Article details: 2013-0002	
Title	Mortality in a large community-based cohort of inner city residents in Vancouver, Canada
Authors	Deans GD, Raffa JD, Lai C and colleagues
Reviewer 1	Robert S. Remis
Institution	Public Health Sciences, University of Toronto, Toronto, Ont.
General comments	This is an interesting analysis of trends in mortality among residents of the Downtown East Side (DTES), an inner-city neighbourhood of Vancouver with many social problems, including widespread drug use. The study provides important new information on trends in mortality from 2003 to 2009 and documents very high compared to those in Vancouver as a whole. My main concern is the representativeness of the population sampled and therefore the interpretation of the results, as follows: 1. The investigators indicate they recruited 2,913 participants from a variety of community-based venues selected according to census tract. Though the types of venues are indicated, the precise methods of recruitment and the criteria used are not. In addition, there is no indication of refusal rates and any bias that this might have produced. I am concerned mostly that this sample may not be representative of the 16,000+ persons living in the DTES. They indicate in the Introduction that 4,700 of residents are injection drug users (active or ever? See Point 2 below) for a rate of about 28%. However, according to the sample characteristics described on Table 1, 38% had injected, suggesting that their sample may not be truly representative. Several other characteristics of the selected sample suggest the unrepresentative nature of their sample. 53% of participants had HCV infection and 18% HIV infection. This seems very high for persons living in this area. HCV and HIV rates in this area are likely high but probably not this high. As a result of this concern (which, incidentally, is not addressed as a limitation in the Discussion), I wonder whether any of the calculations of mortality in the overall sample are valid. The analyses, however, with respect to specific subgroups such as injection drug users or those infected with HIV or HIV are more likely to be probably valid although, even in this case, the investigators should provide evidence of this. It would be interesting to know whether they have any independent data on mortality rates for the DTES that could assure the reader that the rates they observe were in fact representative of the entire DTES. 2. The period of injection drug use is indicated as recent on Page 6, line 42 and less than six months in the footnote on Table 1; I gather these are the same thing. (Incidentally, two different page numbers are printed on each page; I will refer to that indicated as x of 30) It is not stated whether the 4,700 users indicated in the Introduction lifetime or recent. The period of time during which injection drug use is reported should be clearly indicated throughout and be consistent. 3. The mortality rates are expressed in deaths per 10,000. I believe this is unconventional and make their results more difficult to absorb or compare with studies from other areas. I suggest they use percent, per 100 person-years or per 1,000. 4. The authors present numbers and rates of HIV, HCV and HIV-HCV co-infection. It is not clear whether the HIV and HCV data are for these pathogens alone or with or without the other infection. This should be stated early in the manuscript and applied throughout. 5. The Abstract does not indicate the period during which the study was carried out. 6. Page 7, line at 13: I suggest "HCV and HIV testing" rather than all virology testing since the latter may not be the case. 7. Page 7 under Data Collection section: The methods used for the record linkage to the various data sets should be described in greater detail. I gather they used deterministic matching with health care card numbers (for all linkages?) but this should be stated. Also, they should describe any difficulties they experience with regard to linkage. 8. Page 8, line 14: The population for the health service delivery area of Vancouver should be indicated. 9. Page 10, line 6: I am not sure what "external causes" are.

	In summary, this study is informative and important in documenting and updating the high rate of mortality in this very vulnerable population in recent years. The results underline the need for more intensive intervention. It is rather discouraging that, over a period when many interventions were implemented, mortality did not decrease.
