Author's response to reviews

Title: Antioxidants and breast cancer risk - a population-based case-control study in Canada

Authors:

Sai Yi Pan (sai.yi.pan@phac-aspc.gc.ca)
Jia Zhou (zhoujia10@163.com)
Laurie Gibbons (laurie.gibbons@phac-aspc.gc.ca)
Howard Morrison (howard.morrison@phac-aspc.gc.ca)
Shi Wu Wen (sswen@ohri.ca)

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Author's response to reviews: see over
Re: Manuscript: Antioxidants and breast cancer risk – a population-based case-control study in Canada

Dear Editor:

Thank you very much for inviting us to submitting a revised version of above manuscript. We have revised the manuscript according to reviewers’ comments. The point-to-point response is attached below. We hope it is now suitable to be published in BMC Cancer.

I look forward to your reply regarding this paper.

Sincerely,

Sai Yi Pan
Science Integration Division
Centre for Chronic Disease Prevention and Control
Public Health Agency of Canada
785 Carling Avenue, AL: 6807BA
Ottawa, Ontario, Canada, K1A 0K9
E-mail: Sai.Yi.Pan@phac-aspc.gc.ca

Reviewer’s report
Reviewer: Mary Platek
The manuscript is improved but there are still areas that need to be addressed before this paper can be considered for publication. One major issue concerns something that was overlooked on the first review and that relates to supplement use over time. Respondents were not only asked for how long they took supplements but also how often (never, not regularly, fairly and regularly). There is no reporting of this variable. Specific comments are as follows:

Major Compulsory Revisions
1. What happened to “consistency” of supplemental intake? Who are you reporting on? Just regular users? How many were “not regular” or “fair” users? Are responders all lumped together? This is a very important point and needs to be included. Should the real classification of participants be according to consistency of intake per category of number of years of intake? The answers to these questions might change how the rest of the paper is reviewed.

Response: The questionnaire asked for both frequency (how often) and length (years) of supplementation. Only those respondents who were “not regular” and “fairly regularly” users answered the question on “For many years in total”. However, all respondents who answered “No” to the question on frequency were included in the analysis and classified as “0 (never
taken” for years of supplementation in table 3. Therefore, we reported all subjects including those “not regular” and “fairly regular” users. Although most of those “not regular” users were not long term users, there were both users who took supplement only a few years and many years for those “fairly regular” users. However, because of the small numbers for some categories of years of supplement intake, the number would be too small (and the logistic regression analysis would be unstable) for some categories if we classify participants according to consistency of intake per category of number of years of intake.

Note: The following comments may need to be revised depending on the answers to concern number one above.

2. Since dose was not available, please clarify on pages 6, 7 and 8 that you are referring to length of use of supplements.
Response: Clarification (reference to length of use of supplements) has now been made on pages 6, 7, and 8.

3. You now include information regarding antioxidant intake in the Canadian population, but how do your findings relate? What are the median or average dietary intakes of your population by case/control status? A comparison of these dietary intakes and length of use of supplements for each nutrient by case-control status should actually be table 2 (making table 2 and 3, tables 3 and 4).
Response: A table of average dietary intake and average years of supplements of antioxidants by case-control status as well as the relation with the information on antioxidant intake in the Canadian population have now been added (table 2 and text in page 15).

4. In the statistical analysis section on page 8, you need to better explain your regression model. In fact you made categories of low and high and you compared high relative to low…..For Table 4, you should add the reference group for each category for each nutrient and the number of cases and controls
Response: An explanation as well as the reference group for each category for each nutrient and the number of cases and controls have now been added (page 8 and table 4).

5. On page 14, you state that it is difficult to sort out cause and effect. This is an observational study and so you are looking at associations only – never cause and effect – please revise accordingly.
Response: We agree with reviewer’s comment and thus these two sentences have now been deleted (page 14).

6. Please add to your abstract, discussion and conclusions that you were unable to determine total dose or intake.
Response: This has now been added to the abstract (page 2), discussion (page 11) and conclusions (page 15).
7. Your major result is for “long term” supplementation and you should refer to supplementation as “long term” or exactly what it is such as > 10 years….
Response: This has now been modified.

Minor Essential Revisions
1. Tables: Report all p values with the same number of decimal places going out to the one-hundredth place (x.xx). Many of your trends will now be 0.05 and not considered statistically significant but essentially borderline and important and noteworthy – you will then need to change the corresponding text in all areas of the manuscript.
Response: All p values have now been set to be with two decimal places except p values less then 0.01.