PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Effects of a web application based on multimedia animations to support therapeutic exercise for rotator cuff-related shoulder pain: protocol for an open-label randomized controlled trial
AUTHORS	Pérez-Porta, Irene; Flórez-García, Mariano; García-Pérez, Fernando; Fernández-Matías, Ruben; Pérez-Manzanero, M Ángeles; Araujo-Narváez, Aurora; Urraca-Gesto, M Alicia; Fernández-Lagarejos, César; Plaza-Manzano, Gustavo; Pérez-Fernández, Elia; Velasco-Arribas, María

VERSION 1 – REVIEW

REVIEWER	Bilek, Furkan Muğla Sıtkı Koçman University
REVIEW RETURNED	04-Mar-2024

GENERAL COMMENTS	Dear authors, first of all, I would like to thank you for your valuable work. The methodology of your study is very well-founded. My suggestion for your study: You can try to evaluate joint range of motion with image processing. You can administer the questionnaires through a mobile application.

REVIEWER	Şahinoğlu, Ertan Mavi Physiotherapy
REVIEW RETURNED	07-Apr-2024

GENERAL COMMENTS	Thanks to the authors for their effort. Actually, in such initiatives, I always think why don't we shoot video and use this material instead of animation. Isn't animation a more laborious and expensive method? A physiotherapist can also send videos (not animations) of the exercises that wants patients to do to patients' phones via text message (i.e., WhatsApp). For example, we have been doing this in our clinic for years. In this way, problems such as internet connection or not being able to reach the web site are eliminated. Therefore, I question whether there is a need for this type of study. My comments and suggestions in below. - Although both subacromial pain syndrome (in introduction) and rotator cuff related shoulder pain (in title) have similar connotations and there is no clear agreed terminology, it would be more appropriate to use a single term that is representative of your

	population. Please use a corresponding spelling throughout the text. - There is no statistical analysis in the abstract. If you do not exceed word count, it can be implemented. Also, there is no discussion part in the asbtract and manuscript. I am aware that the manuscript is a presentation of a protocol of a study, but some protocol papers presented Discussion part in BMJ Open. - "The effects of adding the videos to the exercise program can depend on the specific exercises prescribed, so the results of this study may not generalize to other exercises." I think, this is not a limitation. If it is a general exercise program for rotator cuff disease, it can be generalized to this population. - " The exercise program of this study will be reported in detail following current recommendations to facilitate its reproducibility and clinical implementation." Doesn't this exercise program include classic exercises? I guess that can't be a strong point of your work. - You indicated that " Nevertheless, the evidence of its superiority over traditional paper-based exercises is not clear." However, in your 25th reference (Emmerson et al.), the authors has been conducted a meta-analysis of randomized-controlled studies and found that " Multimedia approaches to exercise instruction may result in increased adherence compared with instructions provided in written or verbal format...". So there's actually nothing so ambiguous, but maybe there is unclear findings for patients with rotator cuff disease. Please, edit your sentence with referring your population. - You will give an instruction form (text with pictures) in both groups. I think, there is no need the instruction form, or even should not be. Yes, this is randomized controlled study, and both groups are asked to receive the standard practice; however, this is neither a gold standard method nor an accepted treatment. I think, experimental group should be receiving only web-based program. - You indicated that the estimated sample size was calculated as 112 patients, and with 10% drop-out rate 132. However, the calculation should be 112 / (1-0.1) ≈ 125 patients. - Your one of aim is that the investigation of effect of web-based program on adherence to the home-based exercise program. How will you measure it? Please explain in method section, not only in Appendix. - Why won't you use fixed-effect models for continuous variables? In these models, it can be possibility to add covariates. - If your missing data will be "missing at random" or "missing completely at random", will you perform a multiple imputation? Please indicate it.

VERSION 1 – AUTHOR RESPONSE

REVIEWER 1

1. **You can try to evaluate joint range of motion with image processing.**

Dear reviewer, thank you for your suggestion. We appreciate your proposal. When we planned this study protocol, we decided not to include some outcome measures because of time and resources availability within the hospital setting. We did not measured range of motion because in our experience and based on current research, subjects with rotator cuff tendinopathy do not seem to present with great range of motion limitation. Because of the study recruitment and treatment has already begun, we are unable to include any other new outcome measures. However, we will consider this proposal for future clinical trials we may conduct.

2. **You can administer the questionnaires through a mobile application.**

Dear reviewer, thank you for your comment. We have already begun the study, so we are unable to make any changes on the methodology. We decided to measure the questionnaires in the hospital with a traditional paper-based system, because in those review sessions the patients will also be seen by the physical therapist to adjust exercise load. We will consider this suggestion for future clinical trials we may conduct.

