PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Promoting Optimal Physical Exercise for Life (PROPEL) – aerobic exercise and self-management early after stroke to increase daily physical activity: study protocol for a stepped-wedge randomized trial
AUTHORS	Mansfield, Avril; Brooks, Dina; Tang, Ada; Taylor, Denise; Inness, Elizabeth; Kiss, Alex; Middleton, Laura; Biasin, Louis; Fleck, Rebecca; French, Esmé; LeBlanc, Kathryn; Aqui, Anthony; Danells, Cynthia

VERSION 1 - REVIEW

REVIEWER	Neha Gothe Wayne State University
REVIEW RETURNED	02-Feb-2017

GENERAL COMMENTS	This is a well-written manuscript about the design and methods of an aerobic physical activity intervention for stroke survivors. Following are some concerns that can be addressed by the authors to clearly detail some of the study procedures. Since the purpose of the manuscript is to present a “protocol”, providing clear and adequate details will allow for future replication of this work. 1. Page 3, line 33, section 12. Intervention: The “dose” of exercise detailed in the intervention is vague – “up to 3x/week” there can be significant differences in participants who engage in 1x/week versus 3x/week of activity. I recommend the authors to detail the specific dose of exercise in an effort to allow future replication of this work. More detailed outlined in #5, #6 and #7 below. 2. Page 4, line 79, section 13. Key Inclusion and Exclusion Criteria: It is unclear how cognitive impairment will be determined. Will there be diagnostic screening tests that will be administered? More objective details would clarify the procedures. This should also be detailed addressed on page 11, lines 224-225, page 12, lines 229-230. Given the multi-site nature of the program, there is a greater need to determine objective screening measures that can be consistently implemented across the different sites. 3. Page 5, line 81, section 13. Key Inclusion and Exclusion Criteria: Attending less than 4 of the 6 sessions is listed as an exclusion criterion. How can this be determined a-priori/ ahead of time? 4. Page 6, line 119, Ethics and Dissemination: It is unclear how the study findings will be disseminated ‘directly to the participants’. Are the authors providing feedback to the participants about their performance? 5. Page 13, paragraph 6.3.1. Control Intervention – GAE – the protocol description needs more details to allow for potential replication of this work in the future. E.g. what will be the heart rate zone for the participants? How long will each session be? Which version of the Borg’s rating of perceived exertion scale will be used?

	On lines 266-267 it is stated that participants “may receive” individualized home exercise programs – does this imply that some control subjects will receive this and some will not? It is important to ensure homogeneity of the control as well as intervention programs – especially because they are multi-site. Would it be possible to determine some standardized procedures in the form of “control discharge packet” or some form of handouts/materials that can be consistently distributed to all control subjects? 6. Page 13-4, paragraph 6.3.2. Experimental Intervention – PROPEL – Similar to some concerns stated above, some more details need to be reported as part of the intervention. It would be useful to detail the staff who will carry out the different aspects of the intervention. The authors state that a PT will administer the intervention (Page 11, lines 204). Will the PT also conduct the small group discussions? It would be useful to detail the staff and their qualifications – as suited to carry out different aspects of the intervention. The nature and content of the group sessions needs to be reported – how long will each session be? How many (minimum-maximum) subjects are required to hold a session? Which topics will be addressed during the 6 group meetings? Perhaps an appendix/table will the topics and content of the group discussions will aid with the protocol description. 7. It is also unclear what the precise “dose” of the intervention will be. Page 13, line 274 reports that participants will complete group exercises “up to 3 days/week”. Does this imply each participant will receive a different dose of the intervention? E.g. some may only exercise 1x/week over the course of the entire intervention, whereas some may exercise 3x/week? This introduces a potential confounder and the intervention needs to be homogenous within the intervention group to allow comparisons across the control. Other details such as the heart rate zone, duration of each session etc. (as outlined in the earlier comment about the control group) need to be stated. 8. Page 16, paragraph starting on line 325: Could the authors also report some psychometric properties of the BBAQ? Authors have reported the reliability and validity of the other measures proposed. 9. Page 21, paragraph 8.3. Statistical analysis: Could the authors comment on intention to use ITT analyses or other strategies? 10. Minor concern: Enrollment has been spelt as “enrolment” in the manuscript and needs to be corrected.

