PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	An interactive web-based Pulmonary Rehabilitation programme: A randomised controlled feasibility trial.
AUTHORS	Chaplin, Emma; Hewitt, Stacey; Apps, Lindsay; Bankart, M. John; Pulikottil-Jacob, Ruth; Boyce, Sally; Morgan, Mike; Williams, Johanna; Singh, Sally

VERSION 1 - REVIEW

REVIEWER	Huong Nguyen Kaiser Permanente Southern California, USA
REVIEW RETURNED	19-Sep-2016

GENERAL COMMENTS	This is a well written paper on an important issue of testing alternative pulmonary rehab formats for patients with COPD. I've offered some comments/feedback to further strengthen the paper. Major Presentation of abstract results should be more forthcoming regarding the high drop out in the WEB group (57%) especially since this was a key feasibility metric. Your study is in good company as there are many web-based behavioral studies showing attrition of 50-80% though most of these studies do not have the "human" interaction that this study has. Related to the point above, while the authors state there were no significant differences in the baseline characteristics of patients who completed the study versus those who dropped out, they also cite that patients who dropped out of WEB differed from those who completed. Because this is essential information, I would suggest reorganizing Table 1 to try to include a column for the 29 WEB patients who dropped out. Although all patients in the study were agreeable to being randomized to either programs, it's important to know what types of patients may not be a good fit for WEB and for clinical purposes, could be guided/persuaded to participate in clinic-based PR. Figure 2 lists reason for drop out but it is hard to understand key reasons for the early drop out (n=12) and if this could have been modified with changes to the WEB protocol. There was also a fair number of drop outs at Stage 2. Please provide more information/possible explanation re: how Stage 2 activities and components were simplified to improve retention. It would be helpful to provide additional process/usage metrics to understand pattern of use over the 11 weeks, e.g. frequency of login/week, duration of each unique log in, areas of web site where patients spent the most time etc…Since this was a feasibility study

	of WEB, providing more detailed usage information is helpful for readers. Was there a qualitative formative or summative component to the study to better understand patients' experience with WEB? This information is usually very helpful. How did the baseline program preference relate to drop out from either groups? Were patients who were assigned to the discordant group more likely to drop out? Could the authors speak to why the change in the ISWT did not meet the MCID threshold even for the conventional PR group? It would seem that if we accept PR as being effective in improving physical functioning, it's concerning that changes in this PR cohort did not achieve the MCID even though the authors state that this group of patients are different from their typical PR patients. Since completion of the WEB extended longer than the expected 6-8 week period, when exactly was the post WEB assessment completed for subjects who did not drop out? Was this to some extent standardized based on completion of certain modules? Should differences in the follow up time be adjusted for in the analysis? It's not clear what the value was in collecting/describing the health cost/EQD data collection especially since the sample is much too small to conduct a CEA nor were the cost data presented in the paper. Other published studies have collected these information thus presentation of the feasibility data is not entirely informative The authors acknowledge the study was not sufficiently powered as a non-inferiority trial. Did it start out as a non-inferiority trial but due to recruitment challenges, was modified? The conclusion would be more helpful if the authors could address how future studies might be designed to either answer the question of non-inferiority and/or use of preference based RCTs to move the science of PR forward or should we stop doing these head to head comparisons altogether and focus on optimizing technology based solutions because we know patients need to have viable alternatives to clinic-based PR. Minor In abstract, include mention that target sample was COPD patients Strengths/limitations bullets should be in past or present tense not future tense as it is currently What does "signposted" mean on page 6, line 54 Suggest combining Figures 3 & 4 with Table 2 since there's duplicate information and best to streamline data presentation. Also, EQ5D score could be combined in the Table 2 as well.

REVIEWER	Pat Camp University of British Columbia, Canada
REVIEW RETURNED	06-Oct-2016

GENERAL COMMENTS	The purpose of this study was to assess the feasibility of a interactive web-based PR program. Specifically, this involved investigating the recruitment rate, retention and drop out of participants; measuring the impact of the program on a variety of