REVIEWER 2

1. **I always think why don't we shoot video and use this material instead of animation. Isn't animation a more laborious and expensive method? A physiotherapist can also send videos (not animations) of the exercises that wants patients to do to patients' phones via text message (i.e., WhatsApp). For example, we have been doing this in our clinic for years. In this way, problems such as internet connection or not being able to reach the web site are eliminated. Therefore, I question whether there is a need for this type of study.**

Dear reviewer, thank you for your comment. We understand the issues you present here. First, we decided to use video animations because we obtained funding for that specific purpose, through a call for proposals that focused on the use of these technologies. Second, the video animations allowed us to show the patients the performance of the exercises from different points of view (including from above), something that is more difficult to do with recorded videos. And third, we decided not to use any means of communication such as WhatsApp, because the ethics committee of our hospital stated there were legal issues with it in Spain within the public healthcare system. Finally, we understand the limitations of internet connection. The aim of this study is to obtain data regarding the effectiveness and viability of this kind of videos to improve patient’s adherence to treatment and health status. If we obtain good results with our study, we will use it as a justification for apply for more funding, in aim to create a mobile-phone application which does allow the patient to download the prescribed exercise by the health professional into his phone, to solve the issue of internet connection without the need for use applications such as WhatsApp. Since the creation of this kind of applications is more expensive than a webpage, so we decided to do it this way to justify asking for the money for the mobile application, which without preliminary results we would not be able to obtain.

2. **Although both subacromial pain syndrome (in introduction) and rotator cuff related shoulder pain (in title) have similar connotations and there is no clear agreed terminology, it would be more appropriate to use a single term that is representative of your population. Please use a corresponding spelling throughout the text.**

We have modified the terminology within the whole manuscript to always refer to the term “rotator cuff-related shoulder pain” instead of “subacromial pain syndrome”.

3. **There is no statistical analysis in the abstract. If you do not exceed word count, it can be implemented.**

We have added this information within the abstract. It now reads:

“Generalized least squares regression models with an autoregressive-moving average lag 1 correlation structure will be implemented, with an intention-to-treat analysis.”

4. **Also, there is no discussion part in the abstract and manuscript. I am aware that the manuscript is a presentation of a protocol of a study, but some protocol papers presented Discussion part in BMJ Open.**

Dear reviewer, the editorial team told us not to include any discussion section within the abstract of the manuscript, since the structure of the abstract of the journal does not include any discussion section. Regarding the inclusion of the discussion section within the manuscript, we are aware that some authors include this subsection in their protocols. However, we think that it would be difficult and a little bit confusing to discuss about a study protocol, so we would prefer not to include any discussion within the manuscript. Since the BMJ Open rules does not require the inclusion of this subsection, we hope it’s fine to leave the manuscript as it is.

5. **"The effects of adding the videos to the exercise program can depend on the specific exercises prescribed, so the results of this study may not generalize to other exercises." I think, this is not a limitation. If it is a general exercise program for rotator cuff disease, it can be generalized to this population.**

Dear reviewer, thank you for this comment. As you have pointed out, these exercises are some of the ones that are often prescribed to people who have rotator cuff-related shoulder pain, so the results of our study regarding the use of multimedia animations could be generalized to this population. However, there are other exercises that health professionals can prescribe to these patients. Since the effects of the training method can be highly dependent on, for example, the difficulty of the performance of the exercises to be trained on, it may be that the results of our study do not generalize to other exercises prescribed to patients with rotator cuff-related shoulder pain.

6. **"The exercise program of this study will be reported in detail following current recommendations to facilitate its reproducibility and clinical implementation." Doesn't this exercise program include classic exercises? I guess that can't be a strong point of your work.**

Dear reviewer, thank you for bringing this item up for discussion. We are aware that our study includes classic shoulder exercises. However, even a typical shoulder exercise can be performed in different ways. For example, a low row shoulder exercise can be performed at 0 degrees of shoulder abduction, or at 45º degrees of shoulder abduction like in our study. Furthermore, there are other aspects of the exercise program such as criteria for progression and regression on the exercise load that need to be specified within a manuscript. Currently, there is a lack of content reporting of exercise programs within shoulder research (Content reporting of exercise interventions in rotator cuff disease trials: results from application of the Consensus on Exercise Reporting Template (CERT) - PMC (nih.gov)), with a recommendation to improve it and use the CERT template to do it so. That is the reason we have stated this is a strength of our study, since we have detailed as much as possible all the items contained in the CERT checklist, that are usually not specified within current research about clinical trials in patients with rotator cuff disease.

7. **You indicated that "Nevertheless, the evidence of its superiority over traditional paper-based exercises is not clear." However, in your 25th reference (Emmerson et al.), the authors has been conducted a meta-analysis of randomized-controlled studies and found that " Multimedia approaches to exercise instruction may result in increased adherence compared with instructions provided in written or verbal format...". So there's actually nothing so ambiguous, but maybe there is unclear findings for patients with rotator cuff disease. Please, edit your sentence with referring your population.**

We have modified this sentence accordingly. It now reads:

“Nevertheless, the evidence of its superiority over traditional paper-based exercises is not clear in patients with RCRSP.”