REVIEWER	Marco Pang Hong Kong Polytechnic University Hong Kong
REVIEW RETURNED	02-Feb-2017

GENERAL COMMENTS	The paper is well written, and I have only a few minor comments. 1. In the abstract, please briefly describe the statistical methods to address the primary research hypothesis. 2. The authors may want to explicitly state whether "Intention to treat" analysis approach will be used and provide justifications. 3. The increased patient-therapist contact time/total treatment time due to the added weekly discussion sessions in the PROPEL group may confound the results. The better outcomes in the PROPEL group could be attributed to increased total treatment time/attention from the therapist/placebo, rather than the content of the sessions. I am not sure whether such factors can be controlled better (e.g., weekly sessions for the GAE group, but with content irrelevant to the

	hypothesis). Otherwise, please acknowledge this as a limitation. 4. Please summarize the limitations of the study in a separate section/paragraph.

VERSION 1 – AUTHOR RESPONSE

REVIEWER 1
Comment
This is a well-written manuscript about the design and methods of an aerobic physical activity intervention for stroke survivors. Following are some concerns that can be addressed by the authors to clearly detail some of the study procedures. Since the purpose of the manuscript is to present a "protocol", providing clear and adequate details will allow for future replication of this work.

1. Page 3, line 33, section 12. Intervention: The "dose" of exercise detailed in the intervention is vague – "up to 3x/week" there can be significant differences in participants who engage in 1x/week versus 3x/week of activity. I recommend the authors to detail the specific dose of exercise in an effort to allow future replication of this work. More detailed outlined in #5, #6 and #7 below.

Response
We modified this text to indicate that the program is available 3 days per week. Ideally, all participants would attend for three days/week. However, from our pilot study, we noted that some individuals were unable to commit to attending three days per week, mostly due to conflicting schedules with other therapies or inability to travel to the hospital that frequently. Patients who are unable to attend regularly for all three sessions per week will not be excluded from attending the group. However, as has been clarified in Section 6.2, participants will be excluded from the study if they have not attended at least 9 of the group exercise sessions.

Comment
2. Page 4, line 79, section 13. Key Inclusion and Exclusion Criteria: It is unclear how cognitive impairment will be determined. Will there be diagnostic screening tests that will be administered? More objective details would clarify the procedures. This should also be detailed addressed on page 11, lines 224-225, page 12, lines 229-230. Given the multi-site nature of the program, there is a greater need to determine objective screening measures that can be consistently implemented across the different sites.

Response
As explained in Section 6.2, communication and cognitive capacity to participate in the research study will be determined via consultation with the interprofessional healthcare team. We have found in previous studies that diagnostic screening tests (e.g., MOCA or MMSE for cognitive impairment) are not specific enough to adequately determine an individual's ability to participate in a research study. Therefore, we defer to clinical judgement on this matter. Note that it is unlikely that an individual will have sufficient cognitive/communication ability to participate in the exercise intervention, but not sufficient cognitive/communication ability to participate in the study. We have provided further clarification regarding the considerations for cognitive capacity for eligibility for the GAE and PROPEL programs (Section 6.2).

"To be eligible for referral to GAE or PROPEL, patients must be admitted to the facility for rehabilitation after a diagnosed stroke, and must have sufficient cognitive capacity to understand and follow instructions and to convey adverse symptoms with exercise (e.g., pain, excessive exertion)."

Comment
3. Page 5, line 81, section 13. Key Inclusion and Exclusion Criteria: Attending less than 4 of the 6

sessions is listed as an exclusion criterion. How can this be determined a-priori/ ahead of time?

