Author's response to reviews

Title: Examining the challenges of family recruitment to behavioral intervention trials: factors associated with participation and enrollment in a multi-state colonoscopy intervention trial.

Authors:

Rebecca G Simmons (rebecca.simmons@hci.utah.edu)  
Yuan-Chin Amy Lee (amy.lee@hsc.utah.edu)  
Antoinette M Stroup (nan.stroup@hsc.utah.edu)  
Sandra L Edwards (sandie.edwards@hci.utah.edu)  
Amy Rogers (amy.rogers@hci.utah.edu)  
Christopher Johnson (cjohnson@teamiha.org)  
Charles L Wiggins (cwiggins@salud.unm.edu)  
Deirdre A Hill (DAHill@salud.unm.edu)  
Rosemary D Cress (rcress@ccr.ca.gov)  
Jan Lowery (jan.lowery@ucdenver.edu)  
Scott T Walters (Scott.Walters@unthsc.edu)  
Kory Jasperson (kory.jasperson@hci.utah.edu)  
John C Higginbotham (jhiggin@cchs.ua.edu)  
Marc S Williams (mswilliams1@geisinger.edu)  
Randall W Burt (randall.burt@hci.utah.edu)  
Marc D Schwartz (schartm@georgetown.edu)  
Anita Y Kinney (anita.kinney@hci.utah.edu)

Version: 2 Date: 20 March 2013

Author's response to reviews: see over
March 20, 2013

Doug Altman, Curt Furberg, Jeremy Grimshaw, Peter Rothwell
Editors-in-Chief
Trials

Dear Dr.’s Altman, Furberg, Grimshaw and Rothwell,

Thank you very much for the opportunity to revise and resubmit our manuscript, “Examining the challenges of family recruitment to behavioral intervention trials: factors associated with participation and enrollment in a multi-state colonoscopy intervention trial” (MS: 1178713861829232) as an original article in Trials. The reviewers of our initial submission provided meaningful comments that significantly strengthened our paper. Below, we have responded point by point to each of the comments and, where applicable, have identified the page numbers corresponding to changes in the manuscript text.

Handling Editor Comments:

1. **Please ask the authors to edit their paper for English (it isn’t always the most grammatical).**
   We have reviewed our manuscript thoroughly and copyedited accordingly.

2. **Please ask the authors to use the term “multiple regression” or “multivariable” rather than multivariate (which refers to the dependent rather than the independent side).**
   We have used the term “multivariable” regression, rather than multivariate regression, in the revised text.

Reviewer 1’s Comments:

1. **Please use consistent language throughout the manuscript to describe the three phases of recruitment.**
   We have reviewed the manuscript for consistency. All recruitment phases are now referred to as “stages.”

2. **Table of exclusion criteria is not needed.**
   We have omitted Table 2 and have instead included information about inclusion/exclusion criteria on page 9 of the attached track-changes copy of the manuscript.

3. **Figure of return rates is not needed.**
   We agree that Figure 2 in the original documents was superfluous; thus, we have omitted it. Complete information on the number of cases we needed to contact to enroll one participant is now covered on page 14, under the section “Total Study Participation Outcomes.”

4. **Figure on consort document is not needed in the published version. Can be submitted with journal article.**
   We have removed Figure 1 from our article, but have included it as Appendix A, in the event that readers have questions about our recruitment process.
5. **At the end of each description of recruitment stage, include a sentence about the outcomes of that stage.**

   We agree and now provide a more detailed explanation of the recruitment process. As such, we have revised the manuscript and now provide a summary of outcomes for each recruitment stage (pages 8-10). Information on study outcomes, such as response rates and stage predictors of recruitment, is now provided in the Results section (pages 11-14).