8. **You will give an instruction form (text with pictures) in both groups. I think, there is no need the instruction form, or even should not be. Yes, this is randomized controlled study, and both groups are asked to receive the standard practice; however, this is neither a gold standard method nor an accepted treatment. I think, experimental group should be receiving only web-based program.**

Dear reviewer, thank you for your comment into this topic. We are aware of this issue. We decided to provide both groups with the instruction form (paper-based) because of the recommendation to do it so by the ethics committee of our hospital, since this is the current practice for the treatment of this kind of patients in the hospital setting of our country. Furthermore, the objective of our study is to investigate if the addition of these video animations provides additional benefits over the current practice in our hospital setting, but we don’t aim to evaluate if the video animations itself can replace the traditional paper-based system. Finally, as the study has started recruitment and treatment, we are unable to made modifications on assigned interventions.

9. **You indicated that the estimated sample size was calculated as 112 patients, and with 10% drop-out rate 132. However, the calculation should be 112 / (1-0.1) ≈ 125 patients.**

Dear reviewer, thank you for pointing out this mistake. We assumed a 15% drop-out rate, not a 10% as was stated within the manuscript. This issue has been corrected in the manuscript.

10. Your one of aim is that the investigation of effect of web-based program on adherence to the home-based exercise program. How will you measure it? Please explain in method section, not only in Appendix.

We have added this information within the section “2.7 Measurements”. It now reads:

“2.7.5. Patient’s adherence to the exercise program

Patient’s home adherence to the prescribed exercises will be measured with self-registered calendars, as the percentage of days performing the exercises at home over the maximum days available between the first physical therapy session and the last follow-up.”

11. Why won't you use fixed-effect models for continuous variables? In these models, it can be possibility to add covariates.

Dear reviewer, thank you for your comment. Fixed-effect models are appropriate when there is only one measurement per subject and there is no multilevel structure within the data. Our study has a repeated measures design with 2 groups (categorical variable included as fixed effect), and 4 measurements per subject (baseline, 6-week, 12-week, and 24-week). In this situation, it is not possible to implement fixed-effects models. The correct way of analyzing this type of data is to use kind of multilevel model, such as the generalized least squares with autoregressive structure, to take into account the correlation between repeated measurements. Furthermore, we will include within the model the baseline measurement of outcome measure as a covariate, to adjust for the small discrepancies at baseline induced by randomization itself, that has been showed to improve statistical power and precision of estimates.

12. If your missing data will be "missing at random" or "missing completely at random", will you perform a multiple imputation? Please indicate it.

Dear reviewer, we have modified this paragraph accordingly. It now reads: “Multiple imputation (5 to 20 imputations) will be performed if data seems to be missing at random or completely at random. On the other hand, if there seems to be a relationship between baseline variables and missingness, multiple imputation along with sensitivity analyses using worst-best case and best-worst case scenarios will be implemented.”

VERSION 2 – REVIEW

REVIEWER	Şahinoğlu, Ertan Mavi Physiotherapy
REVIEW RETURNED	03-May-2024

GENERAL COMMENTS	Dear authors, Thanks for considered my review. I indicate some points in below. • "The effects of adding the videos to the exercise program can depend on the specific exercises prescribed, so the results of this study may not generalize to I think, this is not a limitation. If it is a

	general exercise program for rotator cuff disease, it can be generalized to this population. I think, your exercises still can be generalized. Yes, in clinical practice, there may be patient-specific exercise selection, but these are already valid for outlier cases. For instance, routine exercise protocols are the same in all experimental studies without discriminating between patients. In fact, if your exercise programme in your application cannot be generalised, your application is not suitable for this patient population. Therefore, I strongly recommend that this statement be removed because a non-specialist reader of the article may be mistaken in thinking that the exercises are not applicable to the general population. • Why won't you use fixed-effect models for continuous variables? In these models, it can be possibility to add covariates. I will not insist on your choice of statistical analysis, but I must inform you that your recommendation for fixed-effect models is incorrect. Fixed-effect model analysis is commonly used in repeated measures (Gunasekara et al. 2014. Fixed effects analysis of repeated measures data. Int J Epidemiol).

VERSION 2 – AUTHOR RESPONSE

REVIEWER 2

- I think, your exercises still can be generalized. Yes, in clinical practice, there may be patient-specific exercise selection, but these are already valid for outlier cases. For instance, routine exercise protocols are the same in all experimental studies without discriminating between patients. In fact, if your exercise programme in your application cannot be generalised, your application is not suitable for this patient population. Therefore, I strongly recommend that this statement be removed because a non-specialist reader of the article may be mistaken in thinking that the exercises are not applicable to the general population.

Dear reviewer, we have deleted this bullet point within the STRENGTHS AND LIMITATIONS section and added a new one. It now reads:

"•The web-based animations require internet connection so patients can watch the exercise videos."

VERSION 3 – REVIEW

REVIEWER	Şahinoğlu, Ertan Mavi Physiotherapy
REVIEW RETURNED	02-Jul-2024

GENERAL COMMENTS	Thank you for considering my feedback. Best wishes for your research.

VERSION 3 – AUTHOR RESPONSE