Author's response to reviews

**Title:** Return to work of breast cancer survivors: a systematic review of intervention studies

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**Author's response to reviews:** see over
Dear Dr. Edmunds,

We would like to resubmit our revised manuscript “Return to work of breast cancer survivors: a systematic review of intervention studies” to your journal. We hereby give a point-by-point response to the reviewers’ comments. We hope that our reply is sufficient and thorough to meet your recommendation for publication. We look forward to your response.

Please note that the order of the authors has changed. In addition, the corresponding author will be Dr Hoving as Dr Broekhuizen is not longer able to do so due to personal circumstances.

On behalf of all the authors,

Yours sincerely,

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The authors’ responses are in italics after each reviewer comment.

Referee 1: reviewer Cathy J. Bradley
A systematic review of only 4 studies seems unnecessary. These studies are highly variable and were conducted over 25 years ago. Breast cancer treatment has changed drastically in the past 25 years. The studies reviewed are highly variable in quality and do not meet typical standards (e.g., RCT) for a "good" study. Knowing that only 4 intervention studies have used return-to-work as an outcome does not sufficiently contribute to the science nor does a critique of the existing studies at anything to the literature. The analysis presented in this paper could be condensed to serve as a background section for a more extensive paper that reports results from a new intervention.

We agree that four studies is not much but in our view this highlights the importance of research in this area as pointed out by the other two reviewers. As one reviewer states, our review is timely and novel, since he is unaware of a similar paper in the literature. We believe that performing a systematic review on this subject warrants publication because of what the impact it may have on future research regarding breast cancer survivors and return-to-work.

Referee 2: reviewer Marja-Liisa Lindbohm
The topic of the paper is relevant because of the growing number of cancer survivors in all Western societies. Information on actions influencing return to work after cancer is needed. Unfortunately, the number of studies detected was only four, and only one of them included a control group. Thus, it is not easy to make conclusions, other than putting more effort to interventions. However, I would have been happy to see more detailed suggestions on the development of interventions.

Thank you for your comments. Following the reviewers suggestions we have made detailed suggestions regarding the content and development of (new) interventions. We have revised the last paragraph of the discussion and give more detailed suggestions on the development of interventions.

We will also address your comments point by point.

Background
1. The authors give as the objective of their paper "to identify intervention studies of breast cancer survivors in which the outcome was return to work”. I think that the aim should also have been to learn something about these studies, i.e. effectiveness of interventions (whether counselling and exercise increases return to work).

   With respect to the objective of our paper "to identify intervention studies of breast cancer survivors in which the outcome was return to work”, we agree and also think that the aim should have been to learn something about these studies. We changed the aim into: “to study the effects and characteristics of intervention studies on breast cancer survivors in which the outcome was return to work”.

Results
2. The table describing the four studies could be made more concise, systematic and congruent. Here are some suggestions how to do this: I suggest that the column “Design” would include only the design, not the number of participants. Now, this number is given in two studies (studies 26 and
27) or three (study 28) different columns, but it could be given only once in column “Participants”. After this correction, the column “Follow-up and outcomes” would include only these topics and it could be entitled “Length of follow-up and outcomes”.

We agree. With respect to describing the four studies in a more concise, systematic and congruent way, we complied to the suggestions given by the reviewer, with regard to:
- the column: “Design” and participants: we only mention the design and not the participants.
- the column: Follow-up and outcomes’: we altered it to “Length of follow-up and outcomes” and included only these topics.

3. All studies: Statement “Work status pre cancer: N=88 (or some other number)” is unclear. I suggest adding 88 employed women.

We agree with the reviewer by not only mentioning the number but also adding employed women in a newly named column “Total number of subjects enrolled”...

4. All studies: I suggest that the expression: Sample and the following text will be excluded from the column “Description, interventions” and this description will be given the text.

We agree with the reviewers’ suggestion for all studies: that the expression Sample and the following text should be excluded from the column “Description, interventions” and this description will be given in the results section.

5. Study 28 by Winnick et al, column “Description” indicates twice that this a post mastectomy rehabilitation group programme. A similar detailed description of counselling content and frequency in this study is given both in the table and the text. A shortened version could be given in the one place and a more detailed in another.

We agree the reviewer and adapted the table: a detailed version of the intervention is given in the study Sachs et al and a shortened version is given in the study Winnick et al.

6. Study 25 by Macquire et al: I suggest that the term EXP will be changed as counselling group.

We agree with the reviewers’ suggestion and changed Exp into counselling group.

7. Study 26 by Fismen et al column “Follow-up and outcomes” includes a statement “Baseline: before rehab programme”. This kind of statement is not included in the description of other studies and it is also unclear what it means. Column “Description, interventions”: description of counselling content is missing.

