Author's response to reviews

**Title:** Clinical characteristics in schizophrenia spectrum disorder patients with or without suicide attempts and non-suicidal self-harm - a cross-sectional study

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**Version:** 2  **Date:** 5 June 2013

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

Thank you for your e-mail and the possibility to resubmit a revised version of MS: 7899180259511766 “Clinical characteristics in schizophrenia patients with or without suicide attempts and non-suicidal self-harm - a cross-sectional study.” We appreciate the reviewer’s comments, to which we respond in the following sections. Revised versions of the manuscript, tables and additional file and figure are uploaded according to your instructions.

Editors request:

**Please document within the methods section of your manuscript the specific name of the organization that granted ethical approval to your study going ahead.**

Reply Editors request
The specific name of the organization that granted the ethical approval is “The Regional Committee for Medical and Health Research Ethics, South East, Norway.” We have added the name of the specific regional committee (South East) to the name already given in the methods section.

Revision, editor’s request:
Methods, first paragraph, last sentence is revised as follows: “The study was approved by The Regional Committee for Medical and Health Research Ethics South East, Norway and by the Norwegian Data Protection Agency.

Reviewer 1

Reviewer's report

Version: 1 Date: 23 April 2013

Reviewer: Christopher Gale

Reviewer's report:
In general, this is a very well written paper that is dealing with an important issue. The data is taken from a survey and at present is descriptive and describing correlations only, but in doing this the
authors have suggested a classification, methods of measurement, and a risk group that would allow further research. Given the controversy as to the meaning of "Suicidality" (which all too often is a proxy measure taken from the PANNS) this paper is also timely. The statistical approach is appropriately conservative and reasonable with one exception, noted below. I have very few suggestions, only one of which is major.

**Major Compulsory Revisions.**

**Reviewer 1, comment 1.** I would redo the multinomial logistic regression analysis using NO self harm as the reference group. It appears that the authors used the Susicide attempt and deliberate self harm (NISSH) groups as the reference, and this makes the table difficult to interpret.

**Reply, comment 1**

As the referee points out, it would be easier to interpret Table 3 if NoSA was reference category in Table 3. On the other hand, the aim of the present study was to investigate whether patients with SA+NSSH have earlier onset of clinical symptoms and report more impulsive aggression, suicidal ideation and depressive symptoms than patients with SA only and NoSA patients. Using NoSA as the reference category precludes statistical comparison of SA only vs SA+NSSH. To meet both these needs we have redone the multinomial logistic regression analysis according to the suggestion from the reviewer and provided the current Table 3 as additional supplementary material. We have revised the text accordingly (see below).

**Revision 1, comment 1**

We have redone the multinomial logistic regression analysis with NoSA as reference category and revised Table 3 accordingly. The table with SA+NSSH as reference category is added as additional supplementary material.

**Revision 2, comment 1**

Results, Multivariate analyses, 1st and 2nd paragraph is revised according to these changes.

**Minor Essential Revisions.**

**Reviewer 1, comment 1.** The authors are using a population with schizophrenia by the narrow, neo-Kraepelilian definition. However the title uses the words schizophrenia spectrum which imply a broader group. I think adjusting the title to make it clear we are discussing people with Schizophrenia with a narrow definition would be wise.

**Reply, comment 1**

We thank the reviewer for pointing this out. We have revised the title and manuscript text accordingly.

**Revision, comment 1**

The title and manuscript text is revised by using schizophrenia and not schizophrenia spectrum disorders throughout the manuscript.

**Discretionary Revisions.**

**Reviewer 1, comment 1.** The authors, quite correctly, included the problem questions for self harm and suicide attempt. A sentence indicating if they were taken from the SCID or similar, and if these questions were semi-structured or part of a fully structured interview would help. (I have seen the response outcomes in both Structured interviews such as the CIDI and semi-structured such as the SCID).

**Reply, comment 1**
The questions about lifetime episodes of suicide attempts and non-suicidal self-harm was collected using a semi-structured interview based on the question about episodes of self-harm adopted from a previous European study of self-harm (the CASE-study, reference 26) and included both open descriptions and questions with given categories. The clinical assessment section is revised to include this information.

