Reviewer’s report

Title: Relaxation and Exercise In Lymphoma survivors (REIL study): a randomised clinical trial protocol

Version: 0 Date: 21 Feb 2019

Reviewer: Alexander R Lucas

Reviewer’s report:

I commend the authors for preparing this study and thank them for the opportunity to review their work. However, I do have a few concerns about how the study protocol is described. Specifically, this is a pilot, feasibility study, unless data already exists showing that either of the intervention arms, as described, have been successfully delivered to lymphoma patients in the home-based setting. While I feel this work is important and that as a group Lymphoma patients certainly warrant further study, your study design needs to be clarified in some areas. For example, with home based interventions, it is likely that maintaining adherence to protocols will be challenging, especially in a population of survivors with high levels of fatigue and possible exercise intolerance. Furthermore, as lymphoma patients undergo fairly intensive chemotherapy regimens and are at risk for cardiotoxicities, how will the study team monitor survivors for adverse events (even response to exercise) to maintain safety? A description of these process is important. One other general area of concern is the tendency to over reach with statements about the likely impact of this work. This is very early stage enquiry and as such should be placed in that context. Completing your study will certainly provide important information, though this will need to be used to conduct definitive studies that may then provide some of the evidence you are seeking.

My specific comments are below:

Abstract

The conclusion is written in language that needs to be walked back. While there is a potential to improve the quality of life of cancer survivors who engage in either exercise or relaxation, a statement to the effect of "becoming a fully functional member of society" is misplaced.

Background

1. The introduction introduces the concerns most commonly reported in cancer survivors in general. While this is fine, the population of patients focused on in this study have lymphoma, which has quite unique characteristics when compared to many other cancer types. Therefore, it seems that the introduction could be more focused on this group.
2. Page 3, paragraph 3 - the statements that exercise and mind-body interventions both have positive effects on physical and psychological symptoms is fairly broad, can the authors provide specific examples?

3. The point about appropriate control groups is well made.

4. Page 4, paragraph 2 - The first sentence describing the approach to addressing gaps previously identified needs revision. For example, "holistic assessment" seems unfinished, do you mean conducting a holistic assessment?

5. Page 4, paragraph 2 - statement regarding building towards development of evidence-based care pathways for lymphoma survivors, may be a bit strong. This study is more appropriately described as a pilot study where you seem to be assessing the feasibility and perhaps preliminary efficacy (given minimal sample size of 18 per group for detecting clinically meaningful change in QOL) of conducting your intervention arms and will likely not be able to definitively state benefit or provide an evidence-base to change clinical practice or care guidelines.

Methods

6. Page 5, paragraph 1 - do you expect to need to stratify your randomization by any further factors? For example, will BMI, age or gender be relevant to your outcomes?

7. Page 8, paragraph 1 - In describing the exercise intervention, it is written "they will be taught resistance exercises for the major upper and lower limb muscles" This seems to introduce a number of questions, such as: Who is teaching them? What is the experience/training of the person teaching the exercises? The authors in a later paragraph describe that both interventions will be taught by the PI at baseline. This information should be presented before the description of the two interventions.

8. Page 8 paragraph 3 - the authors write that participants will be able to contact the PI for additional support. This seems to be a limitation. Why is there no effort to contact the participants on a regular basis, as it is well known that adherence to protocol is often poor without support? Waiting for a participant to contact the study team is unlikely to happen the way described.

9. Page 9, body composition - is the Tanita BC, a bioelectric impedance device? Please clarify what components of body composition you will measure. Body fat only? Or body fat, fat free muscle mass? Is the Tanita also a scale that will be providing body weight to use in conjunction with height to calculate BMI? Please be specific.

10. Page 11, well-being. It is not clear why you are describing the FACT-Lym as a measure of well-being when compared to the EORTC as a measure of QOL? It seems that it is more common and acceptable to use a measure of global well-being to assess this construct. Please clarify how you are operationalizing and differentiating these constructs.
11. Analyses - seem appropriate.

Discussion

12. Page 13, paragraph 2 - talks about the use of a "whole-person" approach. This is new in the manuscript and there is no previous description of what this refers to. I would therefore caution against the use of this term. The authors are also not assessing what the social, psychological or physical needs of your population is. If you were then you would screen for patients who had deficits in these areas. I think you can get your point across in more conservative language.

13. Page 13, paragraph 2, lines 40-43 - "these approaches have been adopted to encourage participation and minimize drop out" It is not clear to the reviewer how the design of the intervention is likely to do this.

14. Page 14, paragraph 1 - as with other places in the manuscript, the writing is a little hyperbolic. This study may provide some feasibility metrics and preliminary support for your approach; however, it is unlikely to provide evidence for feasible, effective, cost-efficient care pathways. I suggest walking it back a little to reflect the scope of your planned study.

15. Page 14, conclusions - placing both cancer and lymphoma patients in the same bucket (lines 24-25) is no advisable. While there may be some overlap between a program designed to maximize benefits (QOL, functional status) in lymphoma patients, this will differ greatly by cancer type, further by disease stage and treatment regimen. Focus on lymphoma patients as that is the population your study examines.

16. Page 14, conclusions - I believe you need to be more precise in stating how you hypothesize your two intervention arms will lead to improvements in QOL. It is likely that exercise will improve physical function to a greater degree, which may then indirectly lead to improvements in aspects of psychosocial functioning while relaxation training will lead to greater psychosocial benefits. Your current design is unlikely to have the power to detect these effects. Another thought is that while many interventions are taught in a group-based setting, this is home based. Therefore, the social benefits may be limited.

Tables and Figures

None.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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