Author's response to reviews

Title: HIV, STI prevalence and risk behaviours among women selling sex in Lahore, Pakistan

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Author's response to reviews: see over
Dear Ladies and Gentlemen

Reference to MS: 1195613815442841 and manuscript entitled “HIV, STI prevalence and risk behaviours among women selling sex in Lahore, Pakistan” by Mohsin S Khan, Magnus Unemo, Shakila Zaman and Cecilia S Lundborg, we are pleased to resubmit the manuscript which is based on the valued contribution and comments of the reviewers. Please find below the comments and the changes to the effect.

Reviewer No. 1

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<th>S. No</th>
<th>Comments of Reviewer No. 1</th>
<th>Response</th>
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<td></td>
<td><strong>Major compulsory revisions</strong></td>
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</table>
|       | A. The 2004 study reported in the introductions seems to have answered the research question proposed in this study, so it is not clear to me what the specific contribution is expected for this study. If HIV and STIs prevalences were already know (even for the same STIs as those measured in this study) as well as behavioural data, why this study is needed? What would add to the knowledge on sex work in Lahore in particular and Pakistan in general? Is there any specific change between 2004 and 2007 (when data for this study was collected) that could affect the observed levels of HIH, STIs and/or behaviours? It seems to me that addressing this issue is very important in order to analyze the relevance of this study. | The 2004 study was the first study to address HIV, STIs and Behaviours of most-at-risk populations. The 2004 study was conducted in one part of Lahore city where the Female Sex Workers have been selling sex. National and provincial AIDS control programs, initiated provision of services for FSWs in three other areas identified through mapping. This is highlighted under Introduction, on page 4, paragraph 2, line 16-20 as following

*Ministry of Health, Government of Pakistan, through the National and Provincial AIDS Control Program introduced preventive interventions among most-at-risk populations in various urban settings in 2005 through public private partnerships. These interventions were focused on provision of curative and preventive services including syndromic management of STIs, provision of condoms, and behaviour change communication.* |

This was followed by initiation of 2nd generation HIV surveillance. But the 2<sup>nd</sup> generation HIV surveillance, that was confined to measure the trends of HIV and related risky behaviours only and that also solely in one part of Lahore. No other study was conducted from 2004 to 2007 in Lahore to determine the prevalence of STIs and associated risky behaviours. This is highlighted as yellow under introduction, on page 4, paragraph 2, line number 21-23 as following.

*However, after 2004, studies among women selling sex have focused mainly on measuring only the HIV prevalence and its related risk behaviours and did not measure the prevalence of STIs to follow a trend (www.nACP.gov.pk).*

The specific changes, as evident from the results and discussion, that our study have been able to document are trend of HIV and STIs and related risky behaviours and a decline in the prevalence of STIs in Lahore among FSWs, in three other areas of Lahore.

My impression is that the introduction is insufficient to contextualize the problem the paper is addressing. More details on what is particular to the country in terms of sex work and how that is different or similar in the study region. It is not clear to me what is the motivation for this study, why in Lahore, what could be learn from it.

The study is part of a larger research project among women selling sex in Lahore, Pakistan. An earlier qualitative study has addressed the issues of sex work in Lahore and its history (please see reference number 7). This has been described on under introduction, page 5, line 2-10 as

*Briefly, the Mughal Dynasty, which ruled most of India, Pakistan, Bangladesh, and Afghanistan for over 4 centuries patronized artists, singers, and dancers by establishing settlements near the palaces where they lived. In these areas music, singing, dancing, and selling sex went on side by side. The social context of the selling was distinctive as nobles sent their sons to these women to be trained for social get together and*
<table>
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<th>C.</th>
<th>In terms of the sampling, sample size calculation seems to be based on a simple random selection; that is, there is no adjustment for clustering. I am not sure how RDS deals with clustering, but at least it is clear for the description that 3 areas where selected, so it is not a simple random sampling, and I would also assume that some adjustment is needed because only seed were randomly selected. More details on these issues are important to assess the sample.</th>
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| | RDS lends statistical rigor to conventional snowball sampling through longer recruitment chains, recruitment limits, and the collection of data used to statistically adjust for the biases inherent in how persons of similar characteristics are networked and likely to recruit each other.

RDS is not a simple random sampling based on a sampling framework. RDS works on networks of participants and with each wave of recruitment adjusts for inclusion probability.

Please refer to page 6, line 4-7, (as well as the references we have included), which is described as

RDS also statistically adjusts for the biases inherent in how individuals of similar characteristics are networked and likely to know and recruit each other. Furthermore, RDS works on networks of participants and with each wave of recruitment adjusts for

learn classical music, poetry, good wine, and beautiful women Over the period of time the profession of selling sex was passed on by these women to their daughters.

