Author's response to reviews

Title: Balance Right in Multiple Sclerosis (BRiMS): A guided self-management programme to reduce falls and improve quality of life, balance and mobility in people with secondary progressive multiple sclerosis: a protocol for a feasibility randomised controlled trial

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Dear Dr Bremner

Many thanks for the feedback regarding our paper submission. We have had the opportunity to review the feedback and make amendments to the manuscript accordingly. We have attached detailed feedback here- our comments are in red text with quotes from the paper in blue. We have also tracked changes on the resubmitted manuscript in blue text.
Reviewer reports:

Reviewer #1: An important subject to be addressed. Very well written description of protocol. I only had a few things which I thought would be worth detailing, mainly around outcome measures, disability balance between the two groups, minimising variability between therapists and raters (considering the study is multicentre) and lack of active control group. All of these are acceptable and present in other intervention trials, but would be worth mentioning as limitations.

In spite of the above-mentioned advantages, I think acknowledging weaknesses would be important. One of them is the fact that the comparison is made to the standard of care, rather than an active control group. Participants receive a lot of input, care, home visits – so the participants in the control group will receive much more attention. Thank you for this feedback- we have added reference to this issue in the discussion (lines 587-591)

More clarity as to why the mentioned outcome measured were chosen is important (especially the 2 minute timed walk instead of 6 minute). These outcome measures could be compared to walking outcome measures from pivotal trials. All the outcome measures have been selected according to best practice guidelines and recommendations. We have updated the information and references in the outcomes section to clarify this (lines 348-360).

In addition, clarification as to whether or not patients would be matched according to the EDSS scale would be important to mention. Patients in this trial are not matched according to the EDSS, and randomization is not stratified on the basis of the EDSS.

Also, the term “self-management” is only partially adequate, as professionals are also involved (physiotherapists). We agree that this is not purely a “self-management programme” given the level of support and input that participants receive – we have used the phrase ‘guided self-management’ throughout the manuscript to make this clear, and have reviewed the manuscript to ensure that this phrase is used consistently when referring to the BRiMS programme.

It would be good to get more information as to how different treating physiotherapists from different centers will receive the same training. The same would be useful for the assessors – to be assured that the inter-rater variability is diminished as much as possible. This has been clarified in lines 390-396.

Minor point: “Active pal” activity monitor appears in figure 1 without previously being mentioned in the text. Apologies- we have clarified this in the figure 1 legend.

Reviewer #2: This protocol adheres to best practice guidelines for the conduct and reporting of feasibility studies and the researchers have provided clear criteria for determining progression to a full trial.

The background section provides good justification for the study.
Just a few points to consider:

Line 120 - I suggest remove the word 'recent' and just write "……. given evidence that…….."
The meaning of the word recent will change with time and the work referenced is 2014, which reported on data up to 2010, so it's not that recent per se.

This has been amended as per your suggestion (new line 122-3)

Line 274-274 - Identifying when these one-to-one sessions occur would be helpful e.g, one at the start of the intervention and one xxx? I think I worked this out from Figure 2 but it's not explicit
The one to one sessions are in weeks one and two- we have added this information in line 275

Line 315 - I'm not clear as to what assessments will be done at baseline. I presume all assessments listed under primary and secondary outcomes will be conducted? Might be good to make this clear for the reader. We hope this has been clarified through the addition of table 1 and the rearrangement of some of the text (lines 316-323)

Line 318 - Can you provide a justification for the outcome timings i.e. why 15 weeks and 27 weeks? What if there's a delay to the start of the intervention? Then 15 and 27 weeks might not correlate with 15 and 27 weeks following commencement of the intervention? Given the nature of the BRiMS programme, the start dates for each group are pre-scheduled, allowing the follow up dates to be scheduled accordingly. The rationale and arrangements have been clarified in the amended text (317-322)

Line 280: I note there is a link to the web based physio site in line 299. It would be helpful to the reader to have a link to the overview of the intervention site around line 280 under the intervention section. This has been added in line 282

Line 300, usual care - are the therapists the same or different to the ones providing the intervention? What is risk of contamination? If they are the same treating therapists then how will risk of contamination be minimised? The treating therapists will not be involved in delivering the usual care for the control group participants. This has been clarified in the manuscript (lines 312-314)

line 343 - Adherence will be measured by the number of web-based log-in sessions - does this include a measure of length of time the person logged in for and how much of the session they completed. It might be worth clarifying this as participants could just log in and not complete the session. How will you measure this? I assume the online exercise diary is separate to or linked to the session? Thank you for your feedback- this will be complicated data to capture, and part of the intention of the feasibility study is to unravel some of these complexities. We will explore all of these aspects with regard to their validity, supported by the data from the participant interviews in order to clarify the most appropriate method of data collection in a future full trial (lines 360-368).

