These information were added to the Methods section and a new reference was inserted to the paper.

- Moreira L, Fuchs F, Moraes R, Bredemeier M, Cardozo S, Fuchs S, Victora C:

Minor essential revisions

-Page 12, first paragraph. Please change the word “confirms” for another most appropriate, such as “supports”.

  Suggestion accepted and the correction was done.

-Table 1: Please clarify what the numbers in parentheses are in alcohol intake.

  The numbers in parentheses are interquartile range of alcohol intake in grams.

- Table 1: You also omitted the p value in hysterectomy (This value is the same of menopausal status). Footnote: expresses should be changed to expressed.

  The p value is the result of the Pearson’s chi-square for the entire set of menopause status (pre-, peri-, postmenopause and hysterectomy). Individual p values for hysterectomy are presented in Tables 3 and 4. The term “expressed” was corrected in the footnote.

-Table 3: Please check 95%CI of menopausal status.

  Values are correct. The hide CIs are due to low number of women in the postmenopause and hysterectomy strata.

Discretionary revisions:

-Your study has more strengths than the one you mention. You might want to highlight them. Don’t be so humble!

  A sentence was added to the Discussion section including the strengths of our study.