PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The Pulmonary Hypertension And Home-Based (PHAHB) Exercise Intervention: Protocol for a Feasibility Study
AUTHORS	McCormack, Ciara; Kehoe, Brona; Hardcastle, Sarah; McCaffrey, Noel; McCarren, Andrew; Gaine, Sean; McCullagh, Brian; Moyna, Niall

VERSION 1 – REVIEW

REVIEWER	Abraham Babu Manipal Academy of Higher Education, Department of Physiohterapy
REVIEW RETURNED	20-Jan-2021

GENERAL COMMENTS	the authors have submitted a protocol for a study that is both important and timely for those with PAH. This group of patients have frequently been excluded from traditional rehabilitation programs. This study will hold great significance to those in Ireland and will also add to the pool of evidence and future meta-analysis. After reviewing the manuscript, I have a few comments and references that could be added to the revised manuscript. Page 6, line 81: this statement can be referenced as well with the following citation https://pubmed.ncbi.nlm.nih.gov/26391300/ Page 6, line 88: I agree that home-based interventions have not been studied adequately. But i think, when that is the case, it is important to highlight the few studies on home-based programs the are there. Please consider adding the following citations https://pubmed.ncbi.nlm.nih.gov/31663077/ https://pubmed.ncbi.nlm.nih.gov/31280830/ For the inclusion criteria, I would suggest you mention which PH group is primarily being included. In the exclusion criteria, are those in Group IV PH included? In the intervention, you mention that patients will be provided an exercise bike at home. Could you clarify how this would be feasible and sustainable beyond the study period? Page 9: Could you please provide more information on how the exercise manual was developed? How did you decide on the content? Page 12, line 231 - do you mean "THERABAND"? Please check the spelling of "teraband"

	Page 12, Line 232-236: Could you please provide details on how respiratory muscle training will be provided? Is any equipment being used? In the same section, please provide more details on the type of yoga that is being provided and who will be delivering the yoga therapy to the participant? Pg 13: The timing of outcome measurement appears to be different from the registered protocol - could you please justify this change from the registered protocol? Also, there is no mention of the 20wk follow up. Pg 16-17: You have mentioned the measurement of kinesiophobia in the Table but have not provided any description of it in the text. This would need to be added. In the statistical analysis, will you be considering any factors as co-variates? That should be considered. The potential for post-hoc analysis could also be mentioned when relevant. Is there a plan to handle missing data (considering the small sample size)? In light of the current pandemic, have you had to modify the protocol in any way? After reviewing the manuscript I have a general comment w.r.t the generalizability and the slight conflict in thoughts from the introduction to the methodology - i.e., you mention that the German model is resource intensive - however your program as well appears to be resource intensive as all the participants are getting an exercise bike and other monitoring devices. I would therefore suggest reframing the sentence in the introduction that currently focuses on being resource intensive to the geographic applicability of only the home-based component - which is not known sufficiently.

REVIEWER	Kathryn Taylor University of Oxford, Nuffield Dept of Primary Care Health Sciences
REVIEW RETURNED	21-Jan-2021

GENERAL COMMENTS	This seems like a worthwhile study but I found this description of the protocol a bit confusing and vague in several places. The objectives of this study are not clear. The protocol states a key objective is “to collate primary outcome measures to help inform the sample size calculations for future outcome trials”, but detailed intervention processes and the measurement of multiple secondary outcomes to test the intervention are also described. I don’t think it would be helpful to state a second objective to correspond with the secondary aim. The National Institute for Health Research (https://www.nihr.ac.uk/glossary) defines a feasibility study as one to estimate important parameters to answer the question of whether the main study can be completed. Feasibility studies do not usually evaluate the outcome of interest, but I see that in order to evaluate the primary outcomes, the participants of the proposed feasibility study need to fully participate in the intervention and the process of evaluating the intervention. Therefore, I think that the objective of the study to evaluate the feasibility, acceptability, utility and safety encapsulates both the primary and secondary aims. Furthermore, I think the protocol would be clearer if this single objective was stated in the introduction and the primary and secondary aims (to meet the broad single objective) were described in the methods. Having “PHAHB Intervention Protocol” as the short title is unhelpful. “PHAHB Intervention Feasibility Study Protocol” would be better

