

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Return to work of cancer patients after a multidisciplinary intervention including occupational counselling and physical exercise in cancer patients: a prospective study in the Netherlands
AUTHORS	Leensen, Monique; Groeneveld, Iris; van der Heide, Iris; Rejda, Tomas; van Veldhoven, Peter; van Berkel, Sietske; Snoek, Aernout; van Harten, Wim; Frings-Dresen, Monique; de Boer, Angela

VERSION 1 - REVIEW

REVIEWER	Anja Mehnert Department of Medical Psychology and Medical Sociology, University Medical Center Leipzig, Germany
REVIEW RETURNED	21-Nov-2016

GENERAL COMMENTS	<p>This is an interesting prospective study evaluating return to work (RTW) outcomes in cancer patients after completing a multidisciplinary intervention. The study addresses an important research area in cancer survivorship given the fact that interventions studies on employment and work issues are relatively sparse so far. The paper is clearly written and the authors adequately address the weaknesses of the design such as the lack of randomization and a control group that limit the interpretation of study findings. I'd like to address the following points that might help to improve the paper:</p> <p>Abstract: Please report the patient response rate.</p> <p>Article summary: The lack of randomization is also a limitation. Possible bias might also include female gender (84% women) and education, for example.</p> <p>Introduction: Well written and logical.</p> <p>Methods: How many patients were eligible for the study? How many patients declined or could not be included due to other (e.g. organizational) reasons. It would be helpful if you could provide a flowchart with eligibility numbers, drop outs etc. also in order to estimate a possible sample bias.</p> <p>Results: The findings show an overall improvement in muscle strengths, fatigue and QoL and increasing RTW rates. We don't know if this is the effect of the intervention program or if that is the usual course of the recovery process particularly since only patients (mostly breast cancer patients) with curative treatment intention were included. How was physical fitness and qol related to RTW in patients with different occupational backgrounds (e.g. years in employment etc?)</p> <p>How many patients completed how many exercise sessions and counseling sessions (1-3). Was there an association between the intensity of the physical exercise program and the number of counseling sessions? Are there any additional results about topics that have been addressed at the individual counseling sessions?</p>
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	<p>Since this study has a variety of methodological limitations, it would be important to provide further details about the occupational counseling outcomes or the program itself, who participated in how many sessions etc. Physical exercise programs are widely proved and the originality of this work lies in the combination of physical exercise and occupational counseling (against the background of different work situations). This combination is not really show in the results.</p> <p>Discussion and limitations: The interpretation of the findings is not easy due to lack of control patients and randomization. However, I'd recommend being more carefully with the conclusion based on these study findings, because this program cannot be recommended since we don't know if it is effective (it might be, maybe also not for all patients, but we don't know that yet). It might be better to address further research needs and recommendation based on the results presented in terms of future intervention studies.</p>
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REVIEWER	Dr Camille Short University of Adelaide, Australia
REVIEW RETURNED	05-Dec-2016

