Author’s response to reviews

Title: Mortality and repeated poisoning after self-discharge during treatment for acute poisoning by substances of abuse: a prospective observational cohort study

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Author’s response to reviews:

Dear dr Khoshnood and reviewers

Thank you for your valuable comments and for the opportunity to revise our manuscript.

Reviewer 1:

Thank you for the opportunity to review this interesting manuscript. The topic is relevant to a global audience, and is well-done. My suggestions are primarily around making minor clarifications. I think there is an opportunity for the authors to describe how this study contributes to the literature, and is more than just an analysis that confirms the results of prior work.

- We have made changes in the Background and Discussion sections to this effect, as suggested below.

Abstract:

In Results section, a sentence starts with a number (266). Please spell the number if you are starting a sentence with a number.

- The text has been changed, and the number is now spelt.
Background:

This section includes the information that should appear in a background section, however, the authors could do a better job summarizing themes rather than summarizing the results of specific studies. What do ALL of the studies find generally (when considered together)? What are the gaps/limitations? How does this article satisfy the gaps left by previous studies?

- In sum, all the studies taken together point out patients self-discharging during treatment for substance use related poisoning as an at-risk group in an at-risk situation. This specific combination of patients and situation has not been previously outlined. We have revised the Background section as suggested, summarizing themes at the start of each paragraph, delineating the gaps left by previous studies, and clarifying the specific background for our aims.

Methods:

In general there should be better data definitions. How did severe mental illness get defined (specific ICD10s? the physician's opinion?)? I know this is listed as a limitation, but I am unclear of how severe mental illness was actually defined during the study.

- Severe mental illness was defined according to the Norwegian judicial term “severe mental illness”, which is a main criterion in assessments of compulsory admittance to psychiatric hospitals. The term encompasses psychosis, bipolar disorder and severe personality disorders. Though not defined by specific ICD-10 or ICPC-2 codes, it is a clinical concept in regular use in psychiatric, general practice, and emergency medical settings in Norway, with clear implications for patient management. In our study, the doctor treating the patient assessed whether there was a previous history of severe mental illness, based on the information available then and there. We have clarified this in the second paragraph of the Data collection and classification subsection.

What defines multiple presentations (2+, 3+, etc.)?

- We defined multiple presentations as presenting twice or more, which means repeating at least once. We have specified the use of multiple in these contexts throughout the text.

A better description of the enrollment process is necessary.

- Patients were enrolled by the doctor treating them. We have added this in the Inclusion subsection.
The time period to define death is not as clean as it could be. It would be better if there was a standard measure of time-to-death, such as 30-day mortality, or 3-month mortality, rather than just death at anytime during the study period. If a patient was enrolled in 1 Dec 2012 and died 1 Jan 2013, they may be different than a patient who enrolled on 1 Jan 2011 and died 31 Dec 2012. The variable time-to-death allowed by this design could potentially bias the results of the study. I think this is a limitation of the study that should be discussed in the limitations section, or the results should be re-calculated on the basis of a meaningful time-to-death measure (like 90-day mortality).

- We agree that our measure of short-time mortality is not as clean as it could be. We could have used 90-day mortality, but chose to use death within the study period (and hence an observation time varying from three to fifteen months) as this would capture more deaths and thus add power to the Cox regression analysis when looking for associations between self-discharge and death. The variation in observation time is handled by the Cox regression analysis and should not bias the hazard ratios. However, it is likely that some of the patients with repeated poisoning had been presenting frequently for some time already before the start of the inclusion period. Accordingly, repeating patients would possibly tend to present for the first time earlier in the inclusion period than non-repeating patients, hence having longer observation times. As we found self-discharge to be associated with repeated poisoning, self-discharging patients could possibly also tend to have longer observation times. This would overestimate the mortality in the self-discharge group when comparing proportions of dead patients between groups. Then again, as the comparison of the proportions is in the same range as the unadjusted hazard ratio from the univariate Cox regression analysis, we do not think that the varying observation times has any impact on our results. We have elaborated on this in a new paragraph in the Strengths and limitations subsection. If we consider an episode of acute poisoning as a possible crisis reaction, it is a clinical question when we may consider that the patient has returned to a steady state. In general, we consider that this will be a rather short time period, perhaps within 1-2 weeks. We think that most patients have been in a steady state long before 90 days, most likely also before 30 days. So if we should analyze mortality in relation to the crisis, we think that it should be within two weeks. Our sample size is too small for such an analysis.

How is time of discharge defined for patients that elope (leave without telling anyone)?

- Time of discharge for patients leaving without telling anyone is set when they are registered as not present at the clinic anymore. These patients are seen to rather frequently by the nursing staff at the OAEOC, and when a patient is not found, this is marked in the patient logistics part of the electronic medical records. Thus, observation time is systematically overestimated for these patients, but not by much. I would hazard a guess of on average 10-
15 minutes at the most. We have added a paragraph on this issue in the Strengths and limitations subsection.

What is the distribution of the different types of self-discharge (leaving without being seen, elopement, signing AMA, etc.)? How many eloped, etc.?
- Unfortunately, we did not register different subtypes of self-discharge.

Results:
The tables are clean and easy to read. Results section is short an succinct and does not unnecessarily repeat information in tables/figures.

Are the differences observed in Figure 1 statistically significant? Seems like a chi-square could be utilized here.
- The difference in the distribution of time of discharge between the discharge groups was statistically significant, p < 0.001, both on weekdays and on weekends. We have added a statement on this in Figure 1.

Discussion:
I am confused by what is meant in the third line of the discussion section "short-time mortality was twice as high among self-discharging patients...". I don't see anywhere that the authors looked at a specific short vs. long-term mortality for patients (some patients had relatively short-term deaths while others likely had longer-term deaths since a standard time-to-mortality metric was not used).
- We consider all the mortality measured in our study as short-time mortality. To clarify, we have supplied a definition of short-time mortality in the Outcome measures subsection.

The discussion section repeats a lot of what is in the results section without adding new information, so it comes off as a little repetitive. Additionally, the authors state that their results are largely in agreement with prior results... so how is the present study useful in contributing to new information/ thinking? I think more work should be done to differentiate this paper in the content of what has been done already.

Good discussion of WHY people self-discharge.
Should list strengths of analysis-- not just weaknesses. Why did this study add to the literature base? How does this contribute to what is known/ what we should do?

Overall: This is an interesting manuscript with a small but useful research question. There is room for improvement with respect to describing study operations/ data definitions, as well as describing how this study contributes to the current literature base.

- We have revised the Discussion section thoroughly along the lines suggested, avoiding repetitive passages by moving some and deleting some, putting more emphasis on the strengths of the study, and generally trying to make our contribution appear more clearly.

Reviewer 2

I received your paper entitled "Mortality and repeated poisoning after self-discharge during treatment for acute poisoning by substances of abuse: a prospective observational cohort study" as a reviewer.

In this paper, it seems that you tried to find a relation between self-discharge (against medical advice) and mortality in patients poisoned by substances of abuse, resulted in non-significant mortality increase but considerable re-admission.

I read your paper carefully, and in my opinion you done a correct public-able investigation. But I cannot find the "statement of problem" in introduction part that you tried to reply it with this survey! That would be better to explain why you decided to perform this study (introduction) and how it could change or influence on current practice (discussion). In my opinion the paper would be suitable for publication after minor revisions.

- We have revised the Background section trying to clarify our statement of the problem leading to the aims of the study. We have also revised the Discussion section trying to make our contribution to current knowledge appear more clearly.

On behalf of the authors

Yours sincerely

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