Revision 1, comment 1
Methods, Clinical assessment, second paragraph, second sentence is changed as follows: “Information on lifetime episodes of self-harm was based on a semi-structured interview including the following question adopted from a previous European study of self-harm (CASE-study):”

Reviewer 1, comment 2. In table 3 there is no significant difference between medication use between the three groups. The authors may want to comment on this.

Reply, comment 2
Comments about the univariate association between current medication use and types of self-harm are present in the results section, Current symptoms and behavior and in the Discussion section, 5th paragraph. To highlight that current medication did not contribute to further differentiate the groups in the multivariate analyses, we have added a sentence in the Results section, Multivariate analyses (see below).

Revision, comment 2
Results, Multivariate analyses, 2nd paragraph, the following sentence were added: “Current medication did not significantly differentiate between groups in the multivariate analyses.”

Reviewer 1, comment 3. I'm used to using the term deliberate self harm (DSH) in a very similar manner to the authors NISSH. The authors need to consider if these two terms are equicelent (DSH is not uncommon, and there is a literature on this.

Reply, comment 3
The reviewer is right in pointing out that the term “deliberate self-harm” has in some areas of the world (e.g. the US) been used to describe similar behaviors as non-suicidal self-harm (NSSH). However, the term “deliberate self-harm” (currently only “self-harm” is most often used) has in Europe, Australia and other countries been used to describe self-harm irrespective of intent, i.e. both suicide attempts and non-suicidal self-harm. To avoid any confusion we chose to use the term non-suicidal self-harm.

Reviewer 1, comment 4. In the discussion, the authors need to consider the most recent published papers relating to DSH and suicidality and recovery, suicide and schizophrenia. Most of these papers have similar designs to this, but here are also some follow-up studies that may be of interest.

Reply, comment 4
The aim of the present study was to study whether patients with SA+NSSH have different clinical characteristics to patients with SA only or patients without any history of SA. We agree with the referee that there are recent and important published papers relating to suicidality/suicide attempts and recovery in schizophrenia. However, we have not been able to find any recent studies addressing NSSH specifically or the clinical characteristics associated with different types of self-harm behaviors (e.g. SA vs NSSH or combinations) in schizophrenia or psychotic disorders, which is the aim of the current paper. That notwithstanding, studies, including the follow-up study by Sanchez-Gistau and colleagues, highlight the elevated risk of future SA among adolescents with first-episode psychoses, high suicidality and higher severity of depression at baseline. This is relevant to the finding in our study that those with both NSSH and SA have earlier onset of psychoses, more repeated SA and
higher levels of current depressive symptoms than patients with SA only or no suicide attempts. We have made changes to the discussion to incorporate these aspects.

Revision, comment 4
We have added the following to the end of the Discussion, fourth paragraph: “Severity of depressive symptoms and suicidal behavior are robust predictors of future suicide attempts in adult samples of schizophrenia patients [4, 34] and a recent study of children and adolescents with first episode psychoses also found that depressive symptoms and high suicidality at baseline was associated with increased risk for suicide attempts in the follow-up period [35]. That study did not report on NSSH, but such findings highlights that the higher severity of depressive symptoms and higher current suicidality in patients with both SA and NSSH increase the risk of future suicide attempts.”

Reviewer 2
Version: 1 Date: 3 May 2013
Reviewer: Graham Pluck
Reviewer's report:
This is a generally a good report with a large sample. However, I have some concerns with the representation of the statistics.

Minor Essential Revisions

Reviewer 2, comment 1. Has any of this data been reported previously? In the final paragraph there is discussion of your previous study on a similar topic. This should be referenced. And in the fifth paragraph of the discuss there is the statement ‘Studies of first episode patients (including a subsample of the current) indicate that..’. If any data is being re-reported on the same patients this should be stated clearly.

Reply, comment 1
We thank the referee for pointing out that the reference to our previous study, due to an error, had disappeared from the manuscript. This is now corrected (see revision 1, comment 1).

