Author's response to reviews

Title: Chlamydia trachomatis, Neisseria gonorrhoeae and syphilis among men who have sex with men in Brazil

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Version: 2
Date: 7 May 2015

Author's response to reviews: see over
Manuscript nº 1241572051157835

Title: Chlamydia trachomatis, Neisseria gonorrhoeae and syphilis among men who have sex with men in Brazil

Submission date: 7 May 2015

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Dear Editor,

Thanks very much for sending us the reviews on our manuscript. We found the reviewer’s comments very useful and constructive.

We responded to all comments and did all the solicited modifications and adjustments. Our responses are below, in bold blue.

We hope the revised version of our manuscript to fulfill the expectations.

Sincerely,

Beatriz Grinsztejn

Reviewer's report

Title: Chlamydia trachomatis, Neisseria gonorrhoeae and syphilis among men who have sex with men in Brazil

Version: 1

Reviewer #1: King Holmes
Date: 2 March 2015

Reviewer's report:
This study by Cunha et al documents a high prevalence of anorectal gonorrhea and chlamydial infection, and a high prevalence of syphilis seropositivity in a convenience sample of MSM in Rio de Janeiro, Brazil. Prevalence of any of the STIs was 16.4% in HIV+ MSM and 3.67% in HIV- MSM. Infection was unrelated to anorectal symptoms. Urethral infection was infrequent. Lab Methodology was excellent.

The message of the potential value of screening the population for anorectal GC and CT, and for syphilis is valid and important.

1 - Minor essential revisions: The manuscript could be more clearly written, in fewer words – perhaps as a brief report (I found myself compulsively making revisions throughout, to make the writing explicit and coherent). Perhaps Dr Gaydos could help with the rewrite.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published.

The manuscript was thoroughly reviewed by a native English speaker and language corrections were performed.

Statistical review: No, the manuscript does not need to be seen by a statistician.

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

Reviewer #2: Birgit van Benthem

Title: Chlamydia trachomatis, Neisseria gonorrhoeae and syphilis among men who have sex with men in Brazil
Reviewer's report:

Major compulsory revisions

Methods:

1- It is not clear from the methods section how the MSM were recruited into the cohort study. Please give information on inclusion and exclusion criteria of the original cohort study or refer to a paper that explains it. There were much more HIV-positive men than HIV-negative men included into the study. Can this be explained by the inclusion or exclusion criteria or the way study participants were recruited?

We added in the manuscript clarification language about recruitment, inclusion and exclusion criteria for parent study, and also referred to another manuscript previously published with data from the same cohort (http://www.ncbi.nlm.nih.gov/pubmed/24742202).

Results:

2- In general it should be clear from the table titles alone that study participants are MSM participating in a cohort study in Rio, Brazil. Titles are too general now.

Table titles were thoroughly reviewed according to the reviewer suggestion.

3- Table 1. Row percentages for HIV-negatives and positives are derived by using total number of study participants, but percentages should be calculated by using the number of HIV positives and number of HIV negatives respectively.

Thank you for the valuable comment. The overall prevalence of each STD was obtained for participants for whom results were available. Thus, percentages in the first line of table 1 are correct and we agree they were derived by using the total number of study participants for whom results were available (numbers in the top of the columns).
Percentages for each individual STDs for MSM according to HIV status were double checked and are correct.

An error was detected in the overall prevalence of “having at least one STD” according to HIV serostatus. We corrected this result in the table and in the manuscript. Thanks again to the reviewer for pointing this out.

4- Line 145. Numbers are incorrect (n=31 and n=6) since they do not add up to 55. Please provide the number of the group that had 3 or more STD.

Thanks for the comment. We checked the data and corrected the numbers provided in the manuscript. Please, see the output below.

<table>
<thead>
<tr>
<th>ndst</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valid 0</td>
<td>237</td>
<td>81.2</td>
<td>81.2</td>
<td>81.2</td>
</tr>
<tr>
<td>1</td>
<td>43</td>
<td>14.7</td>
<td>14.7</td>
<td>95.9</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>4.1</td>
<td>4.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>292</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

5- Information on HIV status, i.e. time since diagnosis, % on treatment is only mentioned in the text. I would provide this important information also in a table.

