Author's response to reviews

Title: Using a state cancer registry to recruit young breast cancer survivors and high-risk relatives: a protocol of a randomized trial testing the efficacy of a targeted versus a tailored intervention to increase breast cancer screening

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Version: 2 Date: 12 January 2013

Author's response to reviews: see over
To BioMed Central Editorial Team

Object MS: 1685282122763858 - Using a state cancer registry to recruit young breast cancer survivors and high-risk relatives: a protocol of a randomized trial testing the efficacy of a targeted versus a tailored intervention to increase breast cancer screening – Maria C. Katapodi, PhD, RN, FAAN et al.

We appreciate reviewers’ comments and take the opportunity to improve the manuscript. We are addressing comments by Reviewer 3, since Reviewers 1 and 2 did not identify any major weaknesses in the study protocol. **Our answers follow in bold.**

Reviewer #1: Paolo Pedrazzoli
Reviewer's report:
The paper reports the protocol of a randomized trial testing the efficacy of a “Targeted” versus an “Enhanced tailored” intervention to increase breast cancer screening in young breast cancer survivors (diagnosed at 20–45 years old) and their high-risk relatives. The principal goal of the proposed study is to contribute to female breast cancer death rate reduction in this specific population. Young breast cancer survivors will be identified in the Michigan Cancer Registry, and eventually the results will be applied to the entire American female population with the same characteristics.

The remarkable points of the study are:
- gain of knowledge on a population (young women survivors and their families) yet to be studied thoroughly;
- emphasis on the importance of “advocacy”, by requiring young women survivors to involve their relatives;
- increase awareness of disease risk in this population of healthy women
- stratification by race; this might help to identify specific factors that may assist to improve and differentiate subsequent interventions.

The study is well designed and the protocol description is clear. It provides clear information for better intervention in BC screening. It is likely that the study will help expanding public health knowledge about breast cancer surveillance practices for young patients and high risk relatives.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

- We appreciate that Reviewer 1 identified many strengths and no weaknesses in the study

Reviewer #2: Ophira Ginsburg, MSc, MD, FRCPC
Reviewer's report:
This study has the potential to make real impact on the many women and families still under-referred/under-utilizing for cancer genetics and breast screening services. It is a nice example of a public health approach to cancer genetics services, risk estimation & risk reduction for breast (and ovarian) cancer. Comprehensive prospective, randomized study design with very clear aims & outcome measures. Good use of resources to not only investigate current utilization (and barriers) of breast screening & genetic counselling services, but to also provide outreach to at-risk relatives.

Strengths: adequate background and rationale for the study, including theoretical framework employed for the two interventions. Important to note that despite previous efforts only 42% of charts in their regional genomics program include documentation of family hx of breast cancer, 98% without documented age at
diagnosis, critical for identifying families who may have hereditary breast/ovarian cancer....phone survey indicating a very low (12) % of women over 40 who received cancer genetics services....and a surprisingly low proportion of at-risk, women who had reported having a mammogram of CBE in the past 12 months. Their estimated number of at-risk, age-appropriate female relatives and likely proportion of eligible participants who consent to the study seem realistic. Use of a "Project Navigator" will help in study flow, study participant satisfaction, as well as increasing the opportunities to identify female relatives who may choose to participate.

Statistics seem solid, and a statistician was involved in the study design.
Weaknesses: no major weaknesses identified.
Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

• We appreciate that Reviewer 2 identified many strengths and no weaknesses in the study

Reviewer # 3 (Edmundo Mauad, MD)
Reviewers report:
Comment #1:
"In our institution's experience with genetic counseling, is noted that a patient with high risk breast cancer comes for consultation with a poor perception about the risks of the disease. In the orientation of these women with high risk cancer the understanding is not always totally absorbed by the patients and their families, due to the emotional aspects (general concerns, anxieties, etc.) social, cultural aspects etc., it takes the health professional (geneticist, nurse) which transmit the information to suit each patient and their family in the transfer of such information. Therefore the proposed intervention by the paper via letter, booklet and brochure not seem appropriate."