We adapted the text according to the reviewers’ suggestions and added information on the description of counselling.

8. In general, the description of the studies could be more analytical and comparative. Which aspects (e.g. aim, intervention, length of follow-up) were common to these studies and which were not?

We acknowledge that the results could be more analytical and comparative and have added some extra information in the results section. However, as there are only four studies reviewed, we also agree with one other reviewer that one of the strengths of our study is to include the descriptions of the individual interventions.
9. Instead of giving the numbers of those returning to work (36 out of 46 women) the author should give the percentage like in the description of other studies (text and table 1).

We agree with the reviewers’ suggestions and have included percentages.

On the other hand I suggest that the sentence “of women who had only a breast removed, a simple mastectomy, 100% (n=2) returned to work…” I suggest saying “Two women had only a breast removed, a simple mastectomy and both returned to work”.

We agree with the reviewers’ suggestions and altered the text “Two women had underwent a simple mastectomy, and both returned to work”.

Discussion

10. First paragraph, lines 6-7: The authors’ conclusion on return to work "at best there may be an indication for a positive trend" seems to be based on only one study which included a reference group and indicated that return to work was more common in the counselling group than in the control group. Other studies reported the frequency of those who return to work, but it is not clear whether the frequency had been lower without counselling and exercise. This should be indicated in discussion and abstract.

We agree with the reviewers’ suggestions and used some of the wording of the reviewer. The conclusion in the discussion section has been changed. “Although return-to-work rates around 75%-85% after up to 18 months follow up seem favourable, the lack of recently published high quality studies limits the strength of the evidence observed in these four studies” We also compared our return to work rates with those of other survey studies on breast cancer in the second paragraph of the discussion.

11. First paragraph, lines 9-10: The authors write that "detailed specifics on the content of counselling sessions were not described" in the four studies. I’m not sure what this exactly means because at least three studies seem to have included a description on the counselling content, as reported in the table and the text

We acknowledge that the counselling content has been described, in general, but there is no detailed description on how return to work was promoted other than the women were encouraged to return to work and become socially active again. We have removed this sentence.

12. The last paragraph: The authors say that the most important finding of their review is the lack of methodologically sound research into interventions of breast cancer survivors with the outcome return to work. I think they could go a little further and indicate here in more detail which type of interventions they think should. This could be made based on these four studies, and on ideas obtained from the intervention studies aiming to improve quality of life (references 11-19 in their paper) and from other studies on return to work among cancer survivors.

We welcome the reviewers’ comment that we could go a little further and indicate in more detail which type of interventions we think should be explored. We have made considerable effort in studying the literature and have made several suggestions in the discussion, in several paragraphs. We think this has added some value to the manuscript.
Discretionary revisions

Background

13. In the third paragraph, the authors describe the topics of earlier studies aiming to improve the quality of life of the breast cancer survivors. In addition to describing the topics, I suggest describing shortly the results of these papers. In other words, which interventions were found effective and what were their effects?

We have added some extra information on the interventions (exercises in particular) studied until now that have measured quality of life. This highlights the fact that there is an absence of evidence on interventions that measure return to work: hence our research question.

Methods

14. I wonder whether the authors are familiar with the paper by Verbeek et al (OEM 2005;62: 682-7) on a search strategy for occupational health intervention studies and whether they have followed this strategy. If not, is it possible that they might have found a few more studies using this strategy?

Thank you for this comment. With respect to the paper by Verbeek et al. on a search strategy for occupational health, we have followed this strategy using best search strings as suggested by Verbeek et al. We have described our search strategy in Appendix A of our review.

Results

15. The statement "The women in these studies had less emotional stress and recovered more adequately" should indicate the comparison group.

Both studies did not have a comparison group. They were both before-and after-design studies. We revised the text according to reviewers’ comments. Both studies used a before-after design and reported that PMRG stimulated women to return to work and to resume normal activities.

Discussion

16. First paragraph, lines 12-13: A reference should be given for the statement starting "The individual treatment characteristics have shown...".

We thank the reviewer for this comment. As we have adapted the discussion, this sentence has been deleted.
Referee 3: reviewer John F. Steiner:

In recent years, a number of high-quality observational studies have been published that demonstrate that most cancer survivors are able to return to work, although some of them continue to suffer from disabilities that affect their work. Since the findings of these papers are clear and generally consistent, the focus of the field is turning to intervention studies. In this context, the careful review of the literature on interventions to facilitate return to work after breast cancer by Broekhuizen and colleagues is timely and novel, since I am unaware of a similar paper in the literature. Strengths of the study include the comprehensive and well-documented search strategy and the rich descriptions of the individual interventions. Their call for randomized trials of such interventions is important, and well substantiated by the poor methodological quality of the studies they review.

