Author's response to reviews

Title: Use of a cancer registry is preferable to a direct-to-community approach for recruitment to a cohort study of wellbeing in women newly diagnosed with invasive breast cancer

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Version: 4 Date: 15 February 2008

Author's response to reviews: see over
15 February 2008

Dear Dr Puebla,

Thank you for the opportunity to respond to the reviewers’ comments about our manuscript:

MS: 1002890308165070
Method of recruiting Victorian women with a primary invasive breast cancer to a cohort study of wellbeing
Marijana Lijovic, Susan R Davis, Pam Fradkin, Maria La China, Helen Farrugia, Graham Giles, Melisa Bagnato, Julie de Crespigny, Rory Wolfe and Robin Bell

We thank the reviewers for their specific comments which we have addressed in order below. However we would initially like to acknowledge the recognition of the reviewers that our paper makes a useful contribution to this field. In particular reviewer 2 indicated the value of documenting the complexity of the process of recruiting through a cancer registry and reviewer 3 indicated that our paper does “address a very important question which, to date, has been overlooked in psycho-oncology research, namely the importance of getting population-based data on quality of life of cancer survivors.”

Reviewer's report 1
Title: Method of recruiting Victorian women with a primary invasive breast cancer to a cohort study of wellbeing
Version: 1 Date: 17 November 2007
Reviewer: Santosh K Chaturvedi
Reviewer's report:
General
The authors should reflect on the generalisability of their results and the clinical implications of their study to readers.
We agree with the reviewer that being able to generalise our findings is pivotal and is linked to the issue of potential sampling bias (see under Major Compulsory Revisions below).

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The authors should provide information on comparison between the eligible versus non eligible women, and between women who refused participation versus those who agreed, to rule out any sampling bias, and to see the generalisability of the observations.

The primary method of recruitment of women to this study through the state-based cancer registry is a truly population-based method of recruitment which would minimise sampling bias. During the recruitment phase, all women who were not excluded from participation on the basis of our specific criteria and who were not prevented from being invited by their doctor and whose notification to the register was received with enough time to contact them (see point 9 under reviewer 3) were invited to participate in the study. Obviously participation in a study such as this one is voluntary, however recruitment through the cancer registry would still be far preferable to convenience samples such as clinic-based samples in terms of minimising recruitment bias.

The privacy restraints on the Victorian Cancer Registry are comprehensive. We are not provided with any information about women who were not recruited to our study as only women recruited to our study have given permission for access to their details. Thus we cannot compare the characteristics of women who were recruited with those who were not recruited. What we can do is report on a limited number of characteristics of all Victorian women newly diagnosed with invasive breast cancer available in the public sector. We provided information on age and place of residence in the original version of the manuscript. We have supplemented this with information about tumour size and grade. All of this data supports our assertion that our recruitment methods have minimised sampling bias.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
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Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
I declare that I have no competing interests.

Reviewer's report 2
Title: Method of recruiting Victorian women with a primary invasive breast cancer to a cohort study of wellbeing
Version: 1 Date: 27 November 2007
Reviewer: Ann M Geiger
Reviewer's report:
General
This is a modestly interesting and unique report on an effort to conduct community-based recruitment for a prospective study of breast cancer.
survivorship. The manuscript is generally well-written; the following comments are offered to assist the authors in further strengthening the work.

On a positive note, Figure 1 is particularly useful and should not be modified or removed. In addition, the data on clinician contact results (page 14) is rarely reported and would be useful to others planning similar studies.

We would like to thank the reviewer for their acknowledgement of the contribution of our manuscript to the literature on this topic.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The numbers of clinics participating and numbers of women approached are very hard to follow throughout the text. Moving some material, as described below in comments 7 and 8, might help. More importantly, a flow chart incorporating the two sources of recruitment and the number of women at each stage (eligible, consenting, replying, etc.) could be quite helpful. The suggestion that a flow chart would be helpful in understanding recruitment to this study is a very reasonable one and the reason for the absence of such a flow chart was a deliberate one on our part rather than an over-sight. We felt that a flow chart would “set in stone” numbers that were estimates rather than actual totals. We are accepting, although disappointed by, the limited number of women recruited to the study. We feel that the emphasis should be on the lack of bias in the methods rather than on the exact proportion of women recruited. Further explanation and estimates have been added to the Results section.