• We understand the reviewer's concern, that a print intervention may not be as efficacious as an in-person consultation. However, we believe that the reviewer misunderstood the scope of the study. The protocol describes a public health intervention. With a target sample of 1,200 Young Breast Cancer Survivors (YBCS) and their High-Risk Relatives (HRR) (Fig 2) it would not be feasible to provide an in-person intervention. The study aims to increase awareness about risk of hereditary breast cancer and self-efficacy about screening (Fig 3) among a sample of high-risk women that otherwise receive no attention. This increased awareness, in turn, will increase the number of women who discuss their breast cancer risk and appropriate screening with their provider. Therefore, although we acknowledge that print interventions may not be as efficacious as in-person consultations, the reviewer's suggestion about the latter approach is not feasible in the context of this study.

Comment #2:
"In the questionnaire, if it were included in the manuscript as an attachment will certainly simplify the understanding of some aspects of the study, since the lack of it ends up generating some questions such as: What types of questions are about family history of cancer, such as "genetic counselors" will choose which family will be included in the study, etc.?"

• We provide the names of instruments that are used in the study and appropriate references (Table 2). Questions that assess family history of cancer have been adapted from the Behavioral Risk Factor Surveillance System, and allow calculations of Gail and
Claus risk models (Table 2). These are commonly used models for calculation of breast cancer risk and, in our opinion, most readers that have an interest in breast cancer are familiar with the risk assessment questions included in the models. However, we clarify that we assess family history of cancer by asking YBCS how many first and second degree relatives had cancer, type of cancer, and the age of onset. Then we ask YBCS to list the first and second degree relatives in the family who are cancer free, their age, and whether they are willing to contact them for the study. We explain this process in the manuscript, on page 11 as follows:

“Questions that assess family history of cancer allow calculations of Gail [12] and Claus [13] risk models. YBCS will be asked how many first and second degree relatives had cancer, type of cancer, and age of onset. Then YBCS are asked to list the first and second degree relatives in the family who are cancer free, their age, and whether they are willing to contact them for the study. The combination of answers in these two sets of questions allows genetic counselors to identify eligible, high-risk relatives.”

Comment #3:

“Since there will be no personal contact, but only written informational material, I really doubt whether the proposed intervention will be effective in the study. Depending on the number of individuals with low education, there may be difficulty in reading and understanding the material. According to the authors, it will only include YBCS and families capable of reading and understanding English. But how the understanding degree will be checked among women who are included in the study? The suspicion that this difficulty will occur is reinforced by the fact that the authors describe on page 9 which will conduct the study with larger samples of black women living in cities with high mortality rate due to breast cancer.”

- Reviewer 3 misunderstood the description of intervention efficacy in the study protocol. On page 13 we explain that “Development of the Targeted version is based on a mailed intervention recommended by the Guide to Community Preventive Services as efficacious in increasing breast cancer screening among older, non-adherent women [19].” Moreover, the intervention materials are at the 9th grade reading level or less. We added this information in the text on page 14 as follows:

“All intervention materials are developed at the 9th grade reading level or less.”

Comment #4:

“It also not clear, the reason why the methodology will be done larger samples in this group of women "underserved". Is there any specific reason? This subgroup has less risk perception?”

- As we explain in the Aims of the protocol and in Figure 2, the outcomes of the study are genetic counseling and breast cancer screening. Women who are medically underserved have the greater barriers to breast cancer screening. The study is not about changing perceived risk, although perceived risk is a moderator variable in the study model. Nevertheless, the aim of the study is to identify what inhibits breast cancer screening in YBCS and their high-risk relatives. In our opinion Reviewer 3 misunderstood the protocol.
Comment #5: "It is also not possible to infer the amount of questions to be answered in the questionnaires before and after
the intervention. As there are many collection tools, there may be low adherence to the test if the number of
questions to be answered is high."

- Table 2 includes all instruments that will be used in the study, and the Times that will be
administered. Completion of the baseline and follow up surveys takes approximately 45
min. We added this information on page 15 as follows:

  “Completion of the baseline and the follow-up questionnaires takes approximately 45 min.”

Comment #6: "Will be invited until two family members at high risk to participate the study? However, if the invitation is not
extended to all family members at high risk (not just one or two), there is a serious risk of selection bias. The
program's effectiveness will obviously be higher among those family members who agreed to participate in the
program. The lack of interest in the study by a relative may indicate, for example, he dismissed as
inappropriate intervention, devoid of significance or judge to not have the ability or time to read all the
material. This question cannot be neglected in the analysis of effectiveness of the intervention."