The data reported in this article has not been reported previously. About 25 % of the current sample constituted about 1/3 of a sample of first episode psychoses patients (FEP) in an article reporting on Suicidality before and in the early phases of first episode psychosis. Both the total sample (FEP vs schizophrenia) and the outcome variable (suicidal ideation/plans or suicide attempt in different phases vs self-harm with or without suicidal intent) were different in the two articles. Thus, no data were re-reported on the same patients. We realize that the parenthesis “(including a subsample of the current)” might be confusing and we have thus deleted the parenthesis.

Revision 1, comment 1
Introduction, final paragraph: The following reference is included in text and reference list:

Revision 2, comment 1
Discussion section, 5th paragraph: The following parenthesis has been deleted: “(including a subsample of the current)”.

Reviewer 2, comment 2. In 'Clinical Assessments' it is not clear what reference 22 refers to, this should be clarified.
Reference 22 referred to the inter-rater reliability. We have revised the text by reporting the inter-rater reliability directly and have thus removed the reference 22.

Methods section, Clinical assessment, first paragraph is changed to the following: “All interviewers participated in interrater reliability testing that entailed rating of patient videos. Inter-rater reliability was acceptable with intra-class correlation coefficients for PANSS subscales ranging from 0.71 to 0.73.

Reviewer 2, comment 3. Duration of untreated psychosis is not defined as DUP in ‘Clinical Assessments’ paragraph 1. It should be.

We have changed the description of the definition of DUP to more accurately reflect what was measured and in accordance with the point made by the referee.

Reviewer 2, comment 3. Methods section, ‘Clinical Assessments’ 1st paragraph, last sentence: We have changed the sentence as follows: “Duration of untreated psychosis was measured as time from psychoses onset until start of adequate treatment for psychotic disorder [24].”

Reviewer 2, comment 4. In the discussion section, second paragraph, your claim to be the first to describe NSSH + SA and its correlates is not really true (e.g. Pluck et al 2012, European Psychiatry). That text should be altered.

We are aware that several previous papers have reported on self-harm (encompassing both SA and NSSH) in schizophrenia. Our intention was to express that to our knowledge, this is the first study to address the clinical correlates of a history of both SA and NSSH as opposed to SA only or no suicide attempt history in patients with schizophrenia. We agree that the intended message could be formulated more clearly and have changed the sentence accordingly.

Reviewer 2, comment 5. A Venn diagram would be useful for understanding the different groups. Consider including one.

We have included a Venn diagram to facilitate understanding of the different groups, in line with the suggestion from the reviewer.

Reviewer 2, comment 6. In Tables 1 and 2, the notation used for Kruskal Wallis tests is x2, which is
confusing. ‘K’ would be better considering there are other chi2 tests reported with the notation x2.

Reply, comment 6
We agree that changing the notation from x2 to K is better and have changed the notation according to the suggestion from the reviewer.

Revision, comment 6
Tables 1 and 2. The notation used for Kruskal Wallis test has been changed to K in the table and table footnotes.

Major Compulsory Revisions

Reviewer 2, comment 7. A general issue about the data in Tables 1 and 2 is that you are comparing three groups, therefore with the ANOVAs, Kruskal Wallis or the Chi2 analyses, there are various pairings which could differ from each other. The p values presented in Tables 1 and 2 are simply for all the differences between the three groups. However in the text (e.g. the section entitled ‘Illness history and medication’) you are presenting the findings as if they show that one group differs from the second group and also differs from the third. The p values as they are don’t give that information. If you want to show that one group is different from both other groups then you would need to show some post-hoc comparisons / planned contrasts. I would recommend re-running the ANOVAS and reporting the contrasts between the ‘SA+NSSH’ group and each of the other two groups (‘SA only’ and ‘No suicide attempt’). Similarly, the simplest solution to this issue for the categorical data may be to perform additional 2x2 Chi2 tests with SA+NSSH vs ‘SA only’ and ‘No suicide attempt’. This is a bit long-winded but it may be the simplest way to get the stats for what it is that you are trying to say.