	outcomes; and identifying the technical difficulties of delivering a web-based program. The investigators employed a feasibility RCT research design and recruited 103 PR participants from a variety of referral sources. MAJOR COMMENTS Comment 1. Overall this was a well-written and interesting paper on an important topic. The largest limitation of this study is the lack of description of exercise prescription (especially intensity) and progression. Web-based, unsupervised exercise training as part of PR has great potential but it is crucial that the exercise training program be developed in such as way as to maximize patient benefit while minimizing the risk of adverse events. Therefore patients are often told to be 'active as tolerated' but this may result in the real risk of minimal improvements in exercise capacity, physical fitness or physical activity. As exercise is the cornerstone intervention for PR, careful attention must be paid to how this component is delivered in a telerehabilitation model. A suboptimal exercise prescription may have contributed to the lack of meaningful effect in the web-based group, and additionally in the traditional group (which also had little clarification of the initial exercise intensity and ongoing progression of exercise). The following questions should be addressed: a) How was the exercise prescription developed for both groups? b) How was exercise monitored and progressed? How did participants alter their exercise program if they felt it was too easy/too hard? How was the progress reviewed and what was the nature of the weekly contact? What parameters did the PT use to determine if the exercise prescription needed to change? What safety parameters were tracked? c) How many sessions of exercise were completed? Were there long gaps (> 1 week) in attendance? Comment 2. In addition, I question the use of QOL as the primary endpoint. While I agree philosophically that how a patient feels is the most important aspect of any healthcare intervention, it seems to me that a web-based program really needs to demonstrate that it can safely and effectively improve exercise-related outcomes in order to be deemed comparable to a traditional program. I feel that this program was not feasible in its current design because of its lack of achieving an important difference on the walk test. Therefore an important next step for the investigators is to spend more time on program design, exercise prescription, and monitoring through a web-based format. A careful discussion of this would make an important contribution to the knowledge of this subject. ADDITIONAL COMMENTS: Comment 3. Page 8, Line 37: Should the word "non-clinical" have something else after it? Comment 4. Page 9, Line 4. What was considered a serious adverse event? Comment 5. Page 9, Line 5: how was the patients' ability to exercise safely monitored? Comment 6. Page 19: What was the Exercise Safety Quiz? Was this similar to the PAR-Q for chronic conditions? Comment 7. Page 20: 111 patients had no internet access and were not eligible. How will this impact the feasibility of this intervention? Is this a typical representation of internet access in the UK? Comment 8. Page 21: There was a high percentage of men. Was this proportion reflective of the 2900 patients who were approached? Comment 9. Page 21: Please add the units for the change in ISWT and ESWT

	Comment 10. Page 23: Can a brief description of the Stages be added to the Table? Comment 11. Page 24: Clarify the timing of the information for the Figure Label: Patient Preference for Program Setting Prior to Randomization Comment 12. The Discussion Section has several grammatical errors, inappropriate use of commas and typos and should be carefully edited prior to publication. Comment 13. There appeared to be no results related to the technical delivery of the program (lack of access, functionality of the website, patient navigation and satisfaction, number of hits etc.)

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Huong Nguyen
Institution and Country: Kaiser Permanente Southern California, USA Competing Interests: None

This is a well written paper on an important issue of testing alternative pulmonary rehab formats for patients with COPD. I've offered some comments/feedback to further strengthen the paper.

Major
Presentation of abstract results should be more forthcoming regarding the high drop out in the WEB group (57%) especially since this was a key feasibility metric. Your study is in good company as there are many web-based behavioral studies showing attrition of 50-80% though most of these studies do not have the "human" interaction that this study has. A sentence regarding this has been added to the abstract results section.

Related to the point above, while the authors state there were no significant differences in the baseline characteristics of patients who completed the study versus those who dropped out, they also cite that patients who dropped out of WEB differed from those who completed. Because this is essential information, I would suggest reorganizing Table 1 to try to include a column for the 29 WEB patients who dropped out. Although all patients in the study were agreeable to being randomized to either programs, it's important to know what types of patients may not be a good fit for WEB and for clinical purposes, could be guided/persuaded to participate in clinic-based PR. This has been added as a separate table (Table 2) and discussed/ referred to in the results/ discussion sections.

Figure 2 lists reason for drop out but it is hard to understand key reasons for the early drop out (n=12) and if this could have been modified with changes to the WEB protocol. There was also a fair number of drop outs at Stage 2. Please provide more information/possible explanation re: how Stage 2 activities and components were simplified to improve retention.This is explained in the discussion but has been expanded on.

It would be helpful to provide additional process/usage metrics to understand pattern of use over the 11 weeks, e.g. frequency of login/week, duration of each unique log in, areas of web site where patients spent the most time etc…Since this was a feasibility study of WEB, providing more detailed usage information is helpful for readers. This has been discussed more in the non-clinical study outcomes section of the results.

Was there a qualitative formative or summative component to the study to better understand patients' experience with WEB? This information is usually very helpful. Yes there were semi structured interviews performed with both completers and dropouts of the web arm. These are being transcribed and written up for publication in a separate paper. This has been made clearer in the outcome

measures section of the methods.