The current study was instrumental to raise issues like quantifying a prevalence of HIV / STIs, we found a new trend of married women selling sex, etc.. This has also been documented on Page 12, line 7-10 as

Among the 730 women selling sex in Lahore, of which 91% were married, 0.7% were infected with HIV and additionally 18.5% were suffering from different curable STIs. Most worrying was that only 19% and 83% of the participants were aware of HIV and AIDS, respectively, and 37% had the correct knowledge about transmission and prevention of AIDS.
D. The sampling assumed a response rate of 100% for both questionnaire and biological samples. While I understand that these assumption are set according to country / region specificities, in my experience I have not seen surveys where all selected participants consented to answer the questionnaire and provided samples that are also all sufficient and adequate for testing. I would think that is a very strong assumption to start with. I think it is important to explain this further so the reader is able to understand these assumptions. With each wave the recruiter was advised to bring in three recruitees who would have known that an interview would be conducted and biological samples would be taken. Therefore each participant when she came to the clinic to be included as part of the study was aware of the processes.

E. The values reported in table 3 (with the associations) may not be correct. If numbers of cases in column 4 are correct, then percentages are not. This is very important because the real percentages derived from the cases would make the ORs not consistent. For example, for condom use and gonorrhea, there is 27 and 28 cases in each category of condom use (a difference of just one case), but a OR of 2. In the following table, I calculated the percentage that the reported number of cases would represent if total size if 730

<table>
<thead>
<tr>
<th>n</th>
<th>% of total is 730</th>
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<tbody>
<tr>
<td>20</td>
<td>2.74%</td>
</tr>
<tr>
<td>36</td>
<td>4.93%</td>
</tr>
<tr>
<td>26</td>
<td>3.56%</td>
</tr>
<tr>
<td>30</td>
<td>4.11%</td>
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<tr>
<td>24</td>
<td>3.29%</td>
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<tr>
<td>32</td>
<td>4.38%</td>
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<tr>
<td>26</td>
<td>3.56%</td>
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<tr>
<td>29</td>
<td>3.97%</td>
</tr>
<tr>
<td>27</td>
<td>3.70%</td>
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</table>

The denominator in table 2 is not 730.

The denominators in table 2 are not 730.

In Table 2, while analyzing the Chlamydia trachomatis, for areas A and C the denominator is 486 and for area B, it is 241 (please see the distribution in table 1 and 2). Also for the clients 1-3 the denominator is 484 and for clients 4-12 it is 246. Likewise the denominator for always condom use is 471 and not always condom use is 259.

For Neisseria gonorrhoeae, the denominator for clients 1-3 is 484 and for clients 4-12 it is 246. Likewise the denominator for always condom use is 471 and not always condom use is 259.

For Trichomonas vaginalis the denominators for areas A and C the denominator is 486 and for area B, it is 241.

Henceforth we humbly pledge that the numerators and their related percentages presented in table 2 are correct.
Minor essential revisions

i) While it is mentioned in the methods, it is not clear to me which table is reporting the multivariate logistic regressions. If it is table 3, it is important to have a foot-note explaining which variables were used as control variables for each regression and also explaining why only STIs are reported as outcome variables.

There is no table that reports the multivariate logistic regression. The variables used in multivariate logistic regression have already been presented on page 4 under the data analysis section, line 4, which reads as “Multivariate logistic regression analysis was employed to indicate influencing factors on HIV/STI prevalence. These included age, education, marital status, religion, place of work, condom use, duration of selling sex, number of sexual partners per day, injecting drug use and blood transfusion. Though we were interested to look at both HIV and STIs, the number of HIV positives was too less to establish any statistically significant relationship. Hence we went on to look at STIs. Page 11, 2nd last paragraph

ii) The discussion start with the following sentence: “Among the 730 married women selling sex in....” According to the data, 730 is the total sample, not just the married.

Thank you for noticing, adequate changes have been made on page 12, line as Among the 730 women selling sex in Lahore, of which 91% were married.

Reviewer No. 2

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<th>S. No</th>
<th>Comments of Reviewer No. 2</th>
<th>Response</th>
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<tr>
<td>1)</td>
<td>Novelty. There have been several other studies with similar findings (Hawkes et al, STI, 2009; Bokhari et al, In J STD AIDS, 2007) so the innovation present in this study needs to be more clearly explained.</td>
<td>This is now further clarified on page 15, line 11-15 as Furthermore, our study had a higher number of participants (almost double) as compared to other studies conducted in Pakistan, as reported by Hawkes and Bokhari [14-15]. Finally, our study</td>
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documented a decline in STI prevalence, which could be attributed to prevention interventions placed by the Provincial AIDS Control Program of Punjab, Pakistan.

