Reviewer’s report

Title: Mortality, cause of death and risk factors in patients with alcohol use disorder alone or poly-substance use disorders: a 19-year prospective cohort study

Version: 0 Date: 04 Jan 2019

Reviewer: Michael Roerecke

Reviewer’s report:

Abstract: There should be more details in the Results section, including confidence limits. Please use past tense. The conclusions should be closer to the results, the statement in the first sentence was not investigated in the study.

The Introduction seems well thought out, however, the cited point estimates for mortality should include confidence intervals.

Most of what is written in the Sample section should be in the Results. The sampling should be described in more detail, I don't think a reference will suffice.

What was the source of the mortality rates of the general population?

In the measurements section, I am unsure if subjects were excluded or not if they did not answer some or all of the measures. Please clarify.

Was age used as a continuous or categorical variable? Please clearly specify all variables and their treatment in the analyses.

On page 8, lines 5-8: Please provide more detail on which disorders were clustered together.

Of 254 patients, 102 died, among those only 20 women. Given this, I am wondering whether the Cox regression models were seriously underpowered. Many interactions were conducted, was this appropriate from a statistical perspective? Please comment or revise.

I am missing a comprehensive Table 1 with the patient characteristics at baseline by total, AUD alone, Poly-disorder. Please provide.

Please provide total N for the current Table 1.

Why are several CMRs and SMRs mentioned in the text, but not shown in Table 2?

Why are some of the HRs in Table 3 negative? Are sometimes HRs and sometimes coefficients reported? This is very confusing. It is further unclear what the reference group and what the units are (for example, No. of psychiatric symptom disorders). Please specify in the Methods section.
Results from the secondary analyses introduced in the Discussion should be moved to the Results section.

Page 15, lines 14-22: Please show that people with opioid disorder did or did not differ from other groups at baseline (this is another reason why a thorough new descriptive Table 1 is needed).

I find the Discussion in general is repeating the results more than it adds to the literature. What clinical implications does the study have? I only find very general statements in the Discussion. Even the Conclusions are mostly a repetition of the results.

It should be more prominently featured that the analyses were only crudely adjusted for other risk factors for death, which is only mentioned in one sentence in the limitations. Please expand and discuss more.

Page 14, line 12: lifetime affective disorder was associated with a decreased…

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Acceptable

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