Author's response to reviews

Title: Methodological Issues in Detecting Gene-Gene Interactions in Breast Cancer Susceptibility: A Population-Based Study in Ontario

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Author's response to reviews: see over
We thank the two reviewers for their comments on our previous revisions and provide below a point-by-point reply to each of them.

**Reviewer 1:** David Goldgar

No specific comments made by the reviewer.

**Reviewer 3:** Marylyn Ritchie

**Minor Essential Revisions** *(such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)*

1. Page two, in the results section, there is a sentence with two periods at the end.

   **This was corrected.**

2. Page 10, in the section on logistic regression. One could do an exhaustive logistic regression followed by a permutation test. You could mention that when you describe the stepwise selection procedure that you used. An exhaustive search procedure is another option.

   We added the following sentence on Page 10: “Instead of using a stepwise selection procedure, one could perform an exhaustive search and select the most significant interactions based on a permutation test or using the FDR principle [41]. This was not done in this study because this strategy is not directly applicable to CART analyses.”

   3. Page 13, Figure 1 needs to have a space between Figure and 1. The first line of the "Strategy” section needs to have the word "to” in between applied and our.

   **This was corrected.**

4. Page 21, the word "do" should be "does" in the sentence about the second approach.

   **This was corrected.**

5. What is meant by "use test statistic" in MDR? I am not sure what "test statistic" the authors are referring to.

   We meant a chi-square test statistic for contingency table. This was added in the paper.