Response
We have clarified in this section that patients will be screened as they come towards the end of the GAE/PROPEL programs. It should be known at this stage if the patients have attended most of the PROPEL discussion sessions.

“Patients will be screened for eligibility for the study within the final two weeks of the GAE/PROPEL programs.”

Comment
4. Page 6, line 119, Ethics and Dissemination: It is unclear how the study findings will be disseminated ‘directly to the participants’. Are the authors providing feedback to the participants about their performance?

Response
Study participants will receive a letter of appreciation at the end of the study, with a summary of study results. This is stated in Section 10.8.

“Study participants will receive a letter of appreciation at the end of the study, which may include a very brief summary of the study results.”

Comment
5. Page 13, paragraph 6.3.1. Control Intervention – GAE – the protocol description needs more details to allow for potential replication of this work in the future. E.g. what will be the heart rate zone for the participants? How long will each session be? Which version of the Borg’s rating of perceived exertion scale will be used? On lines 266-267 it is stated that participants “may receive” individualized home exercise programs – does this imply that some control subjects will receive this and some will not? It is important to ensure homogeneity of the control as well as intervention programs – especially because they are multi-site. Would it be possible to determine some standardized procedures in the form of “control discharge packet” or some form of handouts/materials that can be consistently distributed to all control subjects?

Response
We have added further details of the GAE intervention to Section 6.3.1.

“The control intervention will involve group aerobic exercise only (GAE). The intensity and duration of exercise will be determined for each individual patient from the results of a sub-maximal or maximal aerobic capacity test conducted prior to entry into the program, and considering patients’ medical history and stroke-related impairments.10 In general, the duration of exercise will be 20-30 minutes, and the intensity will be 50-70% of age-predicted maximum heart rate or a rating of 3/10 (‘moderate’) on the Borg category ratio (CR-10) scale.29”

Note that this will be individualized for each patient. Therefore, it is not possible for us to define a specific target intensity or duration of exercise. However, as detailed in Section 6.4.3, frequency, duration, and intensity of exercise will be documented for as participant for the purpose of the study.

“We will document the frequency, intensity, and duration of exercise during in- and out-patient rehabilitation by chart review.”

In terms of home exercise programs, study participants will be individuals who are undergoing

rehabilitation and receiving clinical care from physiotherapists and occupational therapists, among others. We are not in a position to dictate to these professionals how they should provide this care (e.g., in the form of a “control discharge packet”). However, we have clarified in Section 6.4.3 that we will document details of any home exercise programs provided to participants.

“We will also document details of any home exercise program or general advice to be physically active that participants receive (outside of the PROPEL intervention).”

Comment
6. Page 13-4, paragraph 6.3.2. Experimental Intervention – PROPEL – Similar to some concerns stated above, some more details need to be reported as part of the intervention. It would be useful to detail the staff who will carry out the different aspects of the intervention. The authors state that a PT will administer the intervention (Page 11, lines 204). Will the PT also conduct the small group discussions? It would be useful to detail the staff and their qualifications – as suited to carry out different aspects of the intervention. The nature and content of the group sessions needs to be reported – how long will each session be? How many (minimum-maximum) subjects are required to hold a session? Which topics will be addressed during the 6 group meetings? Perhaps an appendix/table will the topics and content of the group discussions will aid with the protocol description.

Response
We have clarified that a PT will lead the GAE and PROPEL interventions, and that PTs at each site will be trained by the study investigators (Section 6.3).

“PTs at each site will receive training in sub-maximal aerobic capacity testing for individuals with stroke, exercise prescription, and leading the PROPEL program from the study investigators (ELI, LB, CJD, and AT).”

We have also added further details regarding the content of the discussion sessions.