	(also with “Study” rather than “Trial” in the main title). The sections are out of order. The aim to inform future trials needs to be stated sooner (see above). The sample size statement could be shortened to refer only to pilot study references and remain where it is (before it referred to primary outcomes before they had been introduced). The timings of the outcome assessments, including Table 1, would be better placed after the outcomes have been stated. The proposed study is for multiple primary outcomes to be evaluated in multiple ways, and some are unclear. For example, the plan to evaluate feasibility by “Implementation process and fidelity of the intervention captured through observation and detailed field notes” and evaluating acceptability and utility of the intervention by self-reported questionnaires and semi structured interviews are vague. A data management plan and data validation plan are mentioned but are not described. The assessment of outcomes expectations is unclear regarding the second set of 5 items. The protocol does not include any dates. The statistical analysis section needs to address the issue of repeated testing. The manuscript also needs a light check for spelling errors e.g. s is missing from assess in two places. pulmonary vascular resistance >= dynes cm^-5 (e is missing)

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 ***Reviewer Name: Mr. Abraham Babu,*** **Manipal Academy of Higher Education** **Please state any competing interests or state 'None declared': None declared**	
Reviewer Comments	**Author's Response**
The authors have submitted a protocol for a study that is both important and timely for those with PAH. This group of patients have frequently been excluded from traditional rehabilitation programs. This study will hold great significance to those in Ireland and will also add to the pool of evidence and future meta-analysis. After reviewing the manuscript, I have a few comments and references that could be added to the revised manuscript.	Many thanks Abraham for your helpful feedback and positive evaluation of our study.
Page 6, line 81: this statement can be referenced as well with the following citation https://pubmed.ncbi.nlm.nih.gov/26391300/	Many thanks for the suggestion. We have included this reference to the manuscript and added to our reference list. Ref [15]
Page 6, line 88: I agree that home-based interventions have not been studied adequately. But i think, when that is the case, it is important to highlight the few studies on home-based programs the are there. Please consider adding the following citations https://pubmed.ncbi.nlm.nih.gov/31663077/ https://pubmed.ncbi.nlm.nih.gov/31280830/	Many thanks for the suggestion and references. We agree and have highlighted the few home-based studies that have been published in the revised manuscript as follows: Please See page 6, Line 106 ''*Although the few studies examining the beneficial effects of home-based exercise training in PH are promising [18-19] none included strategies to maximise adherence"*
	To address any confusion we have now added which

For the inclusion criteria, I would suggest you mention which PH group is primarily being included. In the exclusion criteria, are those in Group IV PH included?	groups are excluded to the exclusion criteria. Please see page 7, line 134 *"Inclusion criteria are male or female > 18 years, with a diagnosis of PH (WHO Groups I and IV) by"* *" Exclusion criteria include PH of any cause other than outlined in the inclusion criteria such as PH from left heart disease or lung disease/hypoxia (WHO PH groups 2 and 3)"*
In the intervention, you mention that patients will be provided an exercise bike at home. Could you clarify how this would be feasible and sustainable beyond the study period?	The subsequent follow up (maintenance phase) will allow us the opportunity to assess whether participants continue to use the bikes provided to inform sustainability and utility. It will help us assess whether the bike is viewed as important or a beneficial addition to future home-based interventions. In relation to feasibility , we agree that some future programs are unlikely to have the resources to provide exercise bikes. It is worth pointing out that the cost of the stationary bikes used in this study was relatively modest cost (~150 – 180 euro). We have address this in the discussion section. Please see page 20, Line 447 " *Furthermore, it will allow us to assess resource needs in future home-based exercise programmes such as the provision of specific exercise equipment and the use of ubiquitous, low cost devices to monitor activity and safety (e.g. bike, wearable activity tracker).*
Page 9: Could you please provide more information on how the exercise manual was developed? How did you decide on the content?	The exercise manual was partly based on the design of previous PA intervention in chronic disease - PPARCS and WATTAP trials which included behavioural change techniques eg. goal setting and also our formative research with PH patients. The formative research (yet to be published) helped to refine the manual content in relation to the lack of understanding of the benefits of exercise and the importance of self-regulation strategies to support motivation and exercise engagement. Concerns of breathlessness and energy management were also evident in interviews with PH patients and