2) Benefit to STI/HIV prevention. Other studies have shown high prevalence of STI among sex workers in Pakistan, so exactly how the present study advances our knowledge of STI/HIV prevention should be clearly presented.

Discussed above, and adequate inclusions have been done in the discussion section of the manuscript!

**SPECIFIC COMMENTS: Minor revisions**

**Introduction:**

1) Prior literature. Better to provide URL link to 2004 study.

Revised as suggested.

2) Introduction to STI services. A more clear description of existing STI services would be important in the introduction.

As explained in the text of the manuscript, the study is part of a larger research project whose goal was to ascertain the health sector’s preparedness for the HIV/STI epidemic in Lahore, Pakistan.

**Materials and Methods:**

1) Survey reliability. The authors mention that their survey was developed in English and pretested, but were the items formally validated?

The questionnaire, which was based on an earlier qualitative research, was developed in English and translated into Urdu and thereafter pre-tested. During the pre testing the responses in Urdu
were compared with the English questionnaires. The questions were revised both in English and Urdu, for language, continuation and sensitivity and pretested again. Please see page 7, line 1-4

<table>
<thead>
<tr>
<th>2)</th>
<th>Syphilis operational definition. Did this include all RPR titres or use a cutoff? This should be more clearly explained.</th>
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<td></td>
<td>We only used RPR as a qualitative test to <strong>screen</strong> for the presence of non-treponemal antibodies, and we performed the assay in full accordance with the instructions of the manufacturer (which has been added in the manuscript). Accordingly, undiluted sera were tested in order to find samples that needed to be tested for treponemal antibodies using TPHA, and we did not measure RPR titres. This is the routine diagnostic algorithm at the laboratory where these assays were run, as well as in many other laboratories, with exception of several laboratories in developed, industrialised countries with a very low syphilis incidence. In these laboratories, automated, expensive systems such as Architect for detection of treponemal antibodies are instead used also for initial screening, which is possible due to the low syphilis prevalence. However, of course they use all quantitative RPR to follow progression of infection, and to effect of treatment.</td>
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**Results:**

1) The content of table could be rearranged. I will suggest table 1 only include demographic data, table 2 include risk factors and STI HIV prevalence, thus all the data for statistical analysis will in the same table.

Table1 and 2 have been merged.

**Discussion:**

1) Area B prevalence. The result show the Area B had the highest prevalence of HIV/STI. What may explain this difference in regional STI/HIV prevalence?

*Explained on page 13, 3rd paragraph, line 14-16*

_In area B, where the women selling sex were Kothikhana based, the always condom use was the lowest and the number of clients was the highest._
<table>
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<th>2) 2004 comparison. The present study results differ from the results in the same area in year 2004, the authors should discuss the disparities between the two studies.</th>
<th>Discussed above, and adequate inclusions have been done in the discussion section of the manuscript!</th>
</tr>
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</table>
| 3) Limitations. The authors need to address limitations of the present study. For example, the limitation to use RPR as screening test might miss untreated cases with a long history. The limits of self-reported behaviors might also be discussed. Differences between different typologies of sex worker were not thoroughly investigated. | We fully agree that some cases can be missed using this screening strategy, which is however used in many countries worldwide due to the high sensitivity to detect primary, secondary and early latent syphilis. We also in this study of course wanted to primarily detect active, infectious cases, and not “old syphilis”. Nevertheless, using this screening strategy rare cases of very early untreated syphilis, previously treated early syphilis, incubating syphilis and very late syphilis may be missed. Syphilis diagnostics using serology (or any methods) is not perfect, but we consider that this strategy was the best and most pragmatic way to do it for our study population. Finally, we have not included any specific discussion regarding these issues in the revised manuscript. This is due to the fact that we are using many different methods to detect several divergent STIs, and it would need too much text to discuss the minor limitations with all these different methods. Accordingly, all methods and diagnostic strategies have limitations, and due to this fact we have only used internationally well-recognized and approved ones. Limitations of self reporting behaviors are presented on Page 14, line 1-4 as 

*Inaccurate self-reporting of risky behaviours is the primary threat to the validity and utility of research among most at risk populations. The validity of self-reported risky behaviours has direct effects on the sensitivity and specificity of the results obtained, which may affect the future strategies and interventions.*
Typologies have been discussed in the discussion as Explained on page 13, 3rd paragraph, line 14-16