Reviewer’s report

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

Version: 2 Date: 16 June 2014

Reviewer: Judith Hahn

Reviewer’s report:

This is an interesting study examining mortality using death records among a large prospective cohort of persons who use drugs in Vancouver. The main goal is to examine patterns of drug use that are significant predictors of mortality. The manuscript is nicely written. My main concern is that all the drugs are considered only individually, and only daily use is considered. The title and the introduction lead one to believe that poly-substance use will be addressed but each drug is only considered individually.

Major compulsory revisions/concerns:

1. This paper is severely limited by how the exposures are considered.
   a. Other than crack, only injection is considered. Why not non-injection heroin, meth, or cocaine use? Benzodiazepines?
   b. Also, for heroin, daily use might not be the relevant variable, given that tolerance would be high for daily use while lower tolerance from less frequent use would be a more likely biological cause of overdose. Please provide reasons for only including daily use or provide alternative measures.
   c. Heavy episodic drinking, which is not necessarily reflected in the daily drinking variable, especially in combination with heroin use might also be an important factor but is not represented by the analyses.
   d. There is no attempt to examine poly-substance use. There is too little detail to determine whether data on concurrent use (e.g. speedball or goofball use, or drinking while doing other drugs? Marijuana will using other drugs?) were collected.
   e. Frequency of injecting is mentioned in the discussion. Could this have been analyzed?

2. It is a bit odd that mortality due to HIV disease is included as an outcome; it seems like very different things are being thrown together and it makes the results hard to interpret. The authors should either remove these cases or make a strong case for their inclusion.

3. There is no description of loss to follow up – how much was there? Is there the possibility of differential loss to follow up might bias the results?

4. The conclusions are limited by the analyses conducted whose limitations are noted in the methods comments.
5. Line 230 – a differential risk of mortality between cocaine injectors and crack smokers is mentioned but the data (mortality rates) are not given.

6. There is no mention of the implications of using drug use in the period before the death occurred, rather than right before the death. This is obviously not possible (at least by self-report) for those who died, but it does have important implications regardless and should be treated as a serious limitation.

7. The findings are less convincing given that the analysis restricted to accidental mortality did not yield the same or similar results.

8. The note in the discussion that cocaine injectors inject much more frequently than heroin injectors is salient – and this should be reflected in the analyses (i.e. exploring not only drugs used by frequency of injecting).

Minor essential revisions:
1. The eligibility criteria with respect to drug use are not described.
2. How do the results compare to studies of factors related to non-fatal overdoses? Almost 60% of the deaths are not classified. Do the authors suspect these are poorly classified overdoses? How many were cardiac arrests?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.