Author's response to reviews

Title: Triglycerides as a biological marker for repeat re-hospitalization resulting from deliberate self-harm in acute psychiatry patients: a prospective observational study

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Author's response to reviews: see over
Dear Editor,

Please find enclosed our revised manuscript, “Triglycerides as a biological marker for repeated re-hospitalization resulting from deliberate self-harm in acute psychiatry patients: a prospective observational study” by John Olav Roaldset et al..

The authors are thankful for the reviewers’ comments and have revised the manuscript on the basis of their suggestions. The authors’ responses to the Editor and reviewers have been typed in red, and follow below.

Sincerely,

John Olav Roaldset
Corresponding author

EDITORS REQUEST:

1. Please include contributions of Dr. Olav M Linaker in your Authors Contribution’s section for your revised manuscript.

Comment: Olav Morten Linaker contributed significantly to the interpretation of the data, to the preparation of the manuscript, and to the final approval of the manuscript.

Change: The sentence: “JOR, OLM and SB contributed significantly to the interpretation of the data, to the preparation of the manuscript, and to the final approval of the manuscript “has been added to “Authors contribution”.

Reviewer’s report (1):

Major Compulsory Revisions:

R1-1: The decision to combine into a single outcome variable suicidal behavior and non-suicidal self-injury is questionable and a possible reason for the discrepancy between this study and previous ones showing the relevance of (low) cholesterol levels. Even though there is an area of overlapping between the two symptom dimensions, suicidal behavior and non-suicidal self-injury differ for a variety of features, including predisposing factors, epidemiological correlates, and pathogenetic mechanisms. It would be interesting to reanalyze the data by separating the two phenomena.

Comment: We agree with the reviewer that suicidal and non-suicidal self-harm are different conditions. In line with this, the outcome variable “self-harm” was recorded as either suicidal or non-suicidal in the project.

However, some patients in the project were at one occasion recorded with a suicidal attempt (i.e severe and life-threatening paracetamol overdose), but at another occasion and at a (completely) different time recorded with non-suicidal self-injury (i.e many abdominal and fore-arm scratches and cuts, having torn out suture wires, etc.). It was difficult to decide if the few persons in our sample who were recorded with
suicidal behavior at one or more occasions and with non-suicidal attempt(s) at other occasion(s) should belong to the suicidal or the non-suicidal group. Hence we decided to categorize a third group, the suicidal + non-suicidal self-harmers, in addition to the (i) only suicidal and (ii) the only non-suicidal self-harmers. A distinct dichotomous understanding of self-harm has also been questioned in the literature by suggesting that in some cases it is difficult to decide whether the intention was suicidal or non-suicidal, and that sometimes the self-harm intention could have both suicidal and non-suicidal aspects [1]. This was not explained well in the manuscript, and it has been clarified in the revised manuscript.

We have previously reported more detailed results of the predictive values of lipids for the three groups: suicidal only, non-suicidal only, and suicidal + non-suicidal [2]. One finding was that low total cholesterol at admission was significantly predictive for inpatient suicidal attempts, but high cholesterol was predictive for suicidal behavior the first three months after discharge (in the suicidal only group).

We agree with the reviewer that this aspect could be more clearly handled in the manuscript, and we have made additions to the text in the revised manuscript. We have also computed the predictive validity of the lipids for the 12-months suicidal only and non-suicidal only patients.

However, we have found no good solution to categorize the “suicidal + non-suicidal” self-harming patients into either suicidal or non-suicidal. Therefore we have kept our original categorization in the revised article. Seventeen of the 18 self-harm repeaters belonged to this suicidal + non-suicidal group.

Changes: Predictive values of the lipids for the 12-months suicidal only and non-suicidal only patients have been added to the revised manuscript; see R1-1 in Results. The text has been changed in the revised manuscript; see R1-1 under Methods / Outcome variables.

Minor Essential Revision

R1-2 • Reading the abstract, it is unclear if low or high levels of triglycerides were a significant predictor of self-harm. Please, specify.

Change: The abstract has been changed to be clearer, see R1-2 in the revised manuscript.

R1-3 • In the first lines of p. 4, the authors state that cholesterol levels and DST are not easy markers to include within clinical routine assessment. This is surely not true for cholesterol levels, at least when compared by the marker used in this study (i.e., levels of triglycerides).

Comment: We agree with the reviewer
Change: See R1-3 in Background in the revised manuscript.

R1-4 • The authors decided to include in multivariate models those predictors that were significant in univariate comparisons. However, it is possible that, sometimes, a multivariate analysis shows the significant impact of a variable that
resulted non-significant in univariate comparisons. I am making this point because I think that age is a crucial variable when focusing on risk factors for suicidal behavior and non-suicidal self-injury (separately classified). Thus, I would suggest to include age into multivariate models.

Comment: We think the reviewer has a good point.

(i) Age has been included in the first step of the multivariate logistic regression analysis and the analyses have been re-computed. The result showed that none of the 10 factors were significant in the last step. We then included triglycerides in the first step to follow the progression of the significance of the triglycerides when new factors were stepwise added in the regression, and re-computed the analyses once more. Table 3 and Results have been changed accordingly. The results from Table 3, step 4, in the first submitted manuscript has been included in the text under Results in the revised manuscript.

(ii) When Age was added to other variables (OV) in the ROC analyses (Table 4), the ROC value of “OV + age” decreased compared with the “OV” alone. Therefore, ROC values were not re-computed.

(iii) Since the cut-offs for the predictive values in Table 5 are derived from the ROC curves we did not re-compute these values.

Change: Multiple logistic regression analyses have been re-computed. See changes in Table 3, and R1-4 under Results in the text.

R1-5 • The authors should explain the rationale and clinical utility to set two different time points (3 and 12 months after discharge) for the analysis.

Comment: Self-harm episodes were recorded during the 0-3, 4-6, 7-9, and 10-12-month periods. Results from the 4-6-months and 7-9-months periods did not add significant information, so results are only given for the 0-3-months and 0-12-months periods. Since psychosocial and biological risk factors may change over time, both the 0-3-months and 0-12-months periods are of clinical interest.

Change: See R1-5 under Methods

R1-6 • Text and style require extensive linguistic revision (e.g. repeat in the title should be “repeated”).

Comments. The revised article has been language-edited (“premium”) by American Journal Experts before re-submission.

Reviewer’s report (2):

Major Compulsory Revisions
R2-1. Some studies indicated that low cholesterol level could be one of risk factors for suicidal behavior especially among subjects with major depressive disorder, which had been described in the background of the manuscript. Table 2 in this study showed that subjects with DSH-R included no one
diagnosed with depressive disorder. I think that this can be important one of different points between this study and other previous ones. The authors should discuss the above that subjects with DSH-R did not include anyone with depressive disorder.

Comment: When looking at co-morbid diagnoses, two patients had unipolar depression and two had bipolar depression. Nevertheless, depression disorders seem to be underrepresented in this group. We found the same trend for all patients in the study; despite that depression is a strong risk factor for self-harm it turned out to be a protective factor in this sample of acutely admitted patients [3]. However, some factors may explain this result: the high prevalence of self-harm, patients with depression are known to be at risk for self-harm and were not discharged before the risk was considered low, or they may have received sufficient treatment and self-harm monitoring after being discharged.

Change: We have added the co-morbid psychiatric diagnoses to Result and a new paragraph to Discussion in the revised manuscript. See R2-1 under Results and Discussion.