2. Additional information on study participants versus all Victorian women diagnosed with breast cancer is essential. Age is presented in the text and in Table 2; this is helpful but insufficient. The authors present information in the text about metropolitan and county Victoria, and this should be incorporated into Table 2 and possibly the Abstract. More importantly, some indication(s) of tumor characteristics also should be presented in the abstract, text and Table 2. The best option would be to present some sort of tumor staging and a breakdown of types of treatment received; alternatives might be tumor size and hormone responsiveness. Characteristics of the tumor determine treatment, and both are important predictors of survivors’ outcomes, so clearly this is vital information for anyone contemplating a similar study or reviewing the results of this study. The issue of generalization of results and the minimisation of recruitment bias is important and we have added two characteristics of the sample (tumor size and grade) in relation to publicly available data on all women diagnosed with invasive breast cancer in Victoria. We have added this information to Table 2. The information about place of residence compares our group with all women in Victoria rather than women with breast cancer, so we have kept this information in the text rather than adding it to table 2.

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

3. The overarching purpose of the cohort study seems somewhat diffuse as described. The Abstract mentions physical, psychosocial and socioeconomic consequences, yet the Introduction goes on at length about hormonal treatments and their after effects. This comment is appreciated and the Introduction has been changed to better fit the aims of the study.
In the Methods there is mention of late treatment effects like recurrence, venous thromboembolism and fracture, implying more broad coverage of after effects. Given the purpose of this manuscript is to describe recruitment, a simple and succinct statement of the cohort study purpose should suffice. This statement should be consistently used throughout the manuscript.

The Introduction and Methods section have been modified to concentrate on the primary aims of the study.

4. The Abstract Conclusion notes a "high recruitment rate" yet no such rate is reported in the Results section of the Abstract, and a reader could disagree with the qualifier "high." The authors might simply report their numbers, and conclude that they were able to recruit from the community.

The conclusion section of the abstract has been changed.

5. The Background section is much too long, and contains a substantial volume of information that does not seem directly pertinent to the manuscript. As stated above we have shortened the Introduction and have made it more immediately relevant to the contents of this manuscript. There is no need to describe breast cancer treatment in detail, nor is it appropriate to discuss community controls (page 6) given there is no mention of such controls in this study. The mention of community controls has been removed.

A medium-length paragraph outlining unanswered questions about breast cancer survivorship should suffice as a foundation for this manuscript; these questions should match the succinct description of study aims mentioned in comment #1 above. The Background also should include a brief discussion of the public health literature on recruiting research participants from the community. This has been added.

6. In the Results, on page 8, there are several exclusions from the study that seem like they should appear in Table 1. A reader skimming the paper and looking primarily at tables would otherwise miss these important details. These have been added to Table 1.

7. The material under Sample Size Calculation in the Methods (page 9) seems misplaced, and likely would fit better elsewhere. This section has been shortened (in accordance with earlier suggested changes) and is now limited to a statement that we had considered the sample size in relation to the modelling of determinants of well being.

The description of the recruitment process, including numbers and cessation at 31 months, seems appropriate for the Results, while the impact on the cohort study should be incorporated into the Discussion. We have changed these sections consistent with the reviewer's suggestion.

8. The third paragraph of the results should come before the second (move from larger number of women to smaller numbers). The order of the presentation of the results section has been changed to be consistent with this suggestion.

9. The Discussion is deficient in terms of addressing the impact of the costly and less-than anticipated recruitment on the cohort study (see comment #5 above). A comment about this has been added to the last sentence of the Discussion. The Discussion also should more clearly note that a major limitation of community recruitment work like this is the inability to truly define a denominator and calculate a response rate. This has been added to the Discussion.
Discretionary Revisions (which the author can choose to ignore)
10. The material about centres participation in recruitment may fit better in the Results, as the flow may work well here in terms of describing the actual experience rather than what was originally planned.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Needs some language corrections before being published

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.

Reviewer’s report 3

Title: Method of recruiting Victorian women with a primary invasive breast cancer to a cohort study of wellbeing

Version: 1 Date: 10 December 2007

Reviewer: Elizabeth Maunsell

Reviewer’s report:
Please note: I have numbered paragraphs in the manuscript, starting at 1 in each new section (introduction, methods, etc) and use these to situate certain remarks.

SUMMARY:
The authors address a very important question which, to date, has been overlooked in psycho-oncology research, namely the importance of getting population-based data on quality of life of cancer survivors. To this end, in this manuscript the authors state their objective as reporting on the challenges associated with two strategies used concurrently to recruit to a large, population-based invasive breast cancer survivor cohort in the state of Victoria, Australia. These two strategies were: 1) a community-based approach involving doctors, breast cancer nurses and a public awareness campaign, and for women who had not volunteered to be part of the study as a result of this community approach, and 2) direct recruitment (with passive physician consent) via the Victorian Cancer Registry (VCR).

We would like to thank the reviewer for acknowledging the importance of this area of work.

