Author’s response to reviews

**Title:** The prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae infections among female sex workers from different categories of sex work venues in China

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

Thank you for your email regarding the responses to the comments from the reviewers. We prepared the point-to-point responses to the comments as follows.

As some of results about HIV and syphilis infections among the study population have been reported elsewhere, we modified the revised version to focus on CT and NG infections only.

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COMMENTS FROM REVIEWER NING WANG
Major Compulsory Revisions

Justification: the study is set up on the premise that most past research on STI in this population focuses on HIV and syphilis, but no clear justification is given for how and why research on CT and NG are necessary and what such research can be expected to add to the field.

Reply:

Thanks for this important point. In addition to HIV and syphilis which were extensively reported, CT and NG are reported as notifiable infectious diseases in national sexually transmitted disease (STDs) surveillance system. These two infections can not only cause serious health complications [Ref. Kamwendo F, Forslin L, Bodin L, Danielsson D. Decreasing incidences of gonorrhea- and chlamydia-associated acute pelvic inflammatory disease. A 25-year study from an urban area of central Sweden. Sex Transm Dis. 1996; 23:384-91] but act as facilitating factors in transmission of human
immunodeficiency virus [Ref. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect, 1999, 75:3–17]. We added this statement in the Introduction section.

# Biological interpretation: there is little to no discussion of the relative transmissibility of these various pathogens and the role that coinfection might play in explaining the observed cross sectional results. It is rather wasteful of the rich data not to do further analysis and interpretation of the interplay between the four different STIs.

Reply:
As the current study was based on design of a cross-sectional observational study and it may be hard to use these data for analyzing any causal associations and/or interplays between these four STIs in addition to the current analyses of the associations.

# The stated implications for future disease control efforts are non-specific and poorly linked to the findings of the analysis. First, the need for better CT and NG surveillance must be justified, at the very least by highlighting the importance of reducing their disease burden. Second, these findings can also likely be reframed as additional insight into what is currently understood about HIV and syphilis risk in this population.

Reply:
Regarding the implications, the current findings can be served as a call for action to draw further attention to control the critical disease burden of CT and NG among this population. Meanwhile, further studies on associations between CT and/or NG infection and protective immunity are needed. This statement was integrated into the revised manuscript.

# FSW as “source population”: many researchers refer to FSW as the source population for STI in the general community. While there may be good reason to believe that this may be true in some places, it appears presumptive to make such statements based on cross-sectional data. At the least such claims should be backed by credible references; if none can be found I suggest removing such sentences.

Reply:
We reworded this statement to be “As FSWs are one of the important populations to drive the STI epidemic …”
Minor Essential Revisions

# Introduction: in the first sentence, it would help to point out that heterosexual contact is the major (dominant?) mode of transmission IN THAT it makes up the largest portion of all HIV infections relative to other modes.

Reply:
We made this in the revised manuscript.

# Introduction: the statement “FSW…are likely to determine how fast the HIV epidemic will spread from high risk group to the general population” needs to be backed by at least one original reference.

Reply:
We cited previous Reference 6 (currently Reference 2) and reorganized the reference list accordingly.

# Methods: in the opening sentence, the nature of the study (name, time, purpose, etc.) should be referenced.

Reply:
We added more details about the nature of the current study, particularly about study sites and relationship with Mega Project.

# Results: in the sub-section “prevalence of infection” the HIV prevalence 0.26% is missing the “%.”

Reply:
Sorry for this mistake. We added this.

# Results: the interpretation that syphilis prevalence increases with age might need to be requalified given the broad overlap of the 95% CI that in some cases include the next estimate.

Reply:
We reworded the descriptions as “As shown in Table 1, compared with that in age group of 15-20 years, older age groups had a significantly higher prevalence of syphilis but lower prevalence of NG or CT.”

# Results: under “risk factors for infection” the outcome of the analyses are unclear. It is also unclear as to why multivariate analysis results are only shown for syphilis and Chlamydia.

