Author’s response to reviews

Title: Behavioral and psychosocial effects of rapid genetic counseling and testing in newly diagnosed breast cancer patients: Design of a multicenter clinical trial

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Author’s response to reviews: see over
Dear Editor,

Thank you for reviewing our manuscript entitled: "Behavioral and psychosocial effects of rapid genetic counseling and testing in newly diagnosed breast cancer patients: Design of a multicenter clinical trial". Enclosed please find a copy of the revised version of our manuscript, and below our point by point responses to the reviewers’ and your comments and questions.

We hope that the revised version of the manuscript will be acceptable for publication in BMC Cancer. We look forward to learning of the editorial decision.

Sincerely,

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1. **Mention of CONSORT guidelines.**

We have referred to the CONSORT guidelines on page 9 of the revised manuscript, and have adhered to all points from the checklist that are applicable to this ‘design’ manuscript.

2. **Discrepancy between sponsors as listed on the trial register versus in the manuscript.**

We have explained this apparent discrepancy between the sponsor listed on the trial registry versus in the manuscript in previous correspondence with the editorial office of the journal. Specifically, in response to an inquiry from Rachel Neilan in June of this year, we explained that, when completed the documentation for the trial registry, we mistakenly interpreted “sponsor” to mean the institutions with which the principal investigators are affiliated (i.e., the Netherlands Cancer Institute and the University Medical Center Utrecht). Subsequently we understood this to mean the source of funding, which is the NutsOHRA Foundation. As I’m sure you can understand, it is essential that we acknowledge the source of financial support for our study in the manuscript.

3. **Description of the qualitative research element of the study.**

We appreciate that reports on qualitative studies need to adhere to the standards outlined in the RATS guidelines. Our study, however, is predominantly quantitative in nature. The more qualitative interview data that we are collecting will be used for illustrative purposes only; that is, to highlight and illustrate results that emerge from the quantitative data (e.g., by using direct quotes). It is not our intent to conduct formal qualitative analyses using structured coding systems. This was not part of the protocol as submitted for IRB approval and to the trial registry. We have added some information on the topics covered during the interview, and the way the data will be used on page 9 of the manuscript.

4. **Clarification of how far along the study is and whether any results have been generated.**

Patient recruitment began in November 2008. We will continue recruiting patients until January 1\textsuperscript{st}, 2011. Since participants complete their last follow-up questionnaire 12 months following their baseline questionnaire, the data collection will be completed in January 2012. No results have been generated or published. The data analysis and publication of results will take place in 2012.

5. **The authors should consider the nature of genetic counseling as portrayed in their study...There is a need to reflect on their very directive approach with very medical outcomes as positive expectations.**

Contrary to what the reviewer has suggested, the form of genetic counseling that is being investigated in this study is relatively non-directive. As described on pages 5 and 6 of the manuscript, the objectives of genetic counseling are to improve knowledge and understanding of 1) the possible genetic basis of disease, 2) personal risks of developing disease, and 3) possible consequences of genetic testing. The intent is to provide counselees with sufficient information to make informed choices regarding genetic testing, and available preventive and treatment options. We hypothesize that rapid genetic counseling and testing (RGCT) will lead to an increase in the uptake of direct bilateral mastectomy (BLM) and delayed contralateral prophylactic
mastectomy (CPM). However, this is not the result of directive counseling. Rather, the timing of RGCT (i.e., counseling and, if desired, DNA testing at the time of diagnosis, prior to receiving primary treatment) facilitates making informed choices about available treatment options. A woman can only consider preventive options if she is aware of them. Thus, by definition, we expect a greater uptake of preventive options in the intervention group, where RGCT is routinely offered, than in the control group, where this is not the case.

6. **Need to provide rationale for RGCT...to convince that the extra time gained by RGCT is in itself beneficial.**

As described in the background section of the manuscript (pages 6-8) RGCT may be beneficial because it facilitates the use of information on the possible familial and/or genetic basis of the breast cancer in decisions regarding primary treatment. For those high-risk women who opt for direct BLM or delayed CPM, there are clear advantages in terms of reduction in the risk of contralateral disease, although an improvement in survival has not yet been convincingly demonstrated. Women who choose for (bilateral) mastectomy can also avoid having to undergo radiotherapy. This, in turn, can improve the results of breast reconstruction Our study will contribute important information on the impact of RGCT, when offered routinely to high-risk women, on medical decision-making, cancer-specific distress, treatment satisfaction and health-related quality of life.

7. **Provide reference for the statement: “However, in current practice, this occurs rarely during the pre-surgery period.”**

A reference has been added.

8. **“et al” should read “et al.”**

This has been corrected.

9. **Reference 53 needs to be corrected.**

This has been done (reference 39 in the revised manuscript).