Reviewer's report

Title: Gender disparities in the survival of HIV-positive drug users admitted to an opioid substitution therapy program in Spain: a cohort study.

Version: 1  Date: 16 April 2014

Reviewer: Catherine Todd

Reviewer's report:

Major Compulsory Revisions

Abstract/Summary:
• The purpose statement does not mention anything about gender difference but the title of the manuscript indicates that this is the focus of the paper. Please revise one or the other.

      • Were death rates significantly different between men and women? Wouldn’t it make more sense to state that directly and then comment on whether key predictors were similar or different by gender? The way the Results are currently presented does not support the manuscript’s title.

      • The conclusion statement does not indicate why mortality among women increased. Please revise the Results section to provide this evidence and then revise the Conclusions statement.

Introduction:
• The first sentence of the last paragraph states that the paper aims to assess differences in survival between injectors and non-injectors. If this is the outcome of interest, why is it not mentioned in the title or abstract? If not, this sentence should be revised to reflect an analysis constrained to IDUs with the outcome of interest being differences in mortality between men and women.

• The description of the calendar periods based on temporal events should be placed in a Measures section of the Methods. The key events that determine the divisions can be mentioned in a sentence or two in the Introduction. This paragraph should instead end with the anticipated value or use of the results for OST/SIF programs in Spain.

Methods:
• While the statement that the study is compliant with the Declaration of Helsinki is appreciated, there needs to be a statement confirming review and approval of this study prior to data collection by an ethical review board. Even though data were collected by chart review, ethical board review is still required, even if they determine the study to exempt from review.

Results:
• The first three paragraphs could be made more concise with this data
incorporated into Table 1 and with columns reporting, for each characteristic, the overall statistic, then specific statistics for men and for women.

- It is only first clear in this section that both injecting and non-injecting users are included in the analysis. The Methods section needs to include a statement to this effect and a rationale for including both groups, given their very different mortality risks.

- History of overdose is not reported in the Results yet seems a probable predictor of mortality. Please add this descriptor or provide explanation in the Methods why this is not possible (may not be available in the MTP charts).

- Line 169: What is an “antecedent of imprisonment”? Does this mean previously incarcerated or were referred to the program directly from prison? Please use a different term for this characteristic, such as prior incarceration.

- Lines 256-264: The paragraph states that female IDUs are at greater risk for not accessing harm reduction, yet this study includes only those patients of MTPs. There was no data presented regarding OST adherence in the results but we must assume that these patients were adherent to have the follow-up data. The authors need to comment on the potential bias in this population. Further, stigma against female IDU is not a new concept – has something happened more acutely to result in the recent upswing in mortality among HIV-infected female IDUs? Is there anything that would contribute to them not getting ART on a regular basis? Possibly incarceration? How many are sex workers and would this increase their risk of arrest and inability to adhere to ART?

Discussion:

- The statement “In addition, a percentage of the mortality is due to gender-specific clinical conditions, such as cervical cancer” has no data to support it from the Results section. Further, this paragraph leads to more questions than it answers. There needs to be corresponding data in the Results about the CD4 count at ART initiation and presence of HIV RNA for male patients to provide an adequate comparison. Also, there is no mention of methadone adherence in HIV deaths for either male or female patients in the Results section. This is an important issue as combined OST-ART therapy models have been successfully tested and improve adherence of both medications as well as adjust methadone doses to remain effective in the presence of ART.

- The second-to-last paragraph does not mention the focus on gender-based differences and there is also no mention of improving mental health service access within MTPs as a recommendation. The manuscript would benefit from closer attention to the analysis purpose in the communicated messages.

- It was surprising that injecting drug use was not independently associated with mortality and is worthy of comment in the Discussion.

- The limitation of not analyzing methadone dose change or interruption over time should be mentioned earlier in the Discussion as this is likely contributing to some of the mortality ascribed to other causes, particularly for HIV-infected patients.
Minor Essential Revisions:

Abstract/Summary:
- The title refers to heroin “users” while the abstract mentions “abusers”. It would be best to use the same term consistently and user is more neutral.
- The meaning of calendar periods is not clear – please define these in the Methods.
- The nomenclature for mortality rates is not standard: it should be the number of deaths/100 p-y, not x100 p-y.

Introduction:
- Line 67: Please spell out U.S. the first time it is used.

Methods:
- Line 109: Should this be “>18 years old”? Also, were these entry criteria for MTPs overall or inclusion criteria for this analysis? Please specify.
- Lines 147 and 148: The terms quantitative and qualitative variables are not standard. Do the authors mean continuous and dichotomous or categorical variables? Please revise.

Results:
- Lines 199, 203-204: The multivariate analysis results are stated in Table 3 and do not need to be repeated in the text.
- The paragraph on mortality trends should indicate whether the rates stated as declining over time describe the population overall or are just for male patients.
- Line 224: IDU is an injecting drug user. Please do not use it as a verb.
- Same comment as in the Abstract for nomenclature for person-years.

Discussion:
- The first paragraph is already communicated in the Introduction; please remove it from the Discussion.

Discretionary Revisions

Some members of the harm reduction community oppose the term “addiction” and instead prefer “drug dependence” or “problem drug use”. The authors may want to consider revising their terminology.
- The information from citation 38 does not appear to support the data in this study – please consider whether it should be included or a better way of phrasing whether the results of this analysis wholly mirror those of other studies or if other studies have mixed results to date.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

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