	integrated into the exercise manual. We have included a short section on how the manual was developed in the revised manuscript. Please see page 13, Line 279 “ The exercise manual was partly based on the design of previous PA intervention in chronic disease - PPARCS [26] and WATTAP [45] trials and also our formative research with PH patients (unpublished). The formative research highlighted the lack of understanding of the benefits of exercise, the importance of self-regulation strategies to support motivation and exercise engagement and the desire for visual picture and instruction of exercise. Concerns of breathlessness and energy management were also evident in interviews with PH patients and integrated into the exercise manual.”
Page 12, line 231 - do you mean "THERABAND"? Please check the spelling of "teraband"	Thank you for the correction. This error has been amend in the revised manuscript See page 13, line 279
Page 12, Line 232-236: Could you please provide details on how respiratory muscle training will be provided? Is any equipment being used? In the same section, please provide more details on the type of yoga that is being provided and who will be delivering the yoga therapy to the participant?	The Respiratory training is explained and demonstrated via video call with the participants during their induction training by our qualified exercise specialist. Participants are provided with the opportunity to practice the exercises during the call to ensure appropriate technique. Visual representation (pictures) and written ques are also contained in the exercise manual. Finally, participants will receive a video clip of a qualified exercise specialist performing the exercises. Participants are encouraged to refer to the video to ensure adherence to correct technique. Respiratory muscle training can be performed with or without the TheraBand, no other equipment is necessary.

	To clarify this, we have added the following line to the respiratory training section in the methods. Please see page 17 line 364 "*Participants can progress to use a TheraBand to complete respiratory training. "* And we have expanded the line on the video clips Please see page 14 line 295 *"Participants will receive video clips of a qualified exercise specialist performing the exercises. Participants will be encouraged to refer to the video to ensure adherence to correct technique* " Page 15– Line 316 – in the original manuscript Outlines the following *' Session 2 - Exercise Safety and Exercise Demonstration*; The session will focus on recognizing exercise limits, warning signs, and managing exercise intensity. Visual demonstrations of breathing techniques and aerobic, strength and respiratory training will be provided, with the opportunity for behavioural practice during the session to check technique and instil confidence' The inclusion of the word "yoga" was an error and has been removed from the revised manuscript.
Pg 13: The timing of outcome measurement appears to be different from the registered protocol - could you please justify this change from the registered protocol? Also, there is no mention of the 20wk follow up.	Thank you very much for highlighting this error . The outcome measurement was updated on the trial register prior to submission of the protocol paper under sections labelled 'Interventions and Outcomes'. However it appears that the section entitled 'What does this study involve' did not change to match the outcomes change and still stated 12 weeks . The request to edit the error on the registered protocol was submitted on 01.02.2021 and the addition of the 20 week follow up phase has now been edited on the trial registry. Due to consequences of COVID the delay in the original start date and the time restriction of completion of the project and funding availability to ensure each participants receives equal opportunity for completion of the trial the length of the exercise component of the trial