Line 377 - Safety monitoring. You need to specify what might constitute an adverse event in this intervention. Would a worsening of the participant's condition be considered an adverse event?
How will you determine whether an adverse event is due to the intervention or deterioration in the person's condition? We will use the standard definitions of an adverse event as per best practice guidance (Medicines for Human Use (Clinical Trials) Regulations, 2004). This has been clarified with a reference in lines 410-12.

Line 419: The detail on the qualitative data analysis is scant and would benefit from a little more detail e.g. Reference to quality and rigor in analysis. What coding framework will be used, how rigor will be demonstrated, such as trustworthiness and credibility etc. These elements are discussed in 2 sections, but additions have been made to both to address your feedback (lines 452-3 and 494-6).

Line 504 - typo chaire should read chair apologies- this has been corrected (line 536)

Line 507: Ethics: I think it would be good to cross reference to the declarations section or indicate that ethical approval has been granted in the main body of the text. This has been updated (line 547) “All ethical approvals will be in place prior to the commencement of trial recruitment activities (see declarations section”).

Line 561 Trial status: this needs to be updated at time of publication. Perhaps change it to when trial recruitment commenced? This has been updated (line 606)

Reviewer #3: This is a comprehensive and detailed protocol. The proposed intervention is well described and addresses an important issue for the quality of life of people with MS. For researchers in a similar area, the protocol would be a useful document to consult, while the results will be much more interesting and valuable for wider audiences when they are published. If space permits, the authors might consider the following:

- Further reflection on the unique components (or combination of components) proposed in the BRiMS intervention. For example, there appears to be a focus on the improvement of self-efficacy, and clearly defined behaviour change strategies have been described in relation to this. Is this an advance on previous interventions? We have limited word count, but have added clarification in the section detailing the BRiMS intervention (lines 269-272)

- Related to the above point, the use of CBT, motivational interviewing type techniques and other supportive strategies to improve self-efficacy requires some level of skill. How will therapists be prepared for this? We have added clarification about the therapist training and support in lines 389-395

… will these skills be assessed in terms of therapists' fidelity to the intervention protocol? It is unclear how the two tools will be used to assess this (Dreyfus and MIT integrity scale)

The fidelity checklist has been designed to evaluate whether the BRiMS programme delivery achieves the aims, content and spirit of the programme, rather than assessment of therapist ‘skill’. The use of the fidelity assessment has been clarified in lines 397-407
- Line 372 proposed that 25% of the delivered sessions will be assessed using audio recordings. Is this 25% of each therapist's sessions? This has been clarified (line 397) “This sample will include at least two recordings of each session type (1:1 assessment, home visit and group sessions) and at least one session from each treating therapist”.

- how will you ensure that the researchers undertaking these assessments of treatment fidelity are trained and equipped to do so? The researchers involved in the fidelity assessment have been involved in the development of the checklist and will work collaboratively to agree their expectations and moderate their scoring between them, with discussions continuing on an ongoing basis. We have revised the text in lines 403-407 to reflect this.

- Participants will be monitored for AEs using their daily diaries and follow-up assessments, but are these checked regularly enough? Is another protocol required for the participants to inform the appropriate research personnel if a SAE (such as a fall or injury) takes place? There are standard operating procedures in place to ensure that the monitoring and reporting processes are prompt and appropriate. This has been clarified in lines 400-403.

- If adherence is calculated as a percentage, why is it then reduced to a dichotomous variable, and what is the justification for classification of 'adherent' as attendance at 50%?

We agree that this statement in the context of a feasibility trial is not appropriate- thus we have changed the wording of this section to clarify how we will utilise the data “This information, alongside the data obtained from qualitative interviews with participants (see E below) will be used to evaluate levels of adherence and to determine whether any amendments to the programme are required to improve engagement”. (lines 364-369). The feasibility data will also inform the selection of an adherence cut off for use within the data analysis of a future full trial.