We added this information in Table 3.

6- Line 160. Total number of HIV positive men with at least one STD mentioned here is 42, whereas in table 1 it is 45.

Thank you for your comment. Among HIV-infected MSM, 45 presented at least one STD. HIV viral load results were available for 42 of them. Line 160 describes the percentage of HIV+ MSM with at least one STD among those who had a detectable HIV viral load (n=19/42). We edited the sentence for clarity.
7- Only 3 lines in the results section were devoted to the multivariable analyses (Table 3). It would be interesting to know if factor for having an STD are different for HIV positive and HIV negative men (did the authors check for interaction?).

Repeating the analyses without HIV status included would be informative as well because than you get more insights into the possible effects of recent behavior. Please change discussions according to these results.

Thank you for your comment. We performed the analysis based on the hypothesis that behavior risk factors associated to others STDs do not differ between HIV positive and HIV negative individuals. Therefore, we did not consider that behavior factors associated with prevalent STDs would be different according to HIV serostatus.

Our main outcome was having at least one of the following STD: rectal and urethral CT and NG and syphilis. We did not check for interaction between *HIV serostatus* and behavior covariates as we do not think that having or not HIV might enhance the role of behavior factors on the main outcome. We do not think we can get more insights into the possible effects of risk behaviors on the main outcome, e.g., STD diagnosis, excluding the *HIV status* from the analysis, once HIV infection and its correlates (CD4, HIV-related illnesses, HIV viral load, etc.) may impact the sexual behavior, and thus the main outcome. For example, HIV-related illness may turn sexual activity less frequent, therefore reducing the risk for other STDs. Unprotected receptive anal intercourse may be more frequent when the HIV viral load is perceived to be undetectable. Thus, HIV viral load may also impact unprotected sexual activity and consequently, the risk for others STD.

**Discussion:**

8- It would be important for the reader to know the HIV situation among MSM in Rio. How many MSM are on treatment, know their HIV status etc. This information would give an idea of how representative the study population is for the MSM population in Rio. Is this information available?
There is no data available about how many MSM in Rio de Janeiro are aware of their HIV serostatus or are under treatment. According to the largest epidemiological study conducted among MSM in Brazil, HIV prevalence among MSM in Rio is around 14%. Roughly 50% of those diagnosed as HIV positive in this study were unaware of their HIV serostatus (Kerr et al AIDS 2013).

The Brazilian AIDS epidemic is an urban epidemic, and Rio de Janeiro is one of the major epicenters of the HIV epidemic in Brazil. Our clinic is the largest HIV/AIDS clinic in Rio de Janeiro, currently providing care for roughly 3500 individuals. We understand that our results are broadly generalizable to urban HIV-infected patients in Brazil.

9- Line 210. Change % according new % to be calculated for table 1.

We corrected the %. Thanks.

Minor essential revisions

Methods:
10- The original study is a cohort study, where study participants are followed-up normally based on regular visits. For the cross-sectional study only the inclusion visit was used?

Yes, this was a cross-sectional study nested within a cohort study underway at the Evandro Chagas National Institute of Infectious Diseases (INI/FIOCRUZ), Rio de Janeiro, Brazil. For the present analysis we only used data from the cohort enrollment visit. We included language clarifying in the manuscript.

11- Please explain if study participants new their HIV-status before or was this the first time they were tested for HIV. If not, it would be relevant to know how long they know their HIV-status and for those HIV-negative when was the last time they were tested?
For the HIV-positive MSM, the median time between HIV diagnosis and enrollment in the study was 75.8 (41.2-162.4) months (line 172 and Table3)".

HIV-negative participants were tested at study entry and also at every follow-up visit to confirm their HIV status. We clarified this in the manuscript.

12- In the sexual behavior questions distinction is made between HIV-positive and HIV-negative partners. For HIV negative partners did you use a time-interval for HIV testing?

No, we did not use a time-interval for HIV-testing, but the participants information. We added a study definition for partner(s) HIV serostatus in the manuscript.

13- The use of alcohol is asked via a question if the study participant was drunk before having sex. It might be that alcohol was used, but the study participant did not consider himself as drunk. When asking alcohol usage in such a way, you get underreporting of alcohol use.