	was reduced from 12 weeks to 10 weeks.
Pg 16-17: You have mentioned the measurement of kinesiophobia in the Table but have not provided any description of it in the text. This would need to be added.	Thank you very much for highlighting this error. The measurement of kinesiophobia should not have been included in the table submission. This has now been amended and removed in the revised manuscript. See Revised Table.1
In the statistical analysis, will you be considering any factors as co-variates? That should be considered. The potential for post-hoc analysis could also be mentioned when relevant. Is there a plan to handle missing data (considering the small sample size)?	Thank you for raising these questions. We have consulted with a statistician (Andrew McCarren) and he has now been added to the research group and will assist with the statistical analysis of the trial. We have now re-written the statistical analysis section to address these points. Please see Page 18 line 393, *"A linear mixed model analysis (MMA) will be used to examine the impact of time in this study . A MMA is a suitable approach to modelling time series data which contains repeated measures (Haapalainen et al., 2008). The MMA does not require complete data sets and does not exclude participants with missing data (Armstrong, 2017; Howell, 2015). Furthermore, MMA has less stringent assumptions than other repeated measures models (such as analysis of variance) and also exhibits increased power to detect treatment effects. The data will adjust for confounding variables, such as gender, age, baseline fitness level, and PH group*."
In light of the current pandemic, have you had to modify the protocol in any way?	Due to the pandemic the option to do laboratory testing was not available to us. As stated above due to COIVD we have reduced the exercise component length from 12 weeks to 10 weeks.
After reviewing the manuscript I have a general comment w.r.t the generalizability and the slight conflict in thoughts from the introduction to the methodology - i.e., you mention that the German model is resource intensive - however your program as well appears to be resource intensive	Thank you for your comment. We understand your view point. However, the Heildberg model is deemed resource intensive due to it being centre based which requires more personnel, facilities. Patients also stay on-site for the 3 weeks. Within our introduction we have alluded to how home-based may overcome the barriers to participation in

as all the participants are getting an exercise bike and other monitoring devices. I would therefore suggest reframing the sentence in the introduction that currently focuses on being resource intensive to the geographic applicability of only the home-based component - which is not known sufficiently.	terms of geography and travel. We understand that our intervention may seem resource intensive with the inclusion of the equipment, however since this is a feasibility study it is essential that we can objectively measure physical activity and safety in order to inform future trials. As mentioned above we have included this in our discussion. Please see page 20, Line 447 " *Furthermore, it will allow us to assess resource needs in future home-based exercise programmes such as the provision of specific exercise equipment and the use of ubiquitous, low cost devices to monitor activity and safety (e.g. bike, wearable activity tracker).*

Reviewer: 2 **Dr. Kathryn Taylor, University of Oxford**	
This seems like a worthwhile study but I found this description of the protocol a bit confusing and vague in several places. The objectives of this study are not clear. The protocol states a key objective is "to collate primary outcome measures to help inform the sample size calculations for future outcome trials", but detailed intervention processes and the measurement of multiple secondary outcomes to test the intervention are also described. I don't think it would be helpful to state a second objective to correspond with the secondary aim. The National Institute for Health Research (https://www.nihr.ac.uk/glossary)	We thank Dr Taylor for her constructive comments and helpful feedback. We have removed the statement regarding primary and secondary aims from the introduction. Please see page 7, line 121 **"***The aim of this study is to assess the feasibility, acceptability, utility and safety of a novel home-based exercise training programme for PH patients. "*

defines a feasibility study as one to estimate important parameters to answer the question of whether the main study can be completed. Feasibility studies do not usually evaluate the outcome of interest, but I see that in order to evaluate the primary outcomes, the participants of the proposed feasibility study need to fully participate in the intervention and the process of evaluating the intervention. Therefore, I think that the objective of the study to evaluate the feasibility, acceptability, utility and safety encapsulates both the primary and secondary aims. Furthermore, I think the protocol would be clearer if this single objective was stated in the introduction and the primary and secondary aims (to meet the broad single objective) were described in the methods.	
Having “PHAHB Intervention Protocol” as the short title is unhelpful. “PHAHB Intervention Feasibility Study Protocol” would be better (also with “Study” rather than “Trial” in the main title).	Thank you for the helpful suggestion. We agree and have amended the main title by removing the word trial and replace it with study and the amended the short title to “PHAHB Intervention Feasibility Study Protocol” as suggested.
The sections are out of order. The aim to inform future trials needs to be stated sooner (see above). The sample size statement could be shortened to refer only to pilot study references and remain where it is (before it referred to primary outcomes before they had been introduced). The timings of the outcome assessments, including Table 1, would be better placed after the outcomes have been stated.	Many thanks for your suggestion. We agree and have shortened the sample size statement See page 9, line 171 The outcomes measures have now been moved to page 9 after sample size. The section on outcomes timings and outcomes assessments has not been placed after the comes have been stated on Page 13. Table 1 has been moved to the end of the document.