GENERAL COMMENTS	<p>This study describes the findings from a multidisciplinary intervention study designed to support cancer survivors return to work after cancer treatment. The approach combines counseling from an occupational therapist and physiotherapist, which has not been trialed previously. The program is thought to work by increasing physical fitness and reducing fatigue via exercise, and decreasing barriers to entry through counseling. While the intervention is a good idea, the evaluation is limited by a lack of control group. The authors note that due to this design they are unable to determine if the intervention works. I tend to agree. This limits the usefulness of the results presented.</p> <ol style="list-style-type: none"> 1. The length of the exercise program and the frequency of sessions each week is not clear from the description on page 6. This makes it difficult to assess if it is appropriate. 2. Socio-demographic baseline measures are described under the heading "outcome measurements". These variables are not outcomes. Suggest restructuring this section. 3. The primary outcome was if patients had returned to work in any capacity at the follow-up time points. This measure lacks specificity. Is there a reason why the degree of return to work was not also assessed or reported? Given that number of hours worked was assessed at baseline it seems that this would have also been very useful to collect at follow-up. If survivors had returned to work but were working significantly fewer hours this would be clinically relevant. 4. The rationale for focusing on importance of work is not clear. 5. Bonferroni corrections were performed for some comparisons and not others (i.e., muscle strength and fitness). Why was this the case? 6. What was the response rate? It should be possible to report how many people were invited into the program - or at least provide a
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	<p>rough guide. This has implications for how representative the same is and therefore how reasonable it is to look at population levels of return to work and compare with your findings. Given there is no control group this is essential to draw any meaning from the results. Otherwise your findings could just reflect the normal increase in well-being and return to work after treatment. Longitudinal studies with representative samples have shown this to be the case.</p> <p>7. The results often focus on T1 and T3 but not T2.</p> <p>8. Given lack of control group it would perhaps be more useful for informing future research if the focus was more on process evaluation measures rather than efficacy measures. For example, what was the rate of adherence to the exercise sessions? Was recruitment into the program difficult? Was it expensive to deliver? Were there some participants that increased more than others? For example, if the research shows that people who have worse health at baseline have worse outcomes in the long-term you could see if this was the case for you. If not, it might suggest your intervention worked.</p> <p>9. Strongly suggest that you describe your sample in detail and note how representative it is of the target population. E.g., is it representative in terms of baseline work and health levels. You should then describe population based data on return to work rates... if your sample is slightly biased you would expect slightly better values but it will still give you a yard stick. At this point, I am not convinced that the intervention had an effect (knowing that outcomes naturally improve over time but not sure exactly how much).</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Anja Mehnert

Institution and Country: Department of Medical Psychology and Medical Sociology, University Medical Center Leipzig, Germany

Please state any competing interests or state 'None declared': None declared

This is an interesting prospective study evaluating return to work (RTW) outcomes in cancer patients after completing a multidisciplinary intervention. The study addresses an important research area in cancer survivorship given the fact that interventions studies on employment and work issues are relatively sparse so far. The paper is clearly written and the authors adequately address the weaknesses of the design such as the lack of randomization and a control group that limit the interpretation of study findings.

Thank you.

I'd like to address the following points that might help to improve the paper:

1. Abstract: Please report the patient response rate.

Response rate was 56% (see comment on 'Methods' below). This is added to the abstract.

2. Article summary: The lack of randomization is also a limitation. Possible bias might also include female gender (84% women) and education, for example.

The possible biases with respect of the high number of females in the sample and the relatively high level of education has now been added to the article summary. "Possible biases are in the selection of participants with respect to the type of cancer, the high number of females (84%) and the relatively high level of education. "

3. Introduction: Well written and logical.

Thank you.

4. Methods: How many patients were eligible for the study? How many patients declined or could not be included due to other (e.g. organizational) reasons. It would be helpful if you could provide a flowchart with eligibility numbers, drop outs etc. also in order to estimate a possible sample bias.

During the first four months of our study registration records on the eligibility of newly-diagnosed patients and their willingness to participate were completed by oncologists and oncology nurses. These records contained information about cancer patients at both sites who did not fulfil the inclusion criteria, information on eligible patients willing to participate, and reasons for non-participation. Data from this sub-population were used to assess eligibility and study decline during this period, assuming this could be extrapolated to the total study period. Because these are no actual patient numbers, now flow diagram could be provided. Of the patients treated at the oncology departments of the participating hospitals, 49% were not eligible for participation, the majority of whom because they were older than 60 years. Of the eligible patients, 56% were willing to participate in this study (reach). There was no difference between participants and non-participants in terms of gender and age at baseline. These outcomes are included in our abstract, methods section and results.

5. Results: The findings show an overall improvement in muscle strengths, fatigue and QoL and increasing RTW rates. We don't know if this is the effect of the intervention program or if that is the usual course of the recovery process particularly since only patients (mostly breast cancer patients) with curative treatment intention were included. How was physical fitness and qol related to RTW in patients with different occupational backgrounds (e.g. years in employment etc?)

