Reviewer’s report

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

Version: 1 Date: 11 November 2010

Reviewer: Mary Platek

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The investigation contributes to the literature, but there are major items for consideration before this can be published. In general, I do not think that you can conclude that “supplementation of beta-carotene and vitamin E for greater than 10 years may protect women from developing breast cancer” – the results from your statistical analysis do not support this. Additionally, you conclude that zinc is important in the paper, but you do not include that in your conclusions in the abstract. Specific comments are as follows:

Major Compulsory Revisions

1. Total intake for antioxidants includes both dietary sources and supplemental sources. Total intake for antioxidants is not addressed in this paper. This exposure can not be ignored. There are actually three levels of exposure to look at: dietary antioxidant exposure, supplemental antioxidant exposure and total (dietary and supplemental) exposure. The authors should perform these analyses and include these results in the paper. Since dietary intake was only collected for two years before interview, you can only analyze total intake for the years of supplemental use that relates to this dietary period, but it would be beneficial to understand what the total exposure was for the time prior to interview and you would need to interpret it in that context. You could consider looking at those with so many years of supplement use bundled with high or low intakes based on diet if specific information on dose is not available?

2. Concerning information collected for supplements, what about dose? Perhaps in Canada, each vitamin and mineral supplement available is regulated and amounts are consistent, but this would need to be made known in the paper. Additionally, there is no information provided for the amount of each nutrient that participants received from their supplements. If this particular information was not collected and the focus was solely the number of years of supplement usage, then you need to add this to your discussion. How could different doses over time affect your results?

3. Information regarding recommended intakes for good health in Canada should be included and related to your results. In general, did the diets and/or supplement use of your population seem adequate? If you are unable to evaluate this, can you comment on the level of antioxidant deficiency in the Canadian population?
4. You do discuss your limitation with numbers, but this is a real problem. What power did you have to look at four quartiles of diet and six categories of supplement use divided by pre and post-menopausal breast cancer? The only p for trend in the supplement analysis that was statistically significant was for zinc. Is the p for trends for beta-carotene and vitamin E reported correctly in Table 3? Can you say that supplement use of beta carotene and vitamin E for 10 years or more may decrease breast cancer risk or can you say that compared to those who never took beta carotene or zinc, those who did for 10 or more years had a decrease in breast cancer risk?

5. It does not make sense to include your statistically non-significant results in your discussion unless you see a clear trend and it makes sense. The addition of all of this information just makes for a confusing discussion. You can discuss what you did not see if it is warranted and contributes.

6. You were unable to adjust for essential confounders, most importantly, family history. You should note this as a major limitation.

Minor Essential Revisions

1. Background: Information provided is redundant. You repeat the role that antioxidants play in cancer. This is important, but the introduction should be succinct.

2. Discussion: The literature cited is important but in general this whole section needs be more focused on what you really did and did not find and how this relates to previous findings.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests