Author's response to reviews

Title: Kaposi’s sarcoma associated herpesvirus infection among female sex workers and general population women in Shanghai, China: a cross-sectional study

Authors:

Tiejun Zhang (tjzhangsh@gmail.com)
Ying Yang (yangying@minghang.cdc.com)
Feng Yu (tjzhangsh@gmail.com)
Yanping Zhao (zhaoyangping@minghang.cdc.com)
Feifei Lin (tjzhangsh@gmail.com)
Veenu Minhas (veenu9@yahoo.com.cn)
Charles Wood (cwood@unl.edu.cn)
Na He (nhe@shmu.edu.cn)

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

We sincerely appreciated your and reviewers` comments regarding our revised manuscript. We are encouraged by the reviewers` enthusiasm for this manuscript and their candid and thoughtful comments and suggestions.

Please find here with a revised version R2 of our manuscript 'Kaposi`s sarcoma associated herpesvirus infection among female sex workers and general women in Shanghai, China: a cross-sectional study' (MS: 4023354259994612). We have revised the manuscript and have addressed all issues raised by the reviewers. Below is a point-by-point reply to each reviewer, and the changes are highlighted.

We hope that you will now find this improved manuscript acceptable for publication in BMC Infectious Diseases. Thank you very much for your kind considerations of our revised manuscript.

Please feel free to let us know if you have any question.

Sincerely yours,

Na He, MD., PhD.
Professor of Epidemiology,
Associate Dean for Academic Affairs
School of Public Health,
Fudan University, Shanghai 200032, China
E-mail: nhe@shmu.edu.cn
Point-to-point responses to comments

Review: Dr. Jesse Clark

Reviewer's report:

The revised manuscript has addressed almost all previous comments and has been substantially improved. I have only a few minor comments:

Major Compulsory Revisions

None

Minor Essential Revisions

1) Methods p. 6, "The minimum number of study subjects to achieve a power of 0.95 at a significance level of 0.05 (two-tailed) was calculated as 430 for each group."

Please specify, power to detect what?

Response: Thank you for your valuable suggestion. This sample size estimation focuses on the precision of the estimate. In this study, we calculated the sample size required to estimate the KSHV prevalence with a specified level of confidence and precision. The sample size was calculated based on the prevalence of KSHV (4.8%) among the general population. We speculate that the KSHV prevalence among general women and female sex workers should not be lower than this number. Thus, to estimate KSHV prevalence with 95% confidence and margin of error no larger than 0.02, the required sample is approximately 430 for each group. We have revised in the text as well. Please see Page 6 Para3.
2) Methods pp. 6-7, The authors state that participants were recruited by visiting sex
work venues or households, but how were participants recruited from these sites?
Face to face (if so, who did the invitation)? Posted advertisements? Peer invitation?

Response: Thank you. We apologize for not making this point clear. With regard
to the recruitment procedure, local public health workers visited each of the
selected venues or households and invited qualified individuals by face-to-face in
these sites to participate in the study. Those who were informed consented to
participate in the study were administered with a face-to-face questionnaire
interview by the attending public health workers. (Please see Page 7 Para 2).

3) Methods, pp. 8-9, The authors describe in the manuscript that they have followed
the manufacturer's instructions for the Focus HerpeSelect EIA and state in their
response (though not in the manuscript) that the manufacturer recommended cut-off
value for seropositivity used was 1.1. However, multiple previous studies using this
assay have suggested that, especially in high prevalence populations, the 1.1 cut-off
value results in a high amount of false-positive results and so a higher cut-off value of
3.5 is frequently used now. Obviously it is perfectly acceptable to use the
manufacturer's recommended cut-off value of 1.1, but given the fact that HSV-2
seroprevalence is one of the factors used to determine whether KSHV can be
considered a heterosexual STI in this population, it would be important to at least
comment on the potential limitation of using the lower cut-off value and the
possibility of bias in the estimation of HSV-2 prevalence.

Response: Thank you for your valuable suggestion. We agree with the referee
and have mentioned this potential limitation in the discussion section. Please see Page 17 Para 1.

Discretionary Revisions

1) Abstract (and throughout), the term "general women" is unclear, and it may be better to describe this group as "women from the general population" or "general population women"

Response: Thank you. We have revised as suggested.

2) Page 16, Lines 1-2, "heterosexual contacts is unlikely" should be "are unlikely"

Response: Thanks. Correction has been made as suggested. Please see Page 15 Para 2.

Reviewer: Dr. Anne Buve

Reviewer's report:

MINOR ESSENTIAL REVISIONS

1. Page 6, paragraph on sample size calculation. The authors should explain what the underlying assumptions were for their sample size calculation. Did they want to find a statistically significant difference between FSW and GW; or did they want to assess prevalence with a certain precision.

Response: Thank you for your suggestion. Yes, we want to assess prevalence with a certain precision. Based on our previous study, we want to estimate the
prevalence of KSHV among general women and female sex worker. The sample size was calculated based on the prevalence of KSHV (4.8%) among the general population. We speculated that the KSHV prevalence among general women and female sex workers should not be lower than this number. Thus, to estimate KSHV prevalence with 95% confidence and margin of error no larger than 0.02, the required sample is approximately 430. Please see Page 6 Para3.

2. Page 12, second paragraph. When the authors say that they adjusted for potential confounders "such as age, education and marital status, do they mean that these were the only variables they adjusted for? If so, it would be more elegant to say "after adjusting for age, education and marital status".

Response: Thank you. We have revised the manuscript as suggested. (Please see Page 12. Para2.)

3. Page 15, first paragraph: the English needs to be revised.

Response: Thank you for your suggestion. We have now rephrased the first paragraph on the Page 15.

Reviewer: Dr. Denise whitby

Reviewer's report:

The revised manuscript by Zhang et al is much improved. My remaining concerns are as follows:
1. In the abstract on page 3 the authors state “Transmission via heterosexual contacts might not be a predominate route for KSHV, at least among Chinese women.” Whilst not an advocate of overestimating the significance of data, it seems to me that this is such an underestimation of the findings presented that it casts doubt on them. The findings presented provide strong evidence that KSHV is not heterosexually transmitted in Chinese women, consistent with the majority of studies in other populations. Why are the authors so surprised?

Response: Thanks for the insightful comments. We indeed thought that KSHV was not heterosexually transmitted in Chinese women and have revised the sentence as suggested: “Heterosexual contact is not a predominant route for KSHV transmission among Chinese women”.

2. “Predominate” should read predominant

Response: We apologize for the typo. We have corrected it.

3. On page 4 the authors refer to vertical transmission of KSHV. While there is considerable evidence for mother to child transmission of KSHV, “vertical” usually denotes in utero transmission for which there is no evidence for KSHV. The authors should therefore change “vertical” to “mother to child” throughout the manuscript.

Response: Thank you for the thoughtful comments. We have changed “vertical” into “mother-to-Child” throughout the manuscript.

4. On page 5, the authors refer to KSHV as a sexually transmitted infection. KSHV is transmitted via saliva and while it is associated with markers of sexual activity in MSM it cannot be considered an STI. This should be corrected here and throughout
Response: Thank you. We agree with reviewer and have corrected this description throughout the manuscript.

5. On page 17 the authors state “we cannot eliminate the possibility of horizontal transmission via saliva in our population.” Since there is overwhelming evidence that KSHV is transmitted via saliva this is a very odd statement indeed.

Response: We agree with the referee. This statement has been removed from the manuscript.

6. Also on page 17 the authors conclude “the present study suggests that transmission via heterosexual contacts might not be a predominant route for KSHV, at least among Chinese women.” I suggest this be rephrased more positively as I suggested in point 1.

Response: Thank you, we revised this sentence as suggested.