How did the baseline program preference relate to drop out from either groups? Were patients who were assigned to the discordant group more likely to drop out? 25% of the web withdrawals would have preferred to have attended the classes compared with 54% of patients that attended conventional PR classes preferring to have done the web programme.
This has been reported in the non-clinical study outcomes section of the results.

Could the authors speak to why the change in the ISWT did not meet the MCID threshold even for the conventional PR group? It would seem that if we accept PR as being effective in improving physical functioning, it's concerning that changes in this PR cohort did not achieve the MCID even though the authors state that this group of patients are different from their typical PR patients. More patients were MRC 2 in the PR group than are normally referred to the PR service. The change in ISWT may also have been affected due to the structure of the PR programme which was 7 weeks (4 weeks supervised; 3 weeks unsupervised) for the majority of the patients and did not meet the BTS guidelines of a minimum of 12 supervised sessions. These guidelines were not published until after the trial had started. This has been added to the discussion section. It was discussed at one of the steering group meetings as to whether we should amend the protocol and change this so it was in line with the guidelines. However, a number of patients had already completed the PR arm and it was felt their results would have to be discounted.

Since completion of the WEB extended longer than the expected 6-8 week period, when exactly was the post WEB assessment completed for subjects who did not drop out? Was this to some extent standardized based on completion of certain modules? Should differences in the follow up time be adjusted for in the analysis? Patients were classed as a completer if they had reached stage 3 or above of the web programme, achieving 75% of the programme which is standard in clinical practice for those attending classes. This has been explained in the outcome measures section.

It's not clear what the value was in collecting/describing the health cost/EQD data collection especially since the sample is much too small to conduct a CEA nor were the cost data presented in the paper. Other published studies have collected these information thus presentation of the feasibility data is not entirely informative I agree with this comment and it was done entirely to see if it was feasible to collect the data. This information has been removed from the article.

The authors acknowledge the study was not sufficiently powered as a non-inferiority trial. Did it start out as a non-inferiority trial but due to recruitment challenges, was modified? The conclusion would be more helpful if the authors could address how future studies might be designed to either answer the question of non-inferiority and/or use of preference based RCTs to move the science of PR forward or should we stop doing these head to head comparisons altogether and focus on optimizing technology based solutions because we know patients need to have viable alternatives to clinic-based PR. No this study did not start out as a non-inferiority study. The discussion around non inferiority and preference based studies are addressed in the discussion section

Minor
In abstract, include mention that target sample was COPD patients This has been done
Strengths/limitations bullets should be in past or present tense not future tense as it is currently This has been revised and amended
What does "signposted" mean on page 6, line 54 This has been changed to "directed"
Suggest combining Figures 3 & 4 with Table 2 since there's duplicate information and best to streamline data presentation. Table 2 has been removed and the information represented on the figures.
Also, EQ5D score could be combined in the Table 2 as well. This has been removed as it did not add

value to the paper.

Reviewer: 2
Reviewer Name: Pat Camp
Institution and Country: University of British Columbia, Canada Competing Interests: none declared

The purpose of this study was to assess the feasibility of a interactive web-based PR program. Specifically, this involved investigating the recruitment rate, retention and drop out of participants; measuring the impact of the program on a variety of outcomes; and identifying the technical difficulties of delivering a web-based program. The investigators employed a feasibility RCT research design and recruited 103 PR participants from a variety of referral sources.

MAJOR COMMENTS
Comment 1. Overall this was a well-written and interesting paper on an important topic. The largest limitation of this study is the lack of description of exercise prescription (especially intensity) and progression. Web-based, unsupervised exercise training as part of PR has great potential but it is crucial that the exercise training program be developed in such as way as to maximize patient benefit while minimizing the risk of adverse events. Therefore patients are often told to be 'active as tolerated' but this may result in the real risk of minimal improvements in exercise capacity, physical fitness or physical activity. As exercise is the cornerstone intervention for PR, careful attention must be paid to how this component is delivered in a telerehabilitation model. A suboptimal exercise prescription may have contributed to the lack of meaningful effect in the web-based group, and additionally in the traditional group (which also had little clarification of the initial exercise intensity and ongoing progression of exercise). The following questions should be addressed:
a) How was the exercise prescription developed for both groups?
b) How was exercise monitored and progressed? How did participants alter their exercise program if they felt it was too easy/too hard? How was the progress reviewed and what was the nature of the weekly contact? What parameters did the PT use to determine if the exercise prescription needed to change? What safety parameters were tracked?
c) How many sessions of exercise were completed? Were there long gaps (> 1 week) in attendance?
These points have now been addressed for both the conventional PR programme and the web programme in the methods section. The nature, duration, exercise prescription and progression of the programmes have all been described.