Thank you for your comments. We will address your comments point by point.

Major compulsory revisions – In most reviews such as this one, the table summarizing the findings of the individual studies is the most useful component. The current table could benefit from several revisions to improve clarity:

Results

1. In column 2, the number of subjects enrolled could be omitted (moved to a new column per my next comment). This information is currently duplicated in a subsequent column

   We agree with the reviewers’ suggestion and adapted the table.

2. In at least 3 of the studies, some individuals were included who were not working at baseline. It might be clearer to add a column indicating the total number of subjects enrolled, the number working at baseline, and the number in each arm of the study (for Maguire), since all subsequent results are based on this subset of the original enrollees. This is a particularly confusing in the presentation of the Winick study, since only 371 of the 1700 subjects were working at baseline. Other exclusions (currently in a subsequent column of the table) might also be described here.

   We agree with the reviewers’ suggestions and revised the table: we added a new column: “Total number of subjects enrolled”. Other exclusions are also described.

3. The “Aim intervention” column could be omitted since the aims of all studies are generally similar, and this would provide more space to describe the interventions and their outcomes.

   We adapted the table and text according to the reviewers’ comment.

4. The description of the Maguire intervention should be clarified. As written, it is not clear that the “counselling” weeks and the “control” weeks were the means of allocating subjects. Rather, it sounds like individuals crossed over from intervention to control conditions week by week.

   With regard to the description of the Maguire intervention, we agree it is confusing. We added the following text to the Results section: “Half the weeks during a 24-month period were designated as ‘counselling’ weeks and the other half as ‘control’ weeks using a random number table. Women admitted for mastectomy in these weeks were assigned to the selected group for the duration of the study.”
5. Information about sample sizes can be removed from the “follow-up and outcomes” column since it will have been reported earlier.

We agree it can be removed from the “follow-up and outcomes” column since it will have been reported earlier.

6. It would be helpful to add information from the Fismen study, if available, about the outcomes measured.

We have added some extra information although there was not much detail in the original publication. We did write to the authors without success.

7. The “effect interventions” column could be retitled “proportion returning to work”, since all the data reported in the table is for that outcome.

We agree with the reviewer and revised the table according to the reviewers’ suggestions.

8. If there are other important comments to make about any of the papers, they could be placed in a “comments” column at the end of the table, although this is not necessary.

We do not have other important comments.

Minor essential revisions – The authors could emphasize the limitations of these studies more forcefully, to support their call for randomized trials. In particular:

9. They make the point that physical exercise and counselling were the only interventions provided. Comprehensive occupational rehabilitation, in which specific job skills are assessed and targeted rehabilitation provided, has not been assessed. This is a limitation of these older studies, which (as they note) newer studies in other areas of rehabilitation are now addressing.

We agree with this comment and have used the reviewers comment (and some wording) to make this point in the text. We thank the reviewer for this point.

10. The lack of recent studies is a very important limitation that needs more emphasis, since modern surgical treatment for breast cancer is likely to cause much less residual disability than the radical or modified radical mastectomies received by many women in the older studies they review. Thus, rehabilitation needs may have changed, as well as the likelihood of returning to work.

We agree with the reviewer and revised the text in the discussion.

11. The influence of a review paper like this would be enhanced if they were to propose methodological standards for subsequent studies, rather than simply advocating for randomized trials. In addition, what types of intervention would they proposed, and what types of outcomes (beyond merely whether someone returns to work) would they like to see in these studies?

We thank the reviewer for this comment. We have changed this in the discussion as was also suggested by the previous reviewer.

Discretionary revisions
12. The introduction might flow better if the last paragraph on p. 3 was inserted before the paragraph about interventions.

We agree with the reviewer and revised the introduction according to the reviewers’ suggestion.

13. They state on p. 4 that their objective was to “identify” relevant studies. I would encourage the authors to be more assertive about their goals, and include an objective to “critically review” those studies with the goal of informing the design of intervention trials.

We agree that a critical review would benefit the paper. We altered the text: “The objective of this review was to study the effects and characteristics of intervention studies on breast cancer survivors in which the outcome was return to work”. In the discussion we critically review the studies and give options for interventions.

14. Can we even draw the conclusion that there is a “positive trend” (p. 10) in return to work after these interventions, given the limitations of study design?

We agree. Given the quality of the evidence this is somewhat too positive perhaps. See previous comment to reviewer. We have omitted this sentence and rewritten this paragraph.