Author's response to reviews

Title: A one-year observational study of all hospitalized and fatal acute poisonings in Oslo: Epidemiology, intention and follow-up

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Author's response to reviews: see over
To the Editor of BMC Public Health

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Dear Editor

We would like to thank you for your response to our manuscript, as well as thank the reviewers for their valuable comments.

Reviewer I (Annette Erlangsen):

1. We have now removed some of the data duplications to make the manuscript shorter.

2. The current study was part of a larger multicentre study that included the EMA. However, the current paper only presents data from the hospitalized acute poisonings. The EMA “Legevakten” is an outpatient clinic and is not hospital based. The sentence in the Methods section has been rephrased to: “Poisoned patients are not treated in other clinics (e.g., private) than the EMA and the five hospitals.” Moreover, a sentence under Methods has been rephrased to “As
Akershus University Hospital also treats patients from outside Oslo, the latter patient group was excluded”.

3. TCA and UNODC are now written out the first time they are mentioned, as requested.

4. The EMCDDA and UNODC reported national figures, not regional figures for Oslo. We have now rephrased the sentence to: “This demonstrates that national figures do not always reflect the local clinical reality”.

5. “Strongest predictor” has now been rephrased to “strongest known predictor”, as requested.

6. It would be interesting to compare repetition rates with respect to intention, toxic agents, referral to follow-up, age, gender etc. However, repetition is not an objective in the present study. Assessing the repetition rates would require additional tables and space.

7. “The deaths in and outside hospital were clearly two different populations” has been rephrased to “two distinctively different groups”, as requested.

8. We agree that it would have been preferable to also include younger adolescents (<16 years). However, including this patient group would have been challenging, as we would have needed consent from the patients’ parents. We have added the following phrase to the study limitations: “Adolescents <16 years of age were not included in the present study. This may have limited the evaluation of OTC paracetamol sales, as young adolescents are known to have high rates of attempted suicide, potentially with OTC drugs.”

9. Study period and population has now been specified in the headings of all tables and figures, as requested.

Reviewer II (Anna Jönsson):

Major compulsory revision:

1. Thank you. The sentence under Discussion has been rephrased to: “Double the number of patients (n = 2348) were treated at the EMA in 2008 compared with all Oslo hospitals, making the total incidence of acute poisonings in Oslo higher”. Moreover, the sentence under Methods “As Akershus University Hospital also treats patients from outside Oslo, the latter patient group was excluded” has been deleted, as it probably causes confusion. The EMA (also known as “Legevakten”)
is an outpatient clinic. It is not hospital based and has few diagnostic and treatment options. Moreover, they only have an observation limit of four hours. The main aim of the study was to assess the incidence of hospitalized acute poisonings.

Minor essential revisions:

2. This sentence has been rephrased to: “…and whether a change to over-the-counter sales of paracetamol outside pharmacies had an impact on the frequency of poisonings”.

3. This sentence has been rephrased to: “The number of poisonings caused by paracetamol remained unchanged after the introduction of over-the-counter sales and there were no deaths, so over-the-counter sales may be considered safe.”

4. The inclusion criteria were: “All adults (≥16 years) presenting consecutively with a primary diagnosis of acute poisoning. In cases where poisoning was a secondary diagnosis, the poisoning itself had to warrant admission”. The definition of poisons or toxins is substances that cause damage to the organism when sufficient quantity is absorbed (Wikipedia). In other words, the inclusion criteria were exposure to substances in amounts that may cause damage the organism and warrant hospital admission. This was the treating physicians clinical evaluation. Defining toxic amounts in relation to recommended doses would be problematic, as multiple factors contribute to toxicity (renal failure, enzyme up-regulation, poor metabolizers, drug interaction, frailty etc.). Moreover, defining a toxic dose would be impossible for substances of abuse.