“Specific objectives of the discussion sessions are to: 1) increase participant knowledge regarding the benefits of exercise and physical activity after stroke; 2) build participant skill and self-efficacy for exercise; and 3) establish a feasible post-discharge exercise plan. Through interactive discussions, individualized problem solving, and goal setting, the following topics will be addressed, such that a feasible personal exercise plan is iteratively developed:
• Risks and benefits of exercise;
• Current guidelines and recommendations for exercise;
• Personal barriers to and preferences for exercise;
• Components of an exercise prescription (i.e., frequency, intensity, type and time);
• How to monitor exercise intensity (e.g., using heart rate and rating of perceived exertion);
• How to progress an exercise program;
• How to set short- and long-term goals;
• Strategies to sustain and/or re-engage in exercise;
Additionally, individuals are encouraged to identify and trial appropriate community resources for exercise, and find individualized and realistic strategies for incorporating exercise in a regular routine. The group format helps to promote vicarious experiences. The PROPEL discussions will be led by the PT; access to a health care professional leading the group can increase an individual’s belief about personal skill,32 and support in teaching stroke survivors how to exercise independently, promoting feelings of safety and confidence.33 34”

Comment
7. It is also unclear what the precise “dose” of the intervention will be. Page 13, line 274 reports that

participants will complete group exercises “up to 3 days/week”. Does this imply each participant will receive a different dose of the intervention? E.g. some may only exercise 1x/week over the course of the entire intervention, whereas some may exercise 3x/week? This introduces a potential confounder and the intervention needs to be homogenous within the intervention group to allow comparisons across the control. Other details such as the heart rate zone, duration of each session etc. (as outlined in the earlier comment about the control group) need to be stated.

Response
Please see our responses to comments #1 and #5.

Comment
8. Page 16, paragraph starting on line 325: Could the authors also report some psychometric properties of the BBAQ? Authors have reported the reliability and validity of the other measures proposed.

Response
We have added details of a study reporting the internal consistency of the BBAQ among older adults.

“The BBAQ has good internal consistency among older adults (Cronbach’s α=0.87).42”

We are unaware of any other study that has evaluated the psychometric properties of the BBAQ in any population, including among individuals with stroke. The only other standardized physical activity barriers questionnaire we are aware of is the Stroke Exercise Preference Inventory (SEPI; Bonner et al., 2016), which includes some items on barriers to physical activity. There is evidence to support the validity of the SEPI, but test-retest reliability has not yet been established to our knowledge. Furthermore, the SEPI is not as exhaustive as the BBAQ in terms of evaluating different types of potential barriers. The SEPI is used as a tool within the PROPEL discussion groups; therefore, we wished to use a different tool to evaluate barriers to physical activity for the research study. Our previous research (Mansfield et al., 2016) supports the feasibility of using the BBAQ among individuals recently discharged from stroke rehabilitation, and within this study we have observed a negative correlation between BBAQ total score and participation in physical activity (unpublished data).

Comment
9. Page 21, paragraph 8.3. Statistical analysis: Could the authors comment on intention to use ITT analyses or other strategies?

Response
We have clarified that the analysis will necessarily be ‘per protocol’ as individuals who do not complete at least a minimum amount of the intervention will be excluded from the study. However, all data collected will be analysed.

“Only individuals who complete at least a minimum amount of the intervention will be included in the study; therefore, analysis will necessarily be ‘per protocol’.”

Comment
10. Minor concern: Enrollment has been spelt as “enrolment” in the manuscript and needs to be corrected.

Response

BMJ is a UK-based journal; therefore, we have used UK English throughout the paper and, as such, have used the spelling ‘enrolment’ rather than ‘enrollment’.

REVIEWER 2
Comment
1. In the abstract, please briefly describe the statistical methods to address the primary research hypothesis.

Response
We have added details of the statistical analysis to the Abstract.

“We will compare the proportion of active and inactive individuals at 6 months post-intervention using mixed-model logistic regression, with fixed effects of time and phase and random effect of cluster (site).”

Comment
2. The authors may want to explicitly state whether "Intention to treat" analysis approach will be used and provide justifications.