REVISIONS:

DISCRETIONARY
1. With respect to the population-based study in which these different strategies were tested, why did the authors decide to exclude women with DCIS from it? In Canada and the US, these women are now said to constitute about 13-18% of new breast cancer diagnoses, and they undergo many of the same treatments as women with invasive cancer (surgery, radiotherapy, hormone therapy, although not
chemotherapy). Their exclusion might or might not be the right decision but I suggest that the authors explicitly address the rationale for it directly in future manuscripts reporting on findings from this study. 

*We have added a statement about this issue to the conclusions.*

**MINOR ESSENTIAL**

2. The title of the paper states the subject, but not the conclusion. If as stated, this is BMC policy, the title will need adjustment to give the conclusion.  

*The title of the paper has been changed to better reflect the conclusion.*

**MAJOR COMPULSORY (not always in order of importance, but starting with the key points)**

3. My most important comment on the whole manuscript is that I found the reporting of the key results on the proportion of eligible women recruited, by either method and overall, to be poorly presented. I refer here to the 1st three paragraphs of the results section. While there is a kind of theoretical flow chart for the VCR approach, it seems to me that it would be important to have some tables or a flow chart more clearly documenting actual performance of each method of recruitment. I confess my bias here, that one should move from the larger (ie those eligible) to the smaller numbers here (eventually, those recruited). But in this presentation, different numbers are presented going from small to large and back again.  

*This has been a common theme raised by all three reviewers and we have made extensive changes to the Results section to address this. The reasons why we are unable to provide a simple flow chart have been explained.*

- In the methods, the authors were aiming for 10,000 of 15,000 in a 5-year period, but only recruited 1684.  
- Then in the results, we are told there were 7871 invasive breast cancer cases in a 31-month period, but this number somehow drops to 2898 on the basis of the criteria presented in table 1 (this drop not explained with figures, is this a guess? It would have been nice to see the distribution of reasons, in proportion).  
- I feel that the authors could have presented this with a better synthesis, for example by removing the 63 women reported to be ineligible (but again, I’m not clear because I thought we got from 7871 to 2898 on the basis of ineligibility, or were these guesses?) from both the numerator and the denominator of the proportion participating among eligibles, that is 1747-63, and 2898-63, or 1684 and 2835, respectively.  
- If this is done, 1684 / 2835 = 60% participation and not over 80% (results, paragraph 3) as calculated with a denominator of 2135, who were all contacted women who agreed to participate but not all of whom in fact did. 763 eligible women (2892 – 2135 = 763) have in my view been incorrectly ignored in this calculation.  
- With 60% participation, possible selection bias is of more concern and that is why I think it may be necessary to compare these participants to women with breast cancer generally on other characteristics besides age (a comparison which revealed that older women were underrepresented) (see following paragraph).  

This whole section, which is the heart of the paper, could be quite confusing to the quick reader of this paper it was to me. I also suggest that the authors report the
exact dates (month, year) between which recruitment was conducted in results, paragraph 1.

The dates defining the recruitment period have been added to the results section which has been re-ordered for clarity.

4. The comparison of women recruited on the basis of age (table 2) is good, but limited. Given the 60% participation, and if this cohort is going to be followed up to look at a wide variety of quality of life outcomes (social, marital, and employment outcomes for example), I believe that it would be important to also compare those recruited to those targeted on the basis of percentages married, employed and so forth. If this cannot be done, it should be stated, and perhaps there should be some tempering of conclusions as to the representivity of the cohort recruited.

We have added material about the tumour characteristics. As discussed in the section for reviewer 1, we do not have permission to report on the characteristics of the women not involved in this study. Therefore although appreciating the importance of demonstrating the lack of bias in the recruitment process, we are limited in comparing our participants with published characteristics of women with invasive breast cancer.

5. Little information is provided on the rationale for choosing this two-pronged approach to recruitment, and in particular the addition of the community approach. It is notoriously difficult to recruit women through clinical settings just on the basis of passively presented information (mentioned in paragraph 12, methods) and the brochure given to women, and selection bias using such an approach would be a real possibility. I doubt it was easy or even possible to document the proportion of eligible women to whom this brochure was given, although this is not reported. However, these are the kinds of things I would have expected to see on a paper reporting on and comparing two different approaches. I was unable to find a clear comparison of the proportion of eligible women recruited through this method and the VCR one, and this would seem to be essential.

It was not our intention to formally compare the two approaches to recruitment but to describe that we had used both approaches in an attempt to maximise recruitment.

One of the many drawbacks of the direct recruitment from the community was that we cannot know the denominator for this approach. Our situation was further complicated by the fact that women who notified us directly of their interest in the study were then excluded from recruitment through the Cancer Registry so that those individual women were not approached for this study on more than one occasion.