We agree with reviewer that there is some limitation in assessing alcohol use as we did. Other studies, such as the following, also used such assessment:


We wanted to assess the impact of heavy alcohol use (defined here as being drunk) on sexual behavior, and we may have underestimating the impact of lower alcohol
exposure on sexual behavior. We have included a sentence acknowledging this limitation in the discussion.

**Discussion:**

14- Since anorectal CT is common it would be interesting to know if samples were tested for LGV and how patients were treated.

We do agree with the reviewer it would have been very interesting to test for LGV, but unfortunately we did not have enough funds to perform such testing. Participants with anorectal CT infection were treated with Azithromycin 1 G.

15- Line 205-206. The authors underline the need for STD screening in MSM. Would it be all MSM or especially HIV positive MSM?

STD screening should be offered to all MSM, regardless of HIV serostatus, as already implemented in some countries. We corrected this sentence in the manuscript and added a reference for this recommendation from CDC and STIGMA (STIs in Gay Men Action Group. Sexually transmitted infection testing guidelines for men who have sex with men. 2010).

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

**Quality of written English:** Needs some language corrections before being published.

The manuscript was reviewed by a native person and language corrections were performed.

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

We reviewed all comments and corrected and clarified the issues indicated by the reviewer, improving the quality of the manuscript. And also addressed the comments in this reviewer letter.
Declaration of competing interests:
'I declare that I have no competing interests

Reviewer: Suneeta Soni

Title: Chlamydia trachomatis, Neisseria gonorrhoeae and syphilis among men who have sex with men in Brazil

Version: 1

Date: 8 March 2015

Reviewer's report:
This is a well written paper highlighting the high burden of STDs among young MSM, particularly those who are HIV infected, in Brazil. The findings of the study are striking and, although not novel, they are worthy of publication to add to any existing data on MSM in Brazil.

Major Compulsory Revisions
1. Did the authors use a different confirmatory assay for GC detection?

No, we used the same Nucleic acid amplification tests (NAATs) on the rectal swabs for CT and NG, e.g., APTIMA Combo 2 assay (Gen-Probe/Hologic San Diego, CA) and for urine samples we used the Abbott RealTime NG/CT Amplification Reagent Kit. We added a clarification in the manuscript.

2. The results section is a bit confusing, I'm not sure it follows well. Under the STD prevalence heading there is no detail about the actual STD prevalence seen, these are only depicted in the table. Yet the rest of the results section is extremely wordy and much of it can be cut out as it is does not necessarily add to the findings (eg line 183-185) and/or already depicted in tables.
We included more descriptive results on STD prevalence in the manuscript, and also moved and cut some pieces of the results section to make it flow better.

3. Furthermore the paragraph (lines 149-161) describing the HIV cohort seems out of place under the STD prevalence heading - there is nothing about STD prevalence apart from at the end of the paragraph. It is more about sexual behavior and describing HIV parameters. The paragraph following this then goes back to describing characteristics of those who had one or more STD.

Thanks for your comment. We do agree that the text was not flowing well. As mentioned above, we edited the text and cut some pieces to make it short.

4. Under heading STD symptoms - did any MSM with syphilis present with ulcers?

Yes, 13% of MSM with syphilis presented rectal or genital ulcers.

5. The paper refers to anorectal NG/CT often but neglects to say much about syphilis in the discussion even though syphilis prevalence was as high as rectal CT and the presence of syphilis plays a huge role in the transmission of HIV.

Thanks for this comment and we agree with reviewer. We included syphilis in the discussion section.

Minor Essential Revisions

1. Line 179 and 182 say the same thing.

We edited the manuscript and removed Line 182 for clarity.

Discretionary revisions

1. Line 237 - could number of sexual partners be under-reported?

We do not believe the numbers are under-reported, as we used CASI for collect data on sexual behavior. However, we cannot rule out this possibility. Although we have used
CASI to collect sexual behavior data, we cannot exclude social desirability bias. We added this comment in the manuscript as one possible reason for the higher STD prevalence found among HIV+ MSM, despite their lower risk sexual behavior compared to HIV-negative MSM.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

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