The proposed study is for multiple primary outcomes to be evaluated in multiple ways, and some are unclear. For example, the plan to evaluate feasibility by "Implementation process and fidelity of the intervention captured through observation and detailed field notes" and evaluating acceptability and utility of the intervention by self-reported questionnaires and semi structured interviews are vague.	Thank you for highlighting the confusion within this section. We agree that it is vague and unclear. We have now written the section to clarify any confusion Please see Page 9 , Line 174 ***"Feasibility**: Assessed by participant recruitment (enrolment as a proportion of eligible participants) and retention (proportion that completed all assessments); (ii) engagement with the intervention measured according to attendance at induction sessions and health coaching sessions and adherence, defined as the percentage of home-based exercise sessions recorded by participants who complete the intervention assessed via log books and weekly calls) and (iii) by examining delivery as intended (as per protocol) and health coach perceptions concerning how patients' received the intervention components. This will be captured immediately after each session in order to keep a record of how delivery was received in relation to the planned delivery (e.g., if a participants required extra time or further support following the induction training session).* ***Acceptability and utility;** Assessed through self-report questionnaires completed at T2 and interviews. The questionnaire will assess participant perceptions of intervention appropriateness, effectiveness, quality, accessibility/usability, intrusiveness, and overall enjoyment and attitude towards the intervention. Semi-structured interviews with a sub-set of participants (~ n=12) will be conducted within 2-weeks of completing the T2 assessment. The interviews will further explore acceptability and utility of the intervention including perceptions concerning exercise prescription, adherence to different components of the intervention, in addition to the facilitating and hindering factors to participation. Participants will also be asked to offer suggestions for improvement and implementation. Interviews will be conducted via telephone or online platforms (i.e., Zoom) and will be audio-recorded and transcribed*."
A data management plan and data validation plan are mentioned but are not described.	We apologise for the confusion. We have removed the line "data validation will take place according to the procedures set out in the data management plan and data validation plan'. Our data management section page 18, line 375 outlines the data management plan.

The assessment of outcomes expectations is unclear regarding the second set of 5 items.	Thank you for picking up on this. The second set of 5 items is based on research of PH symptoms. We have now addressed this in the revised manuscript Please see page 12, line 254 *"Ten-items will assess outcome expectations. Five-items are derived from the validated exercise pros subscale [42] and 5-items to assess outcomes related to common symptoms reported in PH, 'such as breathlessness' [43].*
No comment in here?	Due to COIVD-19 the trial began at the end of September 2020 and with rolling recruitment will continue until we achieve our sample size (N=25) , our expected date for completion of the trial is July 2021.
The statistical analysis section needs to address the issue of repeated testing.	Thank you for your comment; we have addressed this issue in the statistical analysis section. We have included the following text in relation to our analytical approach: Please see Page 18 line 393, *"A linear mixed model analysis (MMA) will be used to examine the impact of time in this study . A MMA is a suitable approach to modelling time series data which contains repeated measures (Haapalainen et al., 2008). The MMA does not require complete data sets and does not exclude participants with missing data (Armstrong, 2017; Howell, 2015). Furthermore, MMA has less stringent assumptions than other repeated measures models (such as analysis of variance) and also exhibits increased power to detect treatment effects. The data will adjust for confounding variables, such as gender, age, baseline fitness level, and PH group*."
The manuscript also needs a light check for spelling errors e.g. s is missing from assess in two places. pulmonary vascular resistance >= dynes cm^-5 (e is missing)	Thank you for highlighting this. A thorough spell check was completed on the revised manuscript