To explore differences in the relations between physical fitness and quality of life related to RTW with different occupational backgrounds would be an interesting research question. However, we do not have enough patients in our sample to explore this question because we would have to stratify our sample over the different occupational backgrounds and then examine the relationship between physical fitness and quality of life related to RTW for each stratum. Subsequently, differences in the strength of the associations should be tested between the strata and we do ,unfortunately, not have enough statistical power for that.

6. How many patients completed how many exercise sessions and counseling sessions (1-3). Was there an association between the intensity of the physical exercise program and the number of counseling sessions? Are there any additional results about topics that have been addressed at the individual counseling sessions?

We have added information about the adherence rate of the exercise (86%) and counselling sessions (94%) in the results section (See page 9). To analyse the association between the adherence to the physical exercise program and the number of counselling session, we assessed a Spearman correlation which was 0.22. This is now added to the Methods and Results session. No additional results about topics of the individual counselling sessions were available.

7. Since this study has a variety of methodological limitations, it would be important to provide further details about the occupational counseling outcomes or the program itself, who participated in how many sessions etc. Physical exercise programs are widely proved and the originality of this work lies in the combination of physical exercise and occupational counseling (against the background of different work situations). This combination is not really show in the results.

We have added additional information on who (not) participated in the occupational counselling session with reason for declining further session on page 9: "Regarding the occupational counseling sessions, 94% of the participants attended the first protocolled session, 35% attended the optional second sessions and 8% had a third session with the OOP. Reasons for not attending the second or third included already returned to work (n=27), receiving good support from the company's occupational physician (n=25), receiving good support from their employer (n=18), and not considering further support necessary (n=10)."

8. Discussion and limitations: The interpretation of the findings is not easy due to lack of control patients and randomization. However, I'd recommend being more carefully with the conclusion based on these study findings, because this program cannot be recommended since we don't know if it is effective (it might be, maybe also not for all patients, but we don't know that yet). It might be better to address further research needs and recommendation based on the results presented in terms of future intervention studies.

We do agree that the interpretation of findings is not easy and that we should be careful with our conclusions. Because our current study was not a controlled study it is not possible to draw strong conclusions on the effect of the addition of occupational counselling. Our recommendation to offer this intervention to all eligible cancer patients may therefore have been stated to strongly. We adapted this and recommend to do more research regarding the effects in a controlled study first (see page 13).

Reviewer: 2

Reviewer Name: Dr Camille Short

Institution and Country: University of Adelaide, Australia

Please state any competing interests or state 'None declared': None declared

This study describes the findings from a multidisciplinary intervention study designed to support cancer survivors return to work after cancer treatment. The approach combines counseling from an occupational therapist and physiotherapist, which has not been trialed previously. The program is thought to work by increasing physical fitness and reducing fatigue via exercise, and decreasing barriers to entry through counseling. While the intervention is a good idea, the evaluation is limited by a lack of control group. The authors note that due to this design they are unable to determine if the intervention works. I tend to agree. This limits the usefulness of the results presented.

1. The length of the exercise program and the frequency of sessions each week is not clear from the description on page 6. This makes it difficult to assess if it is appropriate.

The exercise program lasted 12 weeks and provided 1-hour training sessions twice a week. A total of 24 exercise sessions were planned for each participant. The length of the program and frequency of sessions is added to the paragraph 'Multidisciplinary rehabilitation program' (see page 6).

2. Socio-demographic baseline measures are described under the heading "outcome measurements". These variables are not outcomes. Suggest restructuring this section.

Thank you. We have now labelled this section “Measurements” and indicated which measures our outcomes in the subsequent sub headings.

3. The primary outcome was if patients had returned to work in any capacity at the follow-up time points. This measure lacks specificity. Is there a reason why the degree of return to work was not also assessed or reported? Given that number of hours worked was assessed at baseline it seems that this would have also been very useful to collect at follow-up. If survivors had returned to work but were working significantly fewer hours this would be clinically relevant.