6. There is considerable confusion in the presentation of study objectives vs manuscript objectives (which are the two strategies used and barriers to recruitment). The population-based prospective cohort study (with data collection by self-administered questionnaire in the first year and then 1, 2, 4, and 5 years thereafter) is the background to this manuscript’s objectives. Currently, there is a great deal of information about the survivorship study itself (the first nine paragraphs of the method), and some of it, while interesting, may be non-essential (for example, paragraph 4 on the study advisory group). Only by paragraph 10 of the methods section do the authors begin to discuss the two recruitment strategies that would seem to be the focus of this manuscript. The authors might consider considerably summarizing information about cohort study.

We have shortened the Methods section but we consider that what we have retained is necessary for the reader’s overall understanding of our study as well as the recruitment process itself.

7. The assertions in paragraph 5 that effects of breast cancer on family,
employment and socio-economic consequences have not been quantified are in fact not true (although I agree that there is a great need for more studies in these areas), and there have been some population-based studies in these areas as well. I direct the authors to some of the key publications by the following authors: family issues after breast cancer, Dorval et al in Canada; work and economic consequences: Bradley and colleagues in the US; Drolet et al and Maunsell et al and colleagues in Canada, and Gordon and colleagues in Australia. We thank the reviewer for this suggestion. We have now included the most relevant of these publications in the Introduction.

8. Methods, paragraph 6: although entitled “sample size calculation”, this seems to be a bit of a misnomer.
- There is no “calculation” here (as one might expect in deciding how many of the incident cases in Victoria were needed for this cohort in order to be able to compare all relevant quality of life outcomes in subgroups, there is only reporting here that the aim was to recruit 2/3 of the 15,000 Victorian women diagnosed in a 5-year period. This section shows that it would in principle be feasible to recruit a large number of women, but provides little information about what for, which would depend on the outcome in question, and what types of differences could be detected.

We have modified this section and retained a general statement about sample size in relation to the modelling of well being.
- Some results (recruitment was more difficult and expensive than anticipated) are also reported in this same paragraph, which is unusual in the methods section.

This has been reorganised
- Then, in methods paragraph 8, the authors state that the sample size is “more than adequate” for modeling various determinants. This may well be so, but it is not shown in the manuscript, and one wonders which number this judgement is based on, the 10,000 women targeted or the 1684 who in fact completed EQs. I believe this needs clarification.

This has been clarified.

9. One of the barriers to recruitment using the VCR method was the problem of late reporting of incident cases to the registry. Again, although not reported, it would have been of interest to know what proportion of eligibles were recruited, for example, in the first 6 months after diagnosis and then in the next 7-9 months using this method, or something along these lines. Not knowing the proportion of women captured in these two time frames, I wondered whether the decision to cut off recruitment at 9 months was a good one (ie missing a substantial proportion of potentially eligible women?) from a population-based viewpoint, especially as it might be argued that quality of life of women at 12 months and at 15 months post-diagnosis might not be that different (and one could assess the affect of time since diagnosis if there was variation, and adjust for it if necessary).

We have tried to further address the issue of delay in notification to the Cancer Registry. We understand the issues involved in creating artificial cut-offs in relation to recruitment. Having decided to use data for our baseline survey that had been collected within 12 months of diagnosis, we were then forced to create another working cut-off of women notified to the Cancer Registry within 9 months of diagnosis because we knew that the process of communicating first with the managing clinician to get permission to contact the woman, then sending the questionnaire to the woman and having her complete and return it took close to 3 months. We are acutely aware that this was the single biggest limitation to recruitment.
We do realise that women recruited soon after diagnosis will be at a different stage of their disease and its management than women who completed their questionnaire 11 months after diagnosis. We will be considering this variation when we report on the characteristics of the cohort in relation to measures such as well being in due course.

10. Although the authors mention costs of each method which I agree is very interesting information to present - at present this is done unsystematically and only in the discussion. Could some of this information also have been summarized in the form of a table in the results? This is another very important barrier to conducting cohort studies of any kind, and one of interest to those thinking about this kind of study.

We have inserted a comment about costs into the Discussion section. Unfortunately although we are able to quantify the costs for the recruitment through the VCR, we cannot accurately assess our costs for the direct recruitment through the community. However we have now said this explicitly.

11. Some conclusions are speculative, since no data are presented to support them. Two examples:

- It is not surprising that elderly women were less interested in volunteering for the study (discussion, paragraph 4). What is this conclusion based on? Other studies? Other data from this study not reported? We have added that this statement is based on our anecdotal experience.

- where eligible women were invited to participate by the VCR, the relatively low active refusal rate may reflect the success of the public awareness campaign. Is this any quantitative or qualitative data to support this conjecture? We have now specified that this statement is speculative.

12. The introduction is very long (the first five paragraphs) and clinically oriented. Could this could be summarized somewhat because the reader is left wondering what the point of this will be? Getting to the objectives of the paper more quickly would help the reader.

The Introduction has been shortened and made more directly relevant to the manuscript.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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.