VERSION 2 – REVIEW

REVIEWER	Abraham Babu Manipal Academy of Higher Education, Department of Physiohterapy
REVIEW RETURNED	22-Feb-2021

GENERAL COMMENTS	The authors have revised the manuscript and have clarified most of the comments raised. There are however, a few comments that require further attention and clarification: 1. Etiological groups of PH are described using alpha numerical and not Roman numerals. Please make this correction. 2. The short title suggested by Dr. Taylor is not reflected in the revised manuscript 3. Therabands in line 333 should be without the apostrophe mark 4. Please verify the reference numbering - No.52 does not have a reference 5, ‘’Although the few studies examining the beneficial effects of home-based exercise training in PH are promising [18-19] none included strategies to maximise adherence” References 18 and 19 are not reflecting this statement, rather it is 20, 21. Please have all the references verified for accuracy. I strongly urge the use of a reference manager to ensure accuracy in referencing. 6. In the introduction, this statement "Further, patient populations express a preference for unsupervised, self-paced, low-moderate intensity PA, specifically walking [18-19]" could be better referenced with the following citations: https://pubmed.ncbi.nlm.nih.gov/33240490/ 7. In the methodology section on respiratory training you mention "Participants can progress to use a TheraBand to complete respiratory training." How does a Theraband contribute to respiratory training? The respiratory muscle training program is still ambiguous with no specific method of training being mentioned - What kind of device is being used and at what intensity? These details are crucial to the clarity of the intervention. 8. Table 1: 6MWT and Borg's dyspnea index are two different outcomes and need to be separated. Could you please clarify what you mean by the Borg's dyspnea index and provide a description of it in the assessment, along with a reference?

REVIEWER	Kathryn Taylor University of Oxford, Nuffield Dept of Primary Care Health Sciences
REVIEW RETURNED	22-Feb-2021

GENERAL COMMENTS	I am happy with the changes made by the authors but there are two omissions: 1. The authors accepted an amendment to the running title to relfect feasibility study and not the trial but the amendment has not been implemented. 2. The authors have provided dates of the study in their response to reviewers but these dates are not included in the manuscript. The editors of the journal require these dates to be stated in the manuscript. Note that this shoudl read "Due to COVID-19 the study began..... for completion of the study is July 2021". If the above changes are made I will be happy to recommend publication in BMJ Open.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1 ***Reviewer Name: Mr. Abraham Babu,*** **Manipal Academy of Higher Education** **Please state any competing interests or state 'None declared': None declared**	
Reviewer Comments	**Author's Response**
1. Etiological groups of PH are described using alpha numerical and not Roman numerals. Please make this correction.	Many thanks for your comment. The error seems only to be in the reviewer response document as the revised manuscripts states the following: Please see line114, page 7 *"Inclusion criteria are male or female > 18 years, with a diagnosis of PH (WHO Groups I and IV) by right heart catheterisation showing baseline mean pulmonary"* And Please see line119, page 8 *"Exclusion criteria include PH of any cause other than outlined in the inclusion criteria such as PH from left heart disease or lung disease/hypoxia (WHO Groups II and III)"*
2. The short title suggested by Dr. Taylor is not reflected in the revised manuscript	Thank you for this we have now amended the short title in the running header on the revised manuscript as requested and agreed upon.
3. Therabands in line 333 should be without the apostrophe mark	Thank you for this observation we have now removed the apostrophe mark.
4. Please verify the reference numbering - No.52 does not have a reference	We believe there was some errors with the online portal since the revised manuscript previously submitted did contain reference number 52. 52. Dalla Vecchia LA, Bussotti M. Exercise training in pulmonary arterial hypertension. *J Thorac Dis*. 2018;10(1):508-521.