Reply, comment 7
In preparation of this manuscript we have performed those post-hoc comparisons/planned contrasts that are suggested by the reviewer. We agree with the reviewer that these should be reported in the tables. These are now included in tables 1 and 2 in line with the suggestion from the reviewer. The Methods section, statistical analyses has been changed accordingly (revision 2, comment 7). Due to these changes in the analyses of the univariate associations, three changes has been made in the text of the Results and discussion sections, to more accurately reflect the findings (see revision 3, comment 7 below).

Revision 1, comment 7
Tables 1 and 2: A new column “Post hoc”, reporting on significant associations from pairwise comparisons, is included and explained in footnotes.

Revision 2, comment 7
The Methods section, statistical analyses has been changed into: “Group differences were analyzed using Chi-square tests, one-way ANOVAs (post hoc Scheffe’s tests) for normally distributed continuous variables and Kruskal-Wallis test (post hoc Mann–Whitney U tests with Bonferroni corrections) for non-normally distributed continuous variables. Based on the research questions, post-hoc comparisons were performed comparing the SA+NSSH group with the SA only and with the NoSA groups.”

Revision 3, comment 7
Results section, current symptoms and behaviors, third sentence has been changed into: “There was, however, a trend towards group differences on positive symptoms (p=.08), and significant group differences were observed on the delusions and hallucinatory behavior items from the positive symptoms score, with those with SA+NSSH scoring significantly higher than both other groups on current hallucinatory behavior.”
Results section, Illness history and medication, the SA only group has been removed from the last sentence: “One third of the SA+NSSH patients did not use any antipsychotic medication; a significantly higher fraction than among NoSA patients.”

Discussion section, the SA only group has been removed from the last sentence above the Strengths and limitations section: “From this point of view it is important to note that one third of the SA+NSSH patients currently did not use any antipsychotic medication; a significantly lower fraction than among NoSA patients.”

**Reviewer 2, comment 8.** In regards to the current medication chi2 in Table 1. The same problem applies, the contingency table is so big that the significance of the difference doesn’t tell us much. You would have to do more 2x2 tests to really pin-down the significant differences. In light of this, you can’t justify the statement in the paragraph above ‘Strengths and limitations’ in the Discussion, that one third of the SA-NSSH group did not use antipsychotics and that this was a significant difference. Additional statistics should be performed to remedy this.

**Reply, comment 8**
The additional statistics have been performed and explained in the footnotes “f” and “g” in Table 2. See also reply and revisions to comment 7 above.

**Reviewer 2, comment 9.** A related issue is that you are not using the word ‘significant’ to describe your univariate findings in the results section, as the results are currently ambiguous, that’s probably OK. However, if you add the extra analyses as described above, it would be clearer in the text if you use the word ‘significant’ when described those results that are.

**Reply, comment 9**
We have revised the text in the results section to use the word significant in reporting of significant findings.

**Revisions, comment 9**
Results section. We have used the word significant in reporting of significant findings throughout the results section.

**Reviewer 2, comment 10.** In the section entitled ‘Multivariate analysis’, I feel that there isn’t enough information provided to understand the methods. For example, why were some variables selected to be included in Model 1, but not others? Overall, I think this manuscript should be reviewed by a statistician, in which case their advice could override the above major compulsory revisions.

**Reply, comment 10**
Variables regarding the patient’s illness history were included in Table 1 to answer the first aim of the study. Current symptoms, medication and behaviors were added to the analyses in model 2 to also address the second research question. We have made changes to the Results section to make this clearer (see below).

**Revisions, comment 10**
Results section, Multivariate analyses, 1st paragraph, 1st sentence has been changed to: In the first model we investigated the multivariate relationships between group memberships and illness history (Aim 1, i.e. ages at onset of psychosis and depression) together with potential confounding variables of this relationship (here DUP and gender).

Results section, Multivariate analyses, 2nd paragraph, 1st sentence has been changed to: In Model 2 we added current symptoms and behavior to the illness history variables entered in model 1 to address the second aim of this study.
One correction made by the authors
In the process of revising the manuscript, we discovered a typing error in table 1, second column, variable “First treatment for other reason than psychoses”: In the overall group the right numbers should be 70 (29), not 26 (49). This has been corrected in the current submission. It was a typing error and does not influence the reported results, data analyses or discussion of the results.

We look forward to hearing from you.

Best regards,
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