Author's response to reviews

Title: The impact of drug use patterns on mortality among polysubstance users in a Canadian setting: a prospective cohort study

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Reviewer 2:
We thank Reviewer 2 for her comprehensive reassessment of our manuscript. We appreciate her careful evaluation of our edits and have addressed her additional concerns as follows.

1. The Reviewer was satisfied with our addition of multiple drug exposures including non-injection heroin, methamphetamines and speedball use. She specifically requested that we also include intranasal cocaine use. Unfortunately, intranasal cocaine use was not assessed in the cohort questionnaire and therefore could not be included in this analysis. To address this suggestion, the following text has been added to the second to last paragraph of the discussion section:

Finally, certain patterns of drug use, such as intranasal cocaine use, are uncommon in this sample and were not measured in our study.

2. As suggested, we have updated the methods section to indicate that non-daily heroin injecting was defined as any report of heroin use in the last six months. Additionally we examined risk associated with non-daily heroin and amphetamine use defined as any report of use in the last six months.

3. As suggested, we addressed our lack of data on the frequency of injecting in the limitations section. It has been updated to read:

For many variables, including alcohol use, we did not have measures that considered refined patterns of use or frequency of use and were often dichotomized into daily versus less than daily use.

4. The Reviewer was concerned about the unmeasured effect of HIV disease on
our outcomes. However, our multivariate analyses were adjusted for a
time-updated measures of participant HIV status. While we have kept the
analysis as is, we would be happy to further reconsider adding a sensitivity
analysis if the Editor feels it is appropriate.

5. As suggested, the following additional text regarding loss to follow up has
been added to the limitations section:

We censored individuals with long durations (>12 months) from behavioural
measurement to death on the date of last behavioural measurement. This may
have resulted in loss of precision regarding our risk factor measurement.

6. As suggested, the discussion has been updated to mention the finding
regarding accidental mortality. The relevant text reads:

Lastly, when the endpoint was restricted to accidental mortality, daily cocaine
injecting did not remain significantly associated with the time to accidental death,
despite a trend towards an association. This may reflect that accidental deaths,
including accidental poisonings, assault and trauma, are not necessarily
predicted by specific drug use patterns. Future research should seek to identify
predictors of accidental mortality among PWID.

7. We agree that it is important to further describe the main cause of death. The
relevant text has been modified to read:

The primary underlying causes of death included accidental poisonings (22.6%)
and HIV disease (18.5%). The remaining 100 classified categories including
assault (2.3%) and lung malignancy (2.4%) are varied and each individually
contributed less than 5%, with most contributing less than 1% to all-cause
mortality.