Response
We have clarified that the analysis will necessarily be ‘per protocol’ as individuals who do not complete at least a minimum amount of the intervention will be excluded from the study. However, all data collected will be analysed.

“Only individuals who complete at least a minimum amount of the intervention will be included in the study; therefore, analysis will necessarily be ‘per protocol’.”

Comment
3. The increased patient-therapist contact time/total treatment time due to the added weekly discussion sessions in the PROPEL group may confound the results. The better outcomes in the PROPEL group could be attributed to increased total treatment time/attention from the therapist/placebo, rather than the content of the sessions. I am not sure whether such factors can be controlled better (e.g., weekly sessions for the GAE group, but with content irrelevant to the hypothesis). Otherwise, please acknowledge this as a limitation.

Response
We have addressed this is a limitation to the study.

“Participants in the PROPEL phase will have one extra hour per week of interaction with the PT and with other participants in the group. It is possible that this extra attention/interaction alone, rather than the content of the PROPEL discussions, will influence the study results. We opted to not add an attention control activity to the GAE phase (e.g., group discussion on a topic unrelated to physical activity) based on feedback from stakeholders. We designed the GAE phase to resemble clinical practice as closely as possible, while still maintaining controls and standardization necessary for a research study. An unrelated discussion group would be contrived for the purpose of the study and would not reflect clinical practice.”

Comment
4. Please summarize the limitations of the study in a separate section/paragraph.

Response

We have added a ‘strengths and limitations’ section (Section 11), as requested.

We have adopted an ‘integrated knowledge translation’ approach, whereby knowledge users (rehabilitation managers and physiotherapists) have been involved in the study from conception. The interventions are being implemented as part of routine care at each site. This also helps to increase the likelihood that the interventions will continue as part of routine care beyond the end of the study, compared to implementing the interventions for study participants only.
The novel ‘stepped wedge’ trial design is appropriate for evaluating the group-based PROPEL intervention as it is ‘rolled out’ as part of routine practice to each site.27 However, it is possible that factors that change over time will influence the study results. For example, stroke rehabilitation delivery in Ontario is supported by the Ministry of Health and Long-Term Care through the Ontario Health Insurance Program. During the course of the study, it is possible that the Ministry will dictate changes to care delivery, such as changes to lengths of stay. However, ‘vertical’ comparisons between sites can be made at any point in time to account for such secular trends.52 55 An alternative approach would be to have some sites start with the PROPEL intervention and transition to GAE; however, there would be a risk of contamination as staff administering the GAE would have been trained in PROPEL, which might influence how they treat their patients.26 56
Participants in the PROPEL phase will have one extra hour per week of interaction with the PT and with other participants in the group. It is possible that this extra attention/interaction alone, rather than the content of the PROPEL discussions, will influence the study results. We opted to not add an attention control activity to the GAE phase (e.g., group discussion on a topic unrelated to physical activity) based on feedback from stakeholders. We designed the GAE phase to resemble clinical practice as closely as possible, while still maintaining controls and standardization necessary for a research study. An unrelated discussion group would be contrived for the purpose of the study and would not reflect clinical practice.
This large multi-site trial will determine if a simple clinical intervention, delivered during stroke rehabilitation, can increase participation in physical activity after discharge. This work addresses methodological limitations of studies aiming to increase exercise participation post-stroke16 17 by: 1) basing the intervention on principles of behaviour modification; 2) using objective measures of exercise participation; and 3) evaluating long-term self-directed exercise (i.e., 6 months post-intervention). If the study results are positive, translation of this program into practice has the potential to reduce healthcare costs (by reducing risk of cardiovascular events) and increase independence for stroke survivors.

VERSION 2 – REVIEW

REVIEWER	Dr. Neha Gothe Wayne State University
REVIEW RETURNED	08-Mar-2017

GENERAL COMMENTS	The authors have addressed the concerns raised in the earlier peer review. I wish them the best with executing this significant work in the field of stroke survivor-ship and look forward to reading about their findings.