Author’s response to reviews

Title: To what extent is multi-morbidity associated with new onset depression in patients attending cardiac rehabilitation?

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Author’s response to reviews:

The reviewers’ and comments were most helpful and have helped us improve the paper.

Specific response to reviewer’s comments:

Reviewer 1 comments:

Abstract / Methods: Binary logistic regression - what tests were used to run the binary regression model? For example, a likelihood ratio test?

Our response:
Added to abstract methods section please see highlighted text.

Abstract / Results: Odds ratios would be better reported as 'significant predictors' or 'independent predictors' rather than 'significant correlates' to reflect the additional analyses undertaken.

Our response:
The term correlates changed to significant predictors in results section of the abstract.
Abstract / Conclusion: What is meant by individual characteristics in this context? Does this solely refer to people 'from areas with higher levels of social deprivation'? This term could imply personality factors, acute or chronic stress for example. However, from this data it seems to refer to psychosocial factors or cardiovascular risk factors. Please consider modifying this term for clarity. The authors may consider the ESC position paper on psychosocial aspects in cardiac rehabilitation (Pogosova et al. 2015) helpful. The Fava and Sonino 2010 paper 'Psychosomatic medicine' may also be helpful to clarifying terminology regarding individual factors or vulnerability.

Our response:  
The broader term ‘individual characteristics’, although it was used as overarching term for variables used in our analysis, has been changed in accordance with the reviewer’s suggestion based on ESC position paper (Pogosova et al. 2015), please see abstract conclusion section.

Manuscript/ Methods: The type of observational study needs to be specified in the methods. E.g was this a cross-sectional study?

Our response:  
Please, see methods section, line 44, page 5.

Manuscript/ Measures: There are a few minor grammatical errors that could be fixed in this section. E.g. Please try not to use the same word twice in a single sentence. E.g 'population' and 'patients'. Lines 92 and 100 also require attention.

Our response:  
Please, see measures section, line 77, 90, 95 and 103, page 6 and 7.

Manuscript / Statistical analysis: Please change 'associations' to 'statistically significant predictors' in this section to accurately reflect the binary regression undertaken. It would also be helpful to add the (HADS ≥ 8) cut-off score in this section for clarity in defining those with new onset depressive symptoms who were included in the model.

Our response:  
Please, see statistical analysis section, line 147,148, page 8.
Manuscript / Tables: It would be beneficial to the reader to include the numbers included in each analyses as well as the percentages. The total number of included participants should also be included in table 2 and 3 as reported in table 1. The regression coefficient and probabilities could be removed from the table for the benefit of the reader. The number of people who answered the HADS adds up to 109056 rather than 109055. Please check the total represented in the text with the tables and flow diagram. The flow diagram is quite helpful in this section. It could also be helpful to report the proportion/percentage of the NACR population who answered the HADS in the participants section as it is of significance to CR service delivery. The non-parametric effect size calculations were a great addition to the manuscript.

Our response:
In order to ease the readability of the tables the counts have not been added. However, the total number of included participants added in table 2 and table 3 as suggested by reviewer. The probabilities have been removed from the table 4 as suggested, however the regression coefficients have been kept to provide extra information for the readers who may want to see it. The total has been checked, the correction has been made in the table 1, last digit has been changed in HADS<8 group. 109055 remains as total number of patients with HADS record as reported in text and flow diagram. The proportion of patients with HADS measures recorded has been reported in the participants section as suggested, please, see line 69-70, page 6.

Manuscript / Results: Line 154-156. The results should only report the findings rather than how the analyses were completed. There is no need to repeat the use of chi squared tests and independent t tests and what variables these were applied to. Please delete or move this information to the methods section of your paper. This also applies to line 173. Grammatical error line 186.

Our response:
The suggested information have been deleted as recommended. The line 173 has also been changed. Please see, line 170,171, page 11. Grammatical error has been corrected, please, see line 192, 195, page 14.

Manuscript / Discussion:
Please do not re-report the statistical details in the discussion (i.e. the confidence intervals and p values), as this is data is included in the results section of the paper.
Now that the paper has added the regression model, it would be better to highlight the factors that predict early onset depressive symptoms, as this is a stronger analyses when compared with the factors associated with the new onset of depressive symptoms. This will also tighten your discussion, which could be better synthesised. The key implications for cardiac rehabilitation research and practice need to be better highlighted by omitting some of the text that repeats the results. The implications of addressing psychosocial factors as classified by the IMD for cardiac rehabilitation service delivery need to be better discussed. It could be worthwhile discussing how your findings relate to the ESC position paper on psychosocial aspects in cardiac rehabilitation (Pogosova et al. 2015).

Our response:
Statistical details have been reduced please see lines 264, 273, 292, page 17. IMD measurement have already been discussed between lines 294 and 308. In addition, IMD is further discussed please see the lines 308-311, page 18. Our finding has been discussed in relation to ESC position paper, please, see line 312-318, page 18.

Manuscript / Limitations: Please do not re-report results in the discussion section of the paper. Rather, please include the data reporting the characteristics of the sample as a whole in the results section where you report the study population.

Our response:
The reason we have given the population characteristics is that to compare them with the wider population of patients recruited during the study period and support the generalisability of the results based on our sample to wider population of n=277521 which is a strength of the paper.

Conclusion: Given that adjustments were made to the manuscript, the conclusion should reflect the factors generated from multivariate analyses of new onset depression in cardiac rehabilitation, rather than focusing on the associations generated from univariate analyses. The objectives also do not to be restated, so I would recommend deleting the first sentence. The conclusion states that "CR programmes need to raise awareness to patients" but does not make the link to what patients should be made more aware of. Do you mean their increased risk of future cardiovascular events due to their increased psychosocial risk and the presence of multiple comorbidities?

Our response:
The second sentence has been deleted in order to make conclusion more focused on multivariate analyses as recommended. The first sentence has also been deleted as suggested. Please, see the adjustments that have been made to line 332-339, page 19.
Reviewer 2 comments:

I have several concerns, however, primarily with their baseline analyses. Although the statistical methods appear to be well done, I believe their conclusions may be somewhat overstated. Although many of the variables assessed were more commonly seen in patients with a HADS $> 8$ as evidenced by the P-values, with the exception of the HADS anxiety score, the clinical significance of these differences is somewhat unclear as the subjective differences don't appear that large (i.e. a mean age of 64 vs. 66, 2.6 vs. 2.3 comorbidities, BMI of 29 vs. 28). This is reflected in the mostly small effect sizes they report (Cohen's d are all $< 0.20$ in Table 1, with exception of HADS Anxiety Score Measurement). Similar patterns are seen in Tables 2 and 3. Although their linear regression model sheds some additional light and highlights the importance of several factors (namely HADS anxiety score, exercise, male gender and diabetes all of which have an odds ratio of 1.2 or greater), the OR for total number of comorbidities remains subjectively small and clinically unclear despite it's significant p-value.

Overall although I believe their manuscript sheds important light on the characteristics of patients with new onset depression who enroll in CR, I would reframe their ultimate conclusions to highlight that these findings are more likely thought provoking and hypothesis generating at this point. Their summary and conclusions could also benefit from a more open discussion around the small effect sizes and odds ratios seen, instead of simply generally stating that patients with new onset depression overall have a higher number of comorbid conditions because, although that may be true from a purely statistical standpoint, in a practical sense I'm not sure if that's the case.

Our response:
The difference in baseline analysis has already been discussed regarding BMI please, see line 263-269, page 17, and anxiety please see lines 274-280, page 17. Conclusions has been changed and focused only on the results of multivariate analysis as recommended by reviewers.