6. **It would be possible to include a cost per participant recruited to compare across registries. This would be helpful and something that can be done after the fact.**

   We agree that cost is certainly an important aspect of the recruitment process. As such, we have calculated the direct per-participant recruitment costs at each stage (Table 3) and provide cost-specific information on pages 10, 12-13, 16, 18 and 19. Although a complete cost analysis is beyond the scope of our paper, we believe that the information provided is useful.

7. **There is one citation missing from the intro. Bowen et al. did something similar for melanoma families.**

   We have expanded the introduction to provide an overview of all known published studies that provide predictors of recruitment to family cancer screening behavioral intervention trials, and have added Dr. Bowen’s paper (see page 5).

Reviewer 2’s Comments:

1. **On page 5, the risk of developing CRC by type of first-degree relative should be cited separately for parents, siblings, and children. Provide statistics and citations? This is important because risk varies.**

   We agree that providing information about differences in familial risk would be an ideal inclusion in our paper. However, to our knowledge, the relationship of the first-degree relative to the case has not been shown to significantly affect the risk of colorectal cancer. A recent study by Taylor et al. found no differences between sibling and parent-offspring risk, even though the numbers of probands in the study with an affected parent or affected sibling included in the analysis were greater than 31,000 and 47,000 respectively (Taylor DP, Burt RW, Williams MS, Haug PJ, Cannon-Albright LA. Population-based family history-specific risks for colorectal cancer: a constellation approach. Gastroenterology 2010;138:877–885). Thus, we have not included specific risk estimates for types of first-degree relatives in our paper but we note the range of risk. We also note that risk varies with the age of onset of colorectal cancer in family members as well as with the number and type (i.e., first-, second- or third-degree relative).

2. **Also, in this section (page 5) what is the numeric lifetime risk or otherwise for second-degree relatives to develop CRC? How does this risk compare to sporadic risk when there is no familial risk?**

   To our knowledge, no study has addressed the specific, lifetime risk of second-degree relatives. A previous study (Taylor et al., 2010; complete citation is in our reply to the previous reviewer
comment) provided relative risk estimates for family history constellations, but none of these constellations included risk for a diagnosis of only one second-degree relative. Our decision to include second-degree relatives with appropriate family history in the study was based upon the clinical recommendations for increased screening put forward by the American Cancer Society (http://www.cancer.org/cancer/colonandrectumcancer/moreinformation/colonandrectumcancer/colorearlydetection/colorectal-cancer-early-detection-acs-recommendations), which recommends that individuals with two or more second-degree relatives with colorectal cancer start screening at age 40. Thus, although we agree that this information would be interesting to include, we are not able to provide reliable risk estimates at this time. However, to address this concern as best we could, we provided the clinical rationale as to why these individuals were included in our study population on pages 5-6.

3. **A summary table of literature review with studies of family recruitment methods used (in CRC or other cancer), outcomes by R/E could help, if feasible?**

   We agree that information regarding differing recruitment methods used to contact family members would be useful to future researchers interested in designing family recruitment studies. However, to our knowledge there are only three published studies that address this topic. Therefore, we expanded the breadth of our literature review in the Introduction section by including information about these three relevant previous studies, all of which examined predictors of recruitment to family cancer behavioral intervention trials (Bowen et al., Glanz et al., Manne et al.).

4. **What is the breakdown of first-degree vs. second-degree relatives among the 481?**

   We agree that this information is interesting and would be useful to the paper. We have provided a specific breakdown of the number of first-and second-degree relatives per enrolled relative in our CONSORT diagram (Appendix A).

5. **Similar to the last point in Background, authors could improve the concluding paragraph by discussing enrollment strategies they believe should be further explored in future trials.**

   We agree that the information in our study is best-utilized if it is translatable to future research. As such, in the Conclusion section we have provided a more in-depth discussion of where future studies might benefit from or build on our outcomes (page 19).

We appreciate the opportunity to revise and resubmit our manuscript to Trials. We look forward to your response.

Sincerely,

Rebecca Simmons, MPH
Huntsman Cancer Institute
University of Utah