Previous studies have shown that when cancer survivors return to work, this is often for less working hours than prior to diagnoses. In some cases this is only temporary – part time work is part of the recovery program and they gradually increase their working hours. This gradual work resumption is also one of the topics that the OOP discussed during the counseling sessions within our intervention. Therefore we chose to focus on any RTW after the completion of the intervention without a specification of hours.

4. The rationale for focusing on importance of work is not clear.

In our introduction we stated that ‘Additional to this practical support, an OP may help to improve the attitude towards (return to) work or address misconceptions about work ability. Negative expectations about illness, future work capacity and RTW are associated with slower RTW in patients with different types of chronic disorders [22,23]. Also, personal factors such as self-assessed work ability [24] or motivational factors such as the intention to RTW or meaning of work [7], that may affect RTW can be addressed by an OP.’ The importance of work is measured in order to explore the meaning of work as experienced by cancer patients during our study.

To clarify this, a sentence is added to the paragraph ‘Secondary outcome measures’ at page 7.

5. Bonferroni corrections were performed for some comparisons and not others (i.e., muscle strength and fitness). Why was this the case?

Bonferroni corrections were performed in order to correct for multiple comparisons and were applied to analyses incorporating more than 2 repeated measurements. This was the case for the majority of outcome measures as these were measured 4 times (baseline, T1, T2 and T3). Muscle strength and cardiorespiratory fitness were only measured at baseline and at completion of the program. Hence there were only 2 measurements available which justifies the application of a normal paired t-test without corrections for multiple comparisons.

To clarify this, we made small changes to the ‘statistical analyses’ section on page 8.

6. What was the response rate? It should be possible to report how many people were invited into the program - or at least provide a rough guide. This has implications for how representative the sample is and therefore how reasonable it is to look at population levels of return to work and compare with your findings. Given there is no control group this is essential to draw any meaning from the results. Otherwise your findings could just reflect the normal increase in well-being and return to work after treatment. Longitudinal studies with representative samples have shown this to be the case.

This is a relevant remark, also provided by reviewer 1. See our response to this comment above. Of the eligible patients, 56% were willing to participate in this study. There was no difference between participants and non-participants in terms of gender and age at baseline.

7. The results often focus on T1 and T3 but not T2.

We measured various outcome measures at 4 times during our study. We wanted to avoid describing a great range of comparisons in order to improve clarity and readability of the manuscript. That is why our analyses focused on both the difference between baseline and T1, to assess changes during the rehabilitation program, and the difference between T1 and T3 to assess changes over the remaining follow-up period. Although the results measured at T2 are not extensively described they are displayed in all presented tables.

8. Given lack of control group it would perhaps be more useful for informing future research if the focus was more on process evaluation measures rather than efficacy measures. For example, what was the rate of adherence to the exercise sessions? Was recruitment into the program difficult? Was it expensive to deliver? Were there some participants that increased more than others? For example, if the research shows that people who have worse health at baseline have worse outcomes in the long-term you could see if this was the case for you. If not, it might suggest your intervention worked.

Thank you for indicating this very important point.

Reviewer 1 also raised questions about adherence in this study, and we added information about the adherence rate of the exercise (86%) and counselling sessions (94%) in the results section (See page 10, Results)

We performed our analysis based on the total group, for reasons of statistical power hence we were not able to compare subgroups of patients with different health measures at baseline with regard to their long-term outcomes.

However, we think that it might be very useful to compare our study population to that of both the control and intervention groups in the comparable study of van Waart et al (2015). They studied the effects of different exercise programs in a group of breast cancer patients in the Netherlands and also report return to work rates.

