Author's response to reviews

Title: Sex-specific disease outcomes of HIV-positive and HIV-negative drug users admitted to an opioid substitution therapy program in Spain: a cohort study.

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Version: 3
Date: 16 July 2014

Author's response to reviews: see over
Dear Editor,

We are submitting the revised version of the manuscript entitled “Sex-specific disease outcomes of HIV-positive and HIV-negative drug users admitted to an opioid substitution therapy program in Spain: a cohort study.” to be considered for publication in your journal.

We appreciate the opportunity to revise and resubmit and we believe that all the reviewers and editor comments have been addressed.

Looking forward to hearing from you.

Sincerely,

Roberto Muga, MD, MPH
Reviewer's report
Title:
Sex-specific disease outcomes of HIV-positive and HIV-negative drug users admitted to an opioid substitution therapy program in Spain: a cohort study.

Version: 2

Date:
2 July 2014

Reviewer:
Sarah Larney

Reviewer's report:
The authors have completed a thorough revision, taking into account the peer reviews. A few minor points remain:

Methods: It was still a bit unclear to me that the mobile unit and pharmacies are dispensing services under the same MTP. Perhaps says something like “Within the program, methadone is dispensed via a primary care center, a mobile unit and five community pharmacies”.

According to the reviewer’s concern, we have added the recommended sentence and the new sentence now reads (Methods section, first paragraph, last sentence): “… Within the program, methadone is dispensed via a primary care center, a mobile unit since 1993 and five community pharmacies since 1999….”

Results: It might be helpful to note in the first paragraph the proportion of participants not injecting, as it is not clear at first that there are some participants who do not inject.

According to the reviewer we added this information in first paragraph of Results section.
“…The study included 1,678 patients (82.8% men). The median age of first heroin use was 18.6 years (IQR: 16-23 years), median age at MTP admission was 30.7 years (IQR: 26-36 years) and 23.8% of patients were non-IDUs.”

Under ‘follow-up and outcomes’ “…14 deaths occurred during the first month of treatment” – it would be more accurate to say “14 deaths occurred within one month of first entry to treatment” as we don’t know for certain if people were still in treatment when they died.

We reworded the sentence according to the reviewer. Please see 4th paragraph, second sentence of Results section:
 “…At the end of follow up, 441 (26.3%) patients had died and 14 (3.2%) of deaths occurred within one month of first entry to treatment…”
Table 3: The authors have clarified their modelling strategy. What is still unclear is why the multivariate hazard ratio for HIV infection in men differs from the univariate hazard ratio, given that HIV infection is the only variable in the ‘multivariate’ model. Please explain this.

As explained in the Methods section the covariates used for the multivariate analysis were those that were found to be statistically significant in the univariate analysis; then, a stepwise forward selection of covariates was used to identify predictors.

The Hazard Ratio for HIV infection in univariate analysis differs from the multivariate due to the fact that in multivariate Cox models mortality is adjusted by HIV infection AND all other statistically significant covariates from the univariate model (age, period of admission, injection drug use, HCV infection and HBV infection), all these non-significant covariates in multivariate analysis are not shown in Table.

Figure 1 needs a title.

Please note that title of Figure 1 is in a separate sheet according to Journal directions.

This title reads as follows:
Sex-specific mortality rates according to four calendar periods and HIV status among patients admitted to a Methadone Treatment Program in metropolitan Barcelona, Spain, 1992-2010.

Discussion, paragraph 7: It is important to clarify that you are referring to a decline in the number of FIRST TIME admissions to treatment.

We added this specification, and the sentence in 7th paragraph of Discussion section reads as follows:
“...Another finding of this study is the decline in the number of first time admissions to methadone treatment….”

Another limitation is that it was not possible to include information on incident HIV/HCV infections (at least I don’t think it was done?)

According to the reviewer we added the limitation and 8th paragraph, last sentence of Discussion section reads as follows:
“...Third, this study did not analyze neither changes over time regarding methadone dose and treatment interruptions nor changes in HIV and HCV serostatus; in this sense, methadone dose, treatment interruptions and blood-borne infections have been associated with disease outcomes [33, 40]….”

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

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