- According to the study protocol, we will test the feasibility of inviting up to two high-risk
relatives per YBCS. We agree with Reviewer 3, that there is an inherent bias built in this
recruitment method. The first step is for the YBCS to be willing to invite the high-risk
relatives, and the second step is for high-risk relatives to be willing to be part of the study.
However, as Reviewer 3 probably knows, healthcare professionals in the U.S. do not have
direct access to high-risk relatives due to HIPAA regulations. This is a fairly inaccessible
and understudied population. Thus, accessing high-risk relatives through the affected
family member is an innovative approach to increase our access to these women.
Moreover, due to random sample selection from the cancer registry and the random
allocation, study findings can be generalized to all YBCS and high-risk relatives in the state
of Michigan and possibly to other U.S. states with similar demographic composition and
similar availability and accessibility of breast cancer screening services. We believe that
the innovation of the study outweighs its limitations, as explained on page 17 as follows:

  “Due to random sample selection and random allocation, study findings can be generalized
to all YBCS and high-risk relatives in the state of Michigan and possibly to other U.S. states
with similar demographic composition and similar availability and accessibility of breast
cancer screening services. Second, confirmation of family history will occur simultaneously
with identification of the YBCS in the cancer registry followed by outreach to her high-risk
female relatives. By circumventing the typical barriers associated with family history
collection (i.e., client awareness of family history, provider practices regarding family history
collection and referral), the study aims to increase breast cancer screening among women
at greatest risk for breast cancer. This innovative approach of identifying high-risk women
through existing public health data may lead to a new method of family history collection and
breast cancer risk assessment.”

Comment #7: "Figure 2 makes you think mistakenly that the family will be randomized at high risk, when in fact, is the family
unit (defined YBCS) that will be.”
• We are not sure we understand this comment. Figure 2 clearly describes that YBCS with high-risk family members will be randomized as a family unit to either version of the intervention. This is also explained on page 13 of the protocol as follows:

“YBCS (n=960 with high-risk relatives and n=240 without high-risk relatives) will be randomly allocated to receive either the Targeted or the Enhanced Tailored version of the intervention via a computerized program generated by the study statistician. YBCS and high-risk relatives will be randomly assigned as a family unit.”

Comment #8:
“As described on page 9 of the 3000 YBCS around 1200 would accept to participate (40% response rate). This type of recruitment by informational material written may force those who respond tends to be better educated and a group of a better economy class. I suggest doing a most effective strategy to increase the response rate.”

• As explained in the study protocol (p. 9) we randomly select YBCS from the Michigan cancer registry database. Moreover, we stratify the sample by race and we oversample YBCS who are black and living in counties with the highest mortality rates for young women with breast cancer (as shown in Figure 1). This recruitment method ensures that we build the maximum effort possible to have a representative sample of YBCS and high-risk relatives according to race, SES, and access to health care services. This recruitment method is a strength of the study, and it is identified by both Reviewers 1 and 2.

Comment #9:
“In conclusion, the aim of the work is very interesting, with great social responsibility and deserves its development for a project in the medium term. Mutations in the BRCA 1 and BRCA 2 carries predispose to power increase lifetime risk of up to 70% of breast cancers and 65% of ovarian cancer. Besides the per-patient lifetime costs of breast cancer in USA raged from U$ 20,000 to U$ 100,000 and multiples studies confirmed that costs increased with increased stage of the disease. Therefore I suggest the evaluation of the comments made and do not carry out the proposed intervention in the study. This intervention, in my view, should be further studied after the responses obtained in the questions 1 and 2 and that such intervention must be performed later by health professionals trained for this purpose and that is through a personal consultation or group.”

• The study protocol has received funding from the Centers for Disease Control and Prevention after a competitive grant and peer review application process. The study is currently under way. We have already recruited more than 800 YBCS and more than 200 high-risk relatives. As Reviewer 2 identified, this is among the first studies of its kind that incorporates a public health genomics approach. In-person interventions are not feasible in public health research. In our opinion, Reviewer 3 may be familiar with in-patient care, but is not familiar with public health approaches and public health research. In summary, we have addressed concerns of Reviewer 3 by adding clarifying information in the study protocol. We are looking forward to your response.