5. Indeed, more than half of the patients were exposed to more than one toxic agent. As written under Methods (page 6): “In cases where patients were exposed to more than one substance, the substance suspected to be present in the most toxic amount was assumed to be the main agent. (…) Substances suspected to be less toxic were registered as co-agents.” As an illustration, 42% of all patients were exposed to ethanol, but in most cases, that was not the main reason they were hospitalized. Therefore, we made the treating physician evaluate which of the toxic substances he considered most toxic in the amount taken. Ethanol was regarded the main agent (and thus the main reason they were hospitalized) only in 18% of the admissions. We think that defining a main agent provides valuable information where patients are exposed to multiple substances in different amounts. The first column in Table 1 provides numbers of total admissions (main+co-agents) where the different toxic agents were present.
6. There was no use of i.e. in the manuscript prior to revision by the academic English proofreading service Online English (www.onlineenglish.com). We have therefore not made any changes now. However, if you still would like this rewritten, we will of course reconsider.

7. This classification was based on more than one source, as in everyday clinical practice. Under Methods, we have now rephrased: “This was based on the treating physician’s clinical evaluation given the available information, such as statements from patients, companions…” to “…clinical evaluation of all available information…”.

8. The phrase: “It was not possible to differentiate between paracetamol bought in and outside pharmacies” has been added to the study limitations.

9. The sentence has been rephrased to: “However, a quarter of patients who repeatedly poisoned themselves during the 2003-study changed their poisoning intention from suicide attempts to unintentional drug-abuse-related overdoses or vice versa, illustrating co-morbidity between substance abuse and suicidal behaviour.”

10. The first sentence under Conclusions has now been rephrased to “The annual incidence of hospitalized acute poisonings was 2.0 per 1000 for both sexes, which was not significantly different from 2003”.

Reviewer III (Kai Knudsen):

Major compulsory revisions:

1. This study shows that opioid abusers are a high-risk patient group. However, we agree that the effects of follow-up have been incompletely studied. The sentence has been rephrased to “…so preventive measures should be encouraged among substance abusers”.

2. The blood ethanol concentration of 54 mmol/L (250 mg/dL) is arbitrary. The blood ethanol concentration generally regarded as lethal (50% of patients with a blood ethanol concentration of 400 mg/dL dies) is obviously too high to use as inclusion criteria. Moreover, the lethal dose of ethanol becomes lower when
combined with other substances and in the old and frail. Although several papers cite lethal concentrations (in the presence of other substances) that are in the same range as the one we have chosen, we have no reference for that exact limit. Also, the chosen limit was easy to remember for physicians participating in patient inclusion.

3. As written under Methods, the intention categories differed slightly from the four used in 2003, i.e., definite or possible suicide attempt, appeal for help, and accident/intoxication. The phrase: “Moreover, the SIS was not used in 2003” has been added under Methods. The categories “definite suicide attempt” and “possible suicide attempt” were exactly the same in both studies. These numbers are given separately in the discussion. However, we agree that combining these two categories in the conclusion may be imprecise. The sentence under Conclusions has therefore been rephrased to: “In total, 46% of the patients had a suicidal intention.”

Minor essential revisions:

4. The sentence has been rephrased to: “The incidence of hospitalized acute poisonings was similar to that in 2003…”

5. The age ranges for each sex is now provided, as requested: “… and the median age was 41 years (range 18–77), i.e., 41 (range 18–77) for males and 50 (range 19–86) for females”.

6. Thank you. This is now rephrased to: “The proportion of patients referred to follow-ups…”

Discretionary revisions:

7. “Including mortality (inside and outside hospitals)” has been changed to “including mortality”, as requested.

8. The sentence has been rephrased to: “All deaths by poisoning in and outside hospitals were registered at the Institute of Forensic Medicine”, as requested.
9. The sentence has been rephrased to: “All adults (≥16 years) presenting with a primary diagnosis of acute poisoning were included consecutively from the five hospitals”, as requested.

10. The sentence has been rephrased to: “OTC paracetamol accounted for 82% of the acute poisonings with paracetamol, but only 58% of the total doses sold in Norway in 2008”, as requested.

11. A comment has been added under Discussion: “As often observed, males had more poisonings with substances of abuse, while females had more poisonings with pharmaceuticals such as paracetamol, neuroleptics and antidepressants. However, females did not have more poisonings with benzodiazepines.”

Sincerely yours,

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