	doi:10.21037/jtd.2018.01.90. The reference list has now since been updated, and so this reference number has changed in the revised manuscript. We have doubled checked the reference list to ensure all references are accurate.
6. In the introduction, this statement "Further, patient populations express a preference for unsupervised, self-paced, low-moderate intensity PA, specifically walking [18-19]" could be better referenced with the following citations: https://pubmed.ncbi.nlm.nih.gov/33240490/	Thank you for your suggestion. We have reworded the sentence and added this reference as an additional reference to compliment the statement. Page 6, Line 83 *"Further, patient populations, including PH [18] express a preference for unsupervised, self-paced, low-moderate intensity PA, specifically walking [19-20]."*
7. In the methodology section on respiratory training you mention "Participants can progress to use a TheraBand to complete respiratory training." How does a Theraband contribute to respiratory training? The respiratory muscle training program is still ambiguous with no specific method of training being mentioned - What kind of device is being used and at what intensity? These details are crucial to the clarity of the intervention.	The respiratory training in this study uses the protocol established by the Heidelberg PH exercise research group which does not use a device. The exercise professional delivering this component of training attended the Heidelberg Rehabilitation centre in Germany and received training in this component of the program as per their protocol. The use of the TheraBand can be introduced to progress the intensity of the respiratory muscle strengthening exercises. To clarify this section we have re-written it as follows: Page 17, Line 320 *Respiratory Training;* Participants will initially perform 10-min of respiratory training at least twice a week, which will follow the protocol established by the Heidelberg PH research group [50]. This involves a combination breathing techniques (e.g., pursed lip, diaphragmic and slow breathing) emphasising control over their rate of inspiration to expiration and to strengthen the diaphragm , stretching of the chest and thoracic muscles (e.g., cat-to-cow) and respiratory muscle strengthening exercises. Training volume will progressively increase with the goal of completing 15/20 min of accumulated respiratory training on ≥3

	d/week. The intensity of the respiratory muscle strengthening exercises can be progressed using a Theraband.
8. Table 1: 6MWT and Borg's dyspnea index are two different outcomes and need to be separated. Could you please clarify what you mean by the Borg's dyspnea index and provide a description of it in the assessment, along with a reference	Thank you for you observation. We understand that placing "Borg's dyspnea index in Table 1 may have caused confusion. To avoid confusion we have removed "Borg's dyspnea index" from the table 1 completely as the measurement of dyspnoea using the modified Borg Scale will be taking during the 6MWT as per standard procedures in accordance with the European Respiratory Society/American Thoracic Society technical standards guidelines [ref 33] for 6MWT along with heart rate response, Spo2 and fatigue which have been previously described in our description of the Exercise Capacity outcome. To clarify this, we have re-written the sentence and provided a reference of the Borg scale used. *Page 10 , line 176* *Subjective symptoms of dyspnoea and fatigue will be recorded using the Modified Borg Scale (0-10) [34] before and after the test'*

Reviewer: 2 **Dr. Kathryn Taylor, University of Oxford**	
I am happy with the changes made by the authors but there are two omissions 1. The authors accepted an amendment to the running title to reflect feasibility study and not the trial but the amendment has not been implemented	Thank you for noting this omission. We have now amended the short title in the running header of the manuscript document as requested and agreed upon.

2. The authors have provided dates of the study in their response to reviewers but these dates are not included in the manuscript. The editors of the journal require these dates to be stated in the manuscript. Note that this shoudl read "Due to COVID-19 the <u>study</u> began..... for completion of the <u>study</u> is July 2021". If the above changes are made I will be happy to recommend publication in BMJ Open.	We have now added the dates to the Manuscript under data management and timeline. Please see page 18, line 344 *"*Study recruitment began at the end of September 2020 and the study is expected to be completed in July 2021*"*