Although we included patient with several types of cancer, the majority of our population consists of breast cancer patients (84%) with comparable baseline values of reported by van Waart, except that in our population baseline scores for fatigue were slightly higher, indicating more fatigue, and baseline scores for quality of life scales were slightly lower, indicating lower quality of life and health. Our RTW rate of our population was 86%, which is comparable to the RTW rate of the supervised exercise group of van Waart, which was 83%. We believe that this indicate that our intervention had an effect. Especially when compared to the control group of van Waart, which showed a 61% RTW rate. This comparison is discussed in the Discussion, page 13.

9. Strongly suggest that you describe your sample in detail and note how representative it is of the target population. E.g., is it representative in terms of baseline work and health levels. You should then describe population based data on return to work rates. if your sample is slightly biased you would expect slightly better values but it will still give you a yard stick. At this point, I am not convinced that the intervention had an effect (knowing that outcomes naturally improve over time but not sure exactly how much).

We agree that we should describe our sample and compare it to population bases data on RTW rates as much as possible. In our discussion section (page 13) we compare the RTW rates observed in our study with population based data as described by Mehnert et al. We agree that comparison have maximum validity when our population is representative of the target population. Since the population data of Mehnert et al. is based on review data derived from 64 different studies including a variety of diagnoses, legislation of countries, education levels, etc, the work and health-related baseline levels of all these populations are unknown. This makes it hard to compare these baseline levels to our population.

However, we do know that in term of work-related data, our population is representative for the Dutch working population, in term of working hours, type of contract and company size. We do see a

overrepresentation of highly-educated women in our study population which is a result of the high percentage of breast cancer patients included in our study.

The studies included by Mehnert included patient with various cancer types. The fact that the majority of our participants had breast cancer may have biased the comparison to their data. Nevertheless, the population based partial RTW rate in a representative sample of Dutch breast cancer patients only in 2008, was 71% after 1 year (Roelen 2011a) or 2 years (Roelen 2011b). This is lower than the rates we observed in our study. This information is now added to the Discussion, page 13: “As these findings were based on 64 different studies, we cannot assess whether the baseline characteristics of our study population is representative of those reviewed by Mehnert [7]. However, we do know that our participants are representative of the Dutch workforce in terms of working hours, type of contract and company size. We did have, nevertheless, an overrepresentation of highly educated women caused by the inclusion of a high percentage of breast cancer patients. Hence we also compared RTW rates to those of Dutch breast cancer patients only. Most recent findings were 70-71% for partial RTW 12 and 24 months after diagnosis [25,26], which are lower than our findings as well.”

Because of we believe that we should not only compare RTW rates of our population to population based data, but also to RTW rates of a comparable population if available, we can use both the intervention groups and control group of the study of van Waart et al. (2015) (See our discussion and previous comment). This population is comparable to ours and they study the effects of a comparable exercise intervention. The finding that our RTW rate of 86% is comparable to the rate of their intervention group (83%) and higher than the rate of their control group (61%) suggests that our intervention has an effect.

We added some comments on the representativeness of our study population and comparisons to data of other, more comparable, populations in our discussion section (see page 13).

VERSION 2 – REVIEW

REVIEWER	Camille Short University of Adelaide, Australia
REVIEW RETURNED	10-Feb-2017

GENERAL COMMENTS	<p>The lack of control group is a limitation of the study which does restrict the ability of the study to address the research question. However, the authors have provided a reasonable case and I believe this data will be of interest to those working in the field</p> <p>Regarding point 3. I agree that focusing on return to work (at all) is a useful outcome and is a reasonable approach. However, it does seem like it would be useful information to know the extent of return to work too. For example, the authors note that many survivors return to work temporarily. If there is a future trial of this study it would be useful to know if those that returned to work remained in work etc. I don't think the authors need to make any additional changes at this point but something to consider.</p> <p>Regarding point 5. Thank you for providing this explanation. As I understand it, correction for multiple comparisons is often done when there are multiple hypotheses/ outcomes being tested. This is because each time a test is performed you increase the likelihood of finding a false positive result. That said, it is standard practice to only do this when there are two primary outcomes. Given you clearly specify one it seems your approach is somewhat conservative. No additional changes requested.</p>
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