Reviewer’s report

Title: Prognostic factors of a favorable outcome following a supervised exercise program for soldiers with sub-acute and chronic low back pain

Version: 0 Date: 02 Aug 2017

Reviewer: Mark Hancock

Reviewer's report:

Thank you for the opportunity to review this manuscript data from a cohort study of patients who underwent a supervised exercise program. The study aims to develop a clinical prediction rule to predict those who respond positively to the exercise program. The manuscript is clearly written but I have substantial reservations regarding the appropriateness of the study design given the study aims and conclusions.

1. This study is a single arm or cohort study, yet the underlying aim is to identify participants who respond better to this treatment than no treatment. Much has been written on this topic or limitation, in the physiotherapy literature over the last 5 to 10 years. The authors really do not refer to this literature stating the problems and limitations of using single arm studies for this purpose. Simply the single arm cohort study and the analysis methods utilised will most likely identify characteristics of participants who have better outcomes regardless of the intervention (in this case exercise program). The results of this study support this concern as all of the variables in the final model would logically be associated, and in many cases have strong evidence for being associated with, better outcomes regardless of the intervention.

The authors do in places use language such as predicting success or predicting outcome which is somewhat more appropriate given the study design but in other places they use terms such as respond positively and it is obvious that the intention of this study is to identify a treatment subgroup rather than a prognostic subgroup. If this study is accepted then I believe it is essential that major changes are made throughout the manuscript to emphasise that this early hypothesis generating study is identifying baseline predictors of good outcomes but provides no evidence
that these variables are also predictors of a specific response to this intervention. An RCT would need to be conducted to provide preliminary evidence of a treatment subgroup which would require further external validation. Some references to guide this restructure and that should be covered in the manuscript are included.1-3

2. Related to the main point above and the Sun et al reference provided below, it is important that there is some logical rationale when investigating predictors of response to treatment. In the introduction there is no rationale provided or direction of effect hypothesised for the included predictors. Were these predictors selected based on a logical rationale or just available data?

3. The justification for retaining four variables in the final model despite them being non statistically significant is not clear.

4. The terms respond to, predict success, predict outcomes are used interchangeably but have very different meanings.

5. Previous studies have demonstrated that even when predicting outcome different thresholds for the outcome substantially alter the association with predictors. The 50% improvement threshold used in this study is reasonable but should be mentioned that the predictors are likely to be different if a different threshold have been used.

6. The literature warns against using optimised thresholds when dichotomising continuous predictors of these likely overestimate the true association and tend not to generalise well new samples. This should be mentioned as a limitation.

7. It is unclear to me if collinearity of the variables included in the multivariable model was tested.

8. There appear to be approximately 50 variables that were investigated. The high risk of type I error needs to be discussed.
9. The model building process and stages seems a little unusual and it is unclear why some form of stepwise process was not used. This likely needs review by a statistician. Were the rules for keeping or excluding variables from the models specified a priori or not?

10. The * symbols in the tables representing statistical significance (p<0.1) are sometimes in the success group column, sometimes in the non-success group and sometimes in both. This implies that the comparisons may have been between one of the small groups and all subjects rather than between the two groups. This seems odd and needs to be clarified.

11. Given the limited predictive value of the final model and that only one variable was statistically significant is there a strong rationale to go on a test this rule in a randomised controlled trial?

12. Much of the discussion is in my opinion quite speculative and trying to find a justification for the included predictors. A more logical explanation is simply that they are predictors of outcome and this needs to be a focus of the discussion. The discussion should also focus more strongly on how this study meets or does not meet the recommendations such as the Sun et al paper, for producing evidence of treatment subgroup. Don't focus on the CPR literature as it mixes up prognostic CPRs and treatment CPRs. The paper by Kent at al (below) could be used as a framework in the introduction and discussion to present this paper as an early hypothesis generating study.

Minor:
1. I am unclear what the term infiltration means on line 73

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I recommend additional statistical review

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I have written papers arguing against the single arm approach taken in this study.

Otherwise I have no competing interests.

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