Reply:
As HIV was only significantly associated with locating in Guangxi and NG associated with having chlamydial infection, we did not include them in previous Table 2. We have modified the table to include only CT and NG infections.

# Results: in the sentence beginning “In contract” should probably be “In contrast”

Reply:
Sorry for this mistake. We corrected it already.

COMMENTS FROM REVIEWER MARIO CRUCIANI

Major points
For syphilis diagnosis, the Authors use an ELISA screening test and a non-treponemal test (TRUST). However, a case definition of syphilis requires positive treponemal and non-treponemal tests and consistent clinical and physical findings. Actually, a positive treponemal test alongside a positive non-treponemal test could represent an active disease, latent infection, prior treated infection, or a serological scar. The main limitations of non-treponemal tests are their reduced sensitivity in primary syphilis and late latent syphilis, false-positive results due to cross-reactivity, and the potential for false-negative results due to prozone reactions. In the current study, it is not completely clear how were syphilis cases defined. Were both the screening test and non-treponemal test required for a case definition?

Reply:
For sure, the diagnosis of active syphilis should be based on not only testing with treponemal and non-treponemal antibodies but also evaluation of clinical and physical findings. However, as a prevalence survey at population level to estimate the disease burden, the definition of syphilitic infection is usually based on the dual seropositivities of these two kinds of antibodies. We have removed the syphilis part from the manuscript.

In this case the reduced sensitivity of non-treponemal test may have underestimated the actual prevalence of positive syphilis tests. By contrast, the treponemal screening EIAs test and the treponemal tests generally remain reactive for life, and this could be misleading in individuals who no longer have active disease. Thus a diagnosis of active disease require nontreponemal and treponemal tests positivity and clinical signs of active disease; while latent syphilis is diagnosed when nontreponemal and treponemal tests are positive in the absence of symptoms or signs of active syphilis.

Reply:
This is relevant to the above comment. The current study was not conducted to make a diagnosis of active syphilis for specific individuals but to estimate the disease burden of syphilis infection at population level. Majority of published studies on prevalence of syphilis infection among populations are based on the definition of the seropositivities of treponemal and non-treponemal tests. We have removed the syphilis part from the manuscript.

The current study doesn’t provide the results of the confirmation test (the treponemal test). This limit needs to be acknowledged and discussed. Moreover, if possible, the authors should provide more information on stage of disease and previous penicillin treatment of the FSWs with positivity of syphilis test.

Reply:
As mentioned in the manuscript, ELISA is one of treponemal tests. There are still discussions on confirmation of EIA positive sera with TPPA but according to the national guidelines in China, ELISA can be used as alternative for TPPA for clinical practice and epidemiological surveillance as well. We have removed the syphilis part from the manuscript.

What happened to subjects that tested positive for HIV, syphilis or other STD? Were they addressed to a clinical centre in order to receive treatment and follow up? Please, give some information about the post screening management of FSWs

Reply:
In the study, we informed the participants of the testing results in specific schedules according to different pathogen tests. Generally, participants with positive tests received counseling messages and were referred to designated clinics for further evaluation and possible treatment or other interventions according to the national guidelines. This has been integrated into the revised manuscript.

Table 2:
Independent factor: Being 21-25 yrs old in footnote B. There is logical incompatibility between the category “being 21-25 yrs old” and the reference group of FSWs aged 25 yrs or younger. Actually, for a multi-level categorical variable, the reference category cannot overlap the category under examination (“independent factors”)

Reply:
It should be 20 years or younger. We made corrections.
Minor Points

ABSTRACT: AOR: when used for the first time in the text abbreviations should be clearly defined

Reply:
Definition of the acronym “AOR” – “adjusted odds ratio” was added.

Table 2:
NS: I suppose is the abbreviation for not significant. The current sentence (is not the factor…) doesn’t make sense.

Reply:
We deleted this note in Table 2.