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

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Reviewer: Abhijit Nadkarni

Reviewer’s report:

Interesting paper examining mortality in a longitudinal cohort of AUD and SUD patients and comparing it between those two groups. Although the paper makes for a good read, it might benefit from some revisions as suggested below:

1) Please do a careful language check. The language is generally good but has some minor errors such as in the abstract 'Being man and...' should have been 'Being male and...'

2) Study design: Was this a prospective or historical/retrospective cohort i.e. was it set up to examine this particular question and then followed up over 19 years or was it set up to answer some other questions and this question is now being answered retrospectively. This needs to be clarified in the methods

3) Some information about the clinical settings and counties needs to be provided for international readers to make judgement about external validity

4) At baseline, were there no other sociodemographics available beside age and gender?

5) Patients with AUD alone tended more often to be men (77% vs 67%, p = 0.055), be older (45.8 vs 32.1 years, p < 0.001), have fewer lifetime psychiatric disorders (3.2 vs 3.9, p = 0.027), and be less likely to have lifetime affective disorders (57% vs 69%, p = 0.047), lifetime anxiety disorders (76% vs 88%, p = 0.010), and current personality disorders (63% vs 80%, p = 0.003) at baseline than patients with poly-SUDs. This appears to be univariate. Could a multivariate analysis be done with ORs as many of these variables will probably be highly correlated.

6) ‘Sampling, subjects and methods at baseline have been described more extensively elsewhere [23, 24]’. Ideally a brief summary might be useful for those who might not want to go back to the original publications.

7) Were there any repeated measurements in the 19 years follow up? Especially important as AUDs/SUDs follow a relapsing remitting course

8) Were any sample size calculations done at baseline? If this was a convenience baseline sample then it would be useful to show post hoc power calculations i.e. what SMR (95% CI) would be detected at 80% and 90% power given the available sample size
Bivariate comparisons showed that the deceased were more often males (80% vs 67%, p = 0.013), older (44.3 vs 35 years, p < 0.001), less likely to have lifetime affective disorder (52% vs 70%, p = 0.003), less likely to have experienced the first onset of an SUD before 18 years of age (35% vs 51%, p = 0.009), and more likely to have had AUD alone versus poly-SUDs (65% vs 34%, p < 0.001) at baseline than living patients'. Why were multivariate analysis not done?

I am unclear about Model 2. Why are outputs for categorical variables like gender and substance use presented as regression coefficients and not HR?

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

Yes

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

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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