Author’s response to reviews

Title: Feasibility and acceptability of an online mindfulness-based program for patients with melanoma: protocol for a randomised controlled trial

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Author’s response to reviews:

We thank the reviewers for their comments and suggestions. Changes in the manuscript are highlighted in yellow.

Reviewer #1: This is an important and interesting protocol. Here are some minor comments.

BACKGROUND

(1) Page 1, lines 2-4. The sentence is not clear. What risk in the general population is being compared with?

Response: Thank you for your question. We agree that comparison to the general population may confuse the intended message. The sentence has therefore been changed in the manuscript (p.1) from:

“The risk of developing a new melanoma following treatment for the primary tumour is nine times higher than in the general population, and remains elevated more than 20 years after the initial diagnosis.”
To:

“People who have received treatment for melanoma are up to nine times more likely to develop a new melanoma, and this risk remains elevated for more than 20 years after the initial diagnosis.”

(2) Are there any studies of long-term impact of mindfulness-based programs on outcomes?

Response: Thank you for your question, this is a really important issue. We have explored this in detail in a systematic review, which is currently under review. Briefly, long-term impact is not well assessed. Given this is an important point, we have now included a sentence to the discussion outlining the importance of longer term follow-up. The following wording (in yellow) is included in the manuscript (p.19):

“This study will support the design of a full-scale RCT with a longer follow-up period, and information collected from the recruitment process will highlight methodological aspects to address in the planning of a larger scale study.”

METHODS

(1) Page 5, eligibility criteria: is a patient eligible if he/she has experienced recurrence but is not receiving treatment?

Response: Thank you for asking for clarification on this important criterion. A patient who has experienced a melanoma recurrence, but has not received treatment at the time of recruitment would not be eligible to participate as this study. We are exploring the potential benefit of the intervention on fear of cancer recurrence following initial treatment. Eligible participants therefore needed to have successfully completed their treatment.

(2) Randomization: line 132. Which is the 6th strata?

Response: We thank the reviewer for spotting this typographical error. We have updated the text and changed the number to 8.

(3) Description of the intervention: page 7. Additional details about the program are needed. Specifically, following issues were not clear:

(i) How many days in week is the program offered?

Response: The program is offered every day of the week. A sentence has been added in the paper, at the end of the intervention description section to state that:
“Participants will have access to the mindfulness program at any time and every day of the week via the hyperlink sent in the e-mails.”

(ii) What is the length of each daily session?

Response: Participants are instructed to engage in daily meditation practice, and the length of a meditation session will range between 5 to 10 minutes a session. This is detailed in Figure 2 (p.8).

(iii) Is it possible that repeated viewing of the video can lead to a dose-response scenario?

Response: This is a very interesting question, thank you. The possibility that repeated viewing of a video could lead to a dose-response scenario cannot be ruled out. Under “Adherence tracking and meditation log” (p.18) we proposed to track participants’ online activities which includes number of time a video was viewed. Results from this feasibility study will inform the design of a larger randomised controlled trial, which could potentially include a dose-response analysis.

FIGURE 1

(1) Do the participants in the second box (n=327) meet all inclusion criteria?

Response: Participants in the second box would have met clinical inclusion criteria; i.e. stage 2c or 3 melanoma diagnosis, not receiving or scheduled to receive treatment. The final inclusion criteria or access to internet will be determined once patients are approached in the clinic area (fourth box: n=170)

FIGURE 2

(1) The table can be made clearer by including details for each week.

Response: Thank you for the opportunity to clarify the weekly schedule. An extra column was added to Figure 2, and includes information about the videos provided for each weekly topic.

Reviewer #2: I read the TRLS-D-17-00423 protocol paper and I think it is almost ready to be accepted in its current form, although some recommendations are suggested to authors.

Major recommendations

1) Your spirit table has too many missing items. Please note that it would probably require more efforts to justify why you do not report one item than to report it on the text. Please, reduce to the minimum the number of missing items.
Response: Thank you for the opportunity to clarify some aspect of the SPIRIT checklist. The following items have been included in the paper and the corresponding page added in the SPIRIT list:

Item 11b: a section has been included in the paper on p.13
Item 22 (Harms): a section has been included in the paper on p.20
Appendices: A copy of the Participant information and consent form is included

2) Please, mention somewhere that your results paper will be written in accordance to CONSORT 2010 and its extension to Pilot and Feasibility studies (and, if relevant, to other extensions, such as non-pharmacological interventions; or pragmatic trials). Please, consider if the PILOT extension has any advice that may be useful to your feasibility trial at this stage.

Response: Thank you for your advice. The following sentence has been added to page 20 with a corresponding reference to the literature:

“Results of this study will be prepared in accordance to the CONSORT 2010 statement extension to randomised pilot and feasibility trials.”

3) Please, note that now Consort and Spirit suggest ‘as randomized’ instead of ‘ITT’ (line 290). Please, find further useful advice to enhance retention at http://www.nejm.org/doi/full/10.1056/NEJMsr1203730.

Response: We have added an explanation in page 20 to clarify that ITT is equivalent to “as randomised”.

4) Please explain (maybe in the discussion) how will you prevent that masked personal will know the allocated treatment (e.g., from patients spontaneously telling them). If there is any risk to unmasking, please, discuss arguments to prevent risk of biases, such as selection, performance and attrition.

Response: This is a very pertinent comment, thank you. Given the nature of the intervention and the context in which participants are recruited, i.e. outpatient clinic we cannot rule out the usual risks of bias due to participants not being blinded to treatment allocation. However, in this study all surveys are completed online, health practitioners have no involvement in the collection or assessment of any of the trial outcomes. This explanation has been included in the paper (p.9)
5) Regarding your secondary objective, please consider either to avoid selective outcome reporting bias by a fully specified SAP, or to be fully clear about the non-confirmatory aim of this analysis (i.e., changing "evaluate" to "explore" or similar in line 285).

Response: The wording has been changed to “explore” to reflect the non-confirmatory aim of the secondary objective.

Other suggestions:

6) Please, in your future SAP or results' paper, consider table 6 from CONSORT 2010 E&E paper as a useful way to convey information about patient evolution within each group (regression to the mean? Biases due to raters unmasked to baseline or outcome evaluations, or similar observational results in each cohort) and the (experimentally estimated) effect of changing from reference to active treatment.

Response: We thank the reviewer for this advice. We plan indeed to report results in the format shown in Table 6 of the cited paper.

7) As both arms will get access to the 'active' intervention (before or after the outcome evaluation), I do not see the advantages for the 2:1 allocation scheme. Please, consider to justify.

Response: We will only collect data during the study period. Interaction with the website will only be assessed in the intervention group. No data will be collected from the participants in the control arm who will access to the program at the end of the study period. The allocation ratio was decided based on the feasibility and acceptability elements of the study.

8) As the block size is small (just 3 patients), please consider to assess if people recruiting patients could be able to un-conceal next patient allocation.

Response: Thank you for your comment. It is very unlikely for the researcher recruiting patients to identify the treatment to be received by the next patient, because the allocation sequence is concealed and keeping track of the completion of blocks in each of the 8 strata is an impossible task.