Comment 2. In addition, I question the use of QOL as the primary endpoint. While I agree philosophically that how a patient feels is the most important aspect of any healthcare intervention, it seems to me that a web-based program really needs to demonstrate that it can safely and effectively improve exercise-related outcomes in order to be deemed comparable to a traditional program. I feel that this program was not feasible in its current design because of its lack of achieving an important difference on the walk test. Therefore an important next step for the investigators is to spend more time on program design, exercise prescription, and monitoring through a web-based format. A careful discussion of this would make an important contribution to the knowledge of this subject. I agree with this comment and the primary outcome as with most rehabilitation based studies is a change exercise capacity. As this is a feasibility study it should discuss the programme design, how the exercise programme is prescribed and progressed and the technical delivery of the web programme. I have tried to address these points in the revised manuscript.

ADDITIONAL COMMENTS:
Comment 3. Page 8, Line 37: Should the word "non-clinical" have something else after it? No it is in context with the first sentence about clinical measures, which are then described in brackets, before reading about non-clinical measures.

Comment 4. Page 9, Line 4. What was considered a serious adverse event? A serious adverse event was defined as an acute exacerbation of their COPD that resulted in a hospital admission. This has been explained in more detail within the outcome measure section
Comment 5. Page 9, Line 5: how was the patients' ability to exercise safely monitored? Patients carried out an Exercise safety quiz online before starting any of the exercise programme which they had to pass (80% or above). Predisposing co-morbidities that may have meant the patient was unable or was unsafe to exercise unsupervised, were investigated prior to the patient being recruited to the study as per normal clinical practice. The research team were able to monitor the patients through the website administration site and through weekly contact with the patient. This is also described in the supplement.
Comment 6. Page 19: What was the Exercise Safety Quiz? Was this similar to the PAR-Q for chronic conditions? It was created by us, based on the content from the website. We wanted to ensure that the user had read the content and understood the aspects of exercising safely, unsupervised.

Comment 7. Page 20: 111 patients had no internet access and were not eligible. How will this impact the feasibility of this intervention? Is this a typical representation of internet access in the UK? We collected some pilot data on 191 COPD patients to try and understand the technology usage in this population. It was found that although over half the patients owned a computer or mobile phone, usage was limited. The majority of patients that entered the study wanted the website showing that there is a desire for this type of intervention. Both these points are discussed within the discussion section. Even in those that did have internet access, it was found that an in depth specific web based knowledge was required. The web programme therefore develops choice for patients but isn't suitable for everyone.
Comment 8. Page 21: There was a high percentage of men. Was this proportion reflective of the 2900 patients who were approached? Unfortunately we are unable to ascertain how many were male out of the complete mail out. However, the prevalence of COPD is believed to be higher in men than in women (Chapman et al, 2001), and therefore this high percentage maybe reflective of the patients approached.

Comment 9. Page 21: Please add the units for the change in ISWT and ESWT This table has now been removed as per Reviewer 1's comments
Comment 10. Page 23: Can a brief description of the Stages be added to the Table? This has been added to table 3. It is also described in detail in the supplement.
Comment 11. Page 24: Clarify the timing of the information for the Figure Label: Patient Preference for Program Setting Prior to Randomization This has now been added
Comment 12. The Discussion Section has several grammatical errors, inappropriate use of commas and typos and should be carefully edited prior to publication. The manuscript has been edited for the above.
Comment 13. There appeared to be no results related to the technical delivery of the program (lack of access, functionality of the website, patient navigation and satisfaction, number of hits etc.) Patient navigation and satisfaction has been captured in the qualitative interviews which will be published separately. Lack of access is shown on the consort diagram and addressed in the discussion section (as per comment 7). The functionality of the website is reported on in the non-clinical study outcomes section of the results and the changes made due to the high withdrawal rates and patient feedback in the discussion.

I have provided a copy of the manuscript with the tracked changes accepted (version 9) and this is the copy that the response to the reviewers refers to. I have also provided a copy of the manuscript with the changes highlighted by tracked changes in MS word.
I hope that these amendments have made it an acceptable study to publish. The work has been seen and approved by all the authors.

VERSION 2 – REVIEW

REVIEWER	Huong Nguyen Kaiser Permanente Southern California US
REVIEW RETURNED	14-Nov-2016

GENERAL COMMENTS	The authors have been responsive to my feedback. Thank you for the opportunity to re-review