Author's response to reviews

Title: Substance Abuse and Psychiatric Co-morbidity as Predictors of Premature Mortality in Swedish Drug Abusers: A Prospective Longitudinal Study 1970 - 2006

Authors:

Anna Nyhlén (anna.nyhlen@skane.se)
Mats Fridell (mats.fridell@psychology.lu.se)
Martin Bäckström (martin.backstrom@psychology.lu.se)
Morten Hesse (mh@crf.au.dk)
Peter Krantz (rmlu@rmv.se)

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Author's response to reviews:

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Substance Abuse and Psychiatric Co-morbidity as Predictors of Premature Mortality in Swedish Drug Abusers:
A Prospective Longitudinal Study 1970-2006
Anna Nyhlén, Mats Fridell, Martin Bäckström, Morten Hesse and Peter Krantz.
16 APRIL 2011

Dear Angelina Ilievska

Thank you for your comments. We answer the questions from the reviewers below. The revised manuscript is submitted. All changes made in the revised manuscript are highlighted (colored) to make it easier for the Editors.

We omit comments from the two reviewers who were satisfied with our first revision.

Our manuscript has now been revised according to the new comments from two of the reviewers. The concerns are addressed with a point-by-point response below:

With best wishes,

Anna Nyhlén, MD, PhD Mats Fridell, Professor in clin psychology
Tel: +46 (46) 174995
e-mail: mats.fridell@psychology.lu.se
REPLY TO REVIEWER 1
Title: Predictors of Premature Mortality in Swedish Drug Abusers: A Prospective Longitudinal Study 1970 - 2006
Version: 4 Date: 5 March 2011
Reviewer: John Corkery
Reviewer's report:
I have now reviewed this second version in the light of my comments and those of the other reviewers - two of whom are close colleagues, and the authors' responses.

I think that the new version is a much more robust paper, far easier to read, and responds to all the major points raised. I now think it is suitable for publication.

May I suggest a few very minor presentational suggestions?

page 15 - bottom line - number should be 0.87
Answer: this is corrected in the new version of the manuscript, now p 16, first para.

page 19 - para 2, line 11 - insert 'the' before UK
Answer: this is corrected in the new version of the manuscript

Table 2 - replace 'Sex' with 'Gender' so is consistent with text. p values in last column should be preceded by '0' to be consistent with rest of table.
Answer: this is corrected in the new version of the manuscript

Figure 1 - use same scale for y axis as is used in Figure 2.
Answer: we re-made the figures according to your comments. We also think that the figures are more comparable and easier to understand after this modification.

We did not notice this inconsistency until Your comment. It is much better this way.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests

REPLY TO REVIEWER 4
Reviewer's report
Title: Predictors of Premature Mortality in Swedish Drug Abusers: A Prospective Longitudinal Study 1970 - 2006
Version: 4 Date: 21 March 2011
Reviewer: Heinrich Kufner
Reviewer's report:
The following comments are referring to the review 4:
The first two major points are not regarded in the discussion chapter or in any other part of the revised paper.

ad 1:
There is no remark that in predicting premature death during such a long time period it seems highly probable that life events and treatment episodes have been occurred which may have a direct or indirect impact on premature death. If the authors think that there is no influence on the prediction they should argue for their position, but not to mention is not a solution. In my view it is a limitation of the study.

ANSWER: We agree completely with your criticism. Several dimensions you mention might be as important as those we were able to include in the analysis. We now comment upon this in the discussion. We do not however, think that more subtle individual life-events data like those you suggest, could be obtained from any Swedish registers we know of and it should be very difficult, probably close to impossible, to get the permission from the ethical committee to approach significant others with questions about the patients. We feel this demands quite another design, maybe better, but not within the scope of this paper.

Please see the new version of the manuscript p. 20 and 21

In response to your criticism we also suggest a somewhat narrower title of the paper.

Ad 2:
In the authors’ answer the type of the discharge of the patients is mentioned. Premature discharge could be a predictor for treatment outcome and for the long term course of addiction. The issue is not to predict the dropping out of treatment, but the effect of dropout on the long term course or on drug related death. Although the study is not conceptualized as a treatment evaluation study, discharge of treatment should be regarded in prediction analysis as a control variable, if there is no clear argument against the possible influence on the dependent variable of drug related death. I think it would be interesting to know
whether dropout of treatment is a predictor or not or is modifying the predictive value of the other predictors.

ANSWER: 2) We now comment upon the lack of treatment related data in the new version of the manuscript. Sorry we missed to do that in our previous reply.

Please see the new version of the manuscript p. 20 and 21

Dropout is a somewhat complicated variable to include in our analysis. About 80% of the patients had two or more treatment episodes and the same patient did not necessarily drop out during (all) following admissions. Dropout is not a stable characteristic like the ones we have used in the prediction analysis. We are well aware of the fact that some individual patients were repetitive dropouts, but it was definitely not the case for all. Patients who dropped out at the first admission, often stayed longer at later admissions and sometimes became more compliant.

As a response to your criticism we analyzed how many patients died in close connection to the discharge from the unit. There were four who dropped out within three months, but non (in this cohort) who died immediately after discharge. We also analyzed the association between dominant substance of abuse and dropout and found none. Given the limited short term influence of dropout, we believe it is unlikely that this is crucial over the 30-year course of risk of dying from an overdose or other substance-related problems. We do not have valid data to make any safe conclusions from the first admission.

Commented, see para, page 10 and page 13 and page 20 and 21.

In order to analyze the impact of dropout data on long-term outcome, we need a design based on data from each single treatment admission at the unit. Also variation in several other treatment-related aspects should be accounted for.

The other points are completed.