Author's response to reviews

Title: Safety, feasibility and effects of a walking intervention for women undergoing chemotherapy for ovarian cancer: a pilot study.

Authors:

Melissa J Newton (mj.newton@qut.edu.au)
Sandi C Hayes (sc.hayes@qut.edu.au)
Monika Janda (m.janda@qut.edu.au)
Penelope M Webb (penny.webb@qimr.edu.au)
Andreas Obermair (obermair@powerup.com.au)
Elizabeth G Eakin (e.eakin@sph.uq.edu.au)
David Wyld (David_Wyld@health.qld.gov.au)
Louisa G Gordon (louisa.gordon@griffith.edu.au)
Vanessa L Beesley (Vanessa.Beesley@qimr.edu.au)

Version: 2 Date: 9 August 2011

Author's response to reviews: see over
9th August, 2011

Dr Christna Chap
Executive Editor
BMC Cancer


Dear Dr Chap,

Thank you for forwarding the reviewers’ comments on our manuscript. We have given careful consideration to these, with responses outlined below and changes made to the manuscript indicated with yellow highlights in version 2.

Reviewer #1’s comments:

Are the methods appropriate and well described?
- Please provide additional information about how the program was individualised to patients. Please address why longer walker session occurred earlier in the program? How did the program change over time? Why did they exercise longer at the start and shorter later?

The following sentences were amended to clarify how the program was individualised a) at the beginning and b) throughout the intervention. They also clarify that once active, women’s exercise prescription time generally got longer (not shorter).

“Initial targets were based on pre-intervention assessment of physical functioning and level of physical activity. Sedentary women were instructed to begin by taking frequent (most days), but lower-intensity, shorter duration (10 minute) walks. Active women were initially instructed to maintain their current number of sessions and increase firstly the duration and later the intensity.” (page 6, paragraph 2).

“During these weekly sessions, presence and change to treatment-related side-effects were identified, barriers to walking were discussed and resolved when possible, details of previous week’s walking sessions were discussed, and based on this the subsequent week’s walking targets were prescribed per individual.” (page 6, paragraph 2).

It was weekly sessions with the exercise physiologist that were longer in the earlier weeks to accommodate the education component of the intervention. Amendments have been made to the text, to clarify this point: “The weekly session duration with the exercise physiologist was between 20-60 minutes, with longer sessions typically required in the earlier weeks of the intervention to ensure the topics within the education booklet were discussed.” (page 6, paragraph 2).

- Provide additional limitations of the research – limited sample size etc.

The second sentence of the last paragraph summarises the range of limitations of this work including small sample size and non-randomised, single-arm design. To cover these further within the context of the discussion the following sentences were amended:

“While the absence of a randomised control group prevents the establishment of a causal relationship and the small sample size means that some changes did not reach statistical significance, the changes observed are similar to those reported from aerobic exercise interventions in women with breast cancer.” (page 12, paragraph 2)
“…a larger sample with randomised controlled data is needed to confirm whether exercise can assist in improving chemotherapy completion rates.” (page 12, paragraph 3)

Reviewer #2’s comments:

- Early in the paper it would be helpful to introduce the ‘concerns’ that were raised prior to initiating the study.
- What is unique about patients with ovarian cancer (in comparison to breast cancer) that might prohibit them from participating in a walking program? Why do you think they might respond differently than other cancer populations?

During the ethical approval process, many questions were raised over the risks involved with the patients undertaking an exercise program during their adjuvant therapy, including whether it was appropriate and whether they could tolerate the intervention and do so safely. To date, ovarian cancer patients have not been the focus of exercise trials, which may have caused concern with the hospital ethical body. Yet on the other hand, the evidence supporting the role of exercise during and following cancer treatment continues to grow and we have also been questioned regarding the novelty and importance of this work. In response, we have included three statements to further justify the need for this work (statement 1 below, added to the introduction) and to highlight the importance of these preliminary results (statement 2 and 3 below, added to the start and middle of the discussion, respectively:

**Statement 1:** Women with ovarian cancer differ from other cancer groups due to their older age, predominantly late stage diagnosis, poorer prognosis, treatment involving major abdominal surgery and different chemotherapy agents/doses/regimens with significant side-effects. (page 3, paragraph 1)

**Statement 2:** The lack of ovarian cancer patients involved with previous exercise intervention trials created concerns that needed to be overcome during the ethical approval process for this study. (page 11, paragraph 3)

It was a considerable challenge to mount our pilot study, given the prevailing assumption that exercise intervention is not appropriate for women undergoing chemotherapy for ovarian cancer. (page 11, paragraph 4)

- Can you comment on the possibility that the exercise program contributed to the hospitalizations, illness etc?

We have clarified (page 10, paragraph 1) that when participants missed sessions during the exercise intervention this was usually due to cancer treatment-related hospitalization (verses were the cause of hospitalization or illness). How women tolerated their treatment-associated symptoms was patient-specific. Symptoms were tracked weekly along with their participation in the intervention and there was a direct relationship with timing of symptoms and receipt of chemotherapy, with symptom change not being associated with progression or maintenance of walking prescription.

- In the study 13 of 17 women completed 85% of their planned chemotherapy dose; this variable should be calculated for all 17 participants. How does this compare to the 83% reported in women with advanced ovarian cancer? Comment on the effect of this exercise intervention on chemotherapy completion rate.

Range and median percentages of RDI were calculated for all participants and are included in the results section (page 11, paragraph 2). In light of the reviewer’s comment though and with further consideration of the appropriateness of comparing results to others we have now included the median RDI in the discussion and revised the subsequent text accordingly: “It is difficult to compare these data with other reports of chemotherapy completion in ovarian cancer as previous studies have been drug trials that deliver non-standard chemotherapy regimens and limit their samples to women with advance disease.” (page 12, paragraph 3).
- Did the face-to-face weekly contacts with the exercise physiologist involve supervised exercise?

Yes. During each weekly visit (face-to-face group) a walking session was conducted by the participant and supervised by the EP. Additional text has been included in the results section (page 6 paragraph 2) to reflect this. "For the face-to-face group this session included a supervised walk with the exercise physiologist”.

- Overall adherence should be reported as a percentage of all 17 women. Should adherence not be defined as the number of exercise sessions completed/the number of exercise sessions prescribed?

Information presented in the results section now includes the overall group adherence as a percentage. “Overall group adherence was 90% (range 55% to 100%). (page 10, paragraph 1). Adherence was determined by the number of completed sessions divided by the number of scheduled sessions. (page 7, paragraph 2).

Additional comments from the Associate Editor:

In the paper, the authors use the following terms: baseline and follow-up; pre-participation and post-participation; and pre-intervention and post-intervention. Are these the same pair of events?

Yes. Pre- and post-intervention is now the only term used throughout the manuscript to avoid reader confusion.

Once again we thank the reviewers for their comments and believe the amendments improve the quality of the paper. We look forward to hearing the outcome of this submission.

Sincerely,

Melissa Newton