Reviewer 2	Richard Reithinger
Institution	London School of Hygiene and Tropical Medicine, London, UK
Author response	***Responses to the editors' and reviewer's comments are in bold.*** Reviewer's Comments to Author: 1. The investigators indicate they recruited 2,913 participants from a variety of community-based venues selected according to census tract. Though the types of venues are indicated, the precise methods of recruitment and the criteria used are not. In addition, there is no indication of refusal rates and any bias that this might have produced. **We have elaborated on relevant details of the recruitment strategy in the Methods section . We have also elaborated on possible sources and implications of participation or selection bias in the Limitations section. Unfortunately, the refusal rate is not available.** I am concerned mostly that this sample may not be representative of the 16,000+ persons living in the DTES. They indicate in the Introduction that 4,700 of residents are injection drug users (active or ever? See Point 2 below) for a rate of about 28%. However, according to the sample characteristics described on Table 1, 38% had injected, suggesting that their sample may not be truly representative. Several other characteristics of the selected sample suggest the unrepresentative nature of their sample. 53% of participants had HCV infection and 18% HIV infection. This seems very high for persons living in this area. HCV and HIV rates in this area are likely high but probably not this high. As a result of this concern (which, incidentally, is not addressed as a limitation in the Discussion), I wonder whether any of the calculations of mortality in the overall sample are valid. The analyses, however, with respect to specific subgroups such as injection drug users or those infected with HIV or HIV are more likely to be probably valid although, even in this case, the investigators should provide evidence of this. It would be interesting to know whether they have any independent data on mortality rates for the DTES that could assure the reader that the rates they observe were in fact representative of the entire DTES. **We appreciate the reviewer's concerns and have clarified in the manuscript that this study did not employ conventional (that is, randomized or stratified) sampling methods because these are not possible when applied to marginalized and difficult-to-reach populations such as those residing in the Downtown Eastside. We have added a reference to a paper by Magnani et al. that discusses this challenge and the alternative approaches required, one of which is the facility-based sampling used in this study. As also discussed now in the Limitations section, these methods may include selection bias inherent in this approach, but in theory – and concrete practice and results of the present study – provide for the most broadly representative sample possible under the circumstances, particularly when compared to other studies conducted in similar settings.** 2. The period of injection drug use is indicated as recent on Page 6, line 42 and less than six months in the footnote on Table 1; I gather these are the same thing. (Incidentally, two different page numbers are printed on each page; I will refer to that indicated as x of 30) It is not stated whether the 4,700 users indicated in the Introduction lifetime or recent. The period of time during which injection drug use is reported should be clearly indicated throughout and be consistent. **We have removed the term "recent" and clarified that these data were collected with regard to the six months prior to survey. The estimate in the introduction refers to lifetime injection drug use; there are few data available to quantify the prevalence of injection drug use in the Downtown Eastside over more specific timeframes and we feel this estimate provides readers with context regarding the neighbourhood.** 3. The mortality rates are expressed in deaths per 10,000. I believe this is unconventional

	and make their results more difficult to absorb or compare with studies from other areas. I suggest they use percent, per 100 person-years or per 1,000. **We disagree with the reviewer that expressing mortality rates per 10,000 person-years is unconventional. We chose to express rates per 10,000 for these results as the mortality rates for some causes of death are relatively low; if rates were expressed per 100 or per 1000 person-years, the lower rates and especially the lower end of the 95% confidence intervals would require leading decimals which would be less readable and would take up more space in tables and text. Rates have been expressed per 10,000 person-years in related publications by members of this author group and other groups (such as Grebely J et al, J Viral Hepatitis 2011;18:32-41; Walter SR et al, J Hepatology 2011;54:879-86; Amin J et al, Lancet 2006; 368:938-45; Friedman SR et al, PLoS ONE 2013;8(2):e57201).** 4. The authors present numbers and rates of HIV, HCV and HIV-HCV co-infection. It is not clear whether the HIV and HCV data are for these pathogens alone or with or without the other infection. This should be stated early in the manuscript and applied throughout. **We have revised the Methods section to clarify that these are mutually exclusive strata (HCV alone, HIV alone, HCV/HIV, neither) and made this consistently stated throughout the paper. We have added these strata to Table 1 to further clarify their composition.** 5. The Abstract does not indicate the period during which the study was carried out. **We have added the recruitment period as well as the timeframe of linked data results to the abstract.** 6. Page 7, line at 13: I suggest "HCV and HIV testing" rather than all virology testing since the latter may not be the case. **We agree with the reviewer that this phrase is clearer and more accurate, and have made this change.** 7. Page 7 under Data Collection section: The methods used for the record linkage to the various data sets should be described in greater detail. I gather they used deterministic matching with health care card numbers (for all linkages?) but this should be stated. Also, they should describe any difficulties they experience with regard to linkage. **We have revised the Methods section to clarify that record linkage used provincial health number and, for those with no match, name and date of birth. We have added a reference to a document that provides further detail on the proportion of CHASE participants that were linked to various data sets.** 8. Page 8, line 14: The population for the health service delivery area of Vancouver should be indicated. *Added.* 9. Page 10, line 6: I am not sure what "external causes" are. **We have clarified in the identified section that the ICD-10 chapter known as "external causes" includes accidents, assault, and intentional self-harm.**