Author's response to reviews

Title: High prevalence of HIV infection and unprotected anal intercourse among older men who have sex with men in China: A systematic review and meta-analysis

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Response to reviewers

Reviewer: Carla van Tienen

-Major Compulsory Revisions

Q1. For a systematic review and meta-analysis, a protocol describing the exact methodology of searching for papers, in- and excluding papers and extracting data is crucial. Was there a protocol in place for this study? If yes, please provide the protocol in an appendix to this paper, if not, please explain in more detail what methodology was used. I recommend using the PRISMA guidelines for conducting and reporting a meta-analysis (http://www.prisma-statement.org/statement.htm). It is much more detailed and includes many more items than the QATSO score that the authors use. This would take away many issues that are now unclear in this paper and that need to be clarified.

Response: We thank the reviewer’s for the very useful suggestion. We have conducted this meta-analysis in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The check list of PRISMA has been attached as Table S1.

Revised text: In the Methods part (Page 5 Line 20-23)

“This meta-analysis was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) [12].”

Q2. Please add a link to at least one of your saved search strategies in one of the databases that was searched. Also, please add the last date when you performed your database searches. In this way, readers of this paper can repeat the search.

Response: Based on the reviewer’s advice, we have added one link of our saved search strategies in Pubmed and the last date when we performed our database searches.

Revised text: In the Methods part (Page 5 Line 17-20)

“The keywords and medical subject headings “HIV,” “AIDS,” “MSM,” “gay,” “homosexual,” “elderly,” “older,” “aged,” “old,” and “China” were used to search for potentially relevant studies (e.g. http://www.ncbi.nlm.nih.gov/pubmed/?term=old+msm+hiv+china). The last date of literature searching was July 1st, 2013.”

Q3. Please describe in Table 1 what laboratory methods were used to confirm HIV and syphilis infection. For example, in the study by Liu MH,
2005, it is noted that detection of HIV antibodies in urine was used to diagnose HIV infection. This is not a valid way to determine HIV infection and therefore this study should have been excluded. The authors have to describe the laboratory tests that were used in the original papers.

**Response:** We thank the reviewer’s for the very useful suggestion. In order to address this issue, we have excluded the study which using an invalid method to detect HIV and syphilis infection and re-did the meta-analysis. Also, we have noted the methods for HIV and syphilis detections in Table 1.

**Revised text:** Please refer to Table 1.

“a: Blood specimens were detected by Enzyme-Linked Immuno Sorbent Assays (ELISA) and Western Blot assay (WB) to confirm HIV infection in all the included studies; b: Blood specimens were detected by Rapid Plasma Reagin (RPR) and Treponema Pallidum Particle Agglutination assay (TPPA) to confirm syphilis infection in all the included studies; ”

**Q4.** Please explain in Table 1 what the abbreviations are for the different sampling methods plus explain what these methods entail.

**Response:** We have included this in the revision of Table 1 according to your valuable advice.

**Revised text:** Please refer to Table 1.

“c: Mixed: Snowballing or/and RDS or/and convenience sampling were included; d: NR: Not reported; e: RDS: Respond Driven Sampling.”

**Q5.** Please add a table which assesses the quality of the included studies so the authors get more information about these studies. For example, now it is not clear what the exact population was that was studied in the different papers, it is not clear whether there was a random sample taken or not and therefore it is impossible to assess any potential bias in the studies for the reader. Assessing potential bias is crucial in a meta-analysis and is not possible in this format.

**Response:** We thank the reviewer for providing valuable advice. In accordance with the suggestion, we added Table S2 to assess the quality of the included studies.

**Revised text:** Please refer to Table S2.

**Q6.** Please give an exact description of how prevalence data were pooled in the Methodology section.
Response: Thank you for your comments. We have added the description of how the pooled prevalence was calculated in the methods part.

Revised text: In the Methods part (Page 7 Line 7-11)

“The pooled prevalence was calculated using the inverse variance method. The average effect size across all studies is computed as a weighted mean, whereby the weights are equal to the inverse variance of each study’s effect estimator [15]. Larger studies and studies with less random variation are given greater weight than smaller studies [15].”

Q7. The prevalence data in Table 1 differ from the prevalence data in Figure 2. E.g. there are 5 studies in Table 1 where HIV prevalence is reported as 0.00%, yet in Figure 2 one of these studies has a prevalence of up to 10% (Feng F, 2009). This has to be corrected and the meta-analysis repeated if necessary. Also, please use the same units for reporting the prevalence in text, tables and figures; it is confusing for the reader now.

Response: We sincerely thank the reviewer for constructive input. We are sorry for this error, and have corrected it in the revision.

Revised text:

Q8. In the Results section under Study selection it says 59721 younger MSM were identified. Please clarify how this was done. I assume now...
these data come from the same papers that were included in the meta-analysis, but it is not clear from the text or tables. Please include in Table 1 the number of young MSM that were studied in these studies and give HIV, syphilis and UAI prevalence for these men.

**Response:** We have added the number of younger MSM in the revised Table 1 and included the HIV, syphilis and UAI prevalence for younger MSM in the result part according to your valuable advice.

*Revised text: Please refer to Table 1.*

**Q9.** There is no mention of Antiretroviral treatment (ART) in the paper. The authors should comment on ART in China in general and specifically in MSM. It is crucial for public health interventions, individual care of HIV infected persons and for the spread of HIV. Also, if many MSM have been on proper ART for a long time, this could contribute to a higher prevalence among older MSM as they just age with their infection.

**Response:** We thank the reviewer for providing valuable advice. In accordance with the suggestion, we noted the influence of ART in the discussion part.

*Revised text: In the Discussion part (Page 11 Line 8-11)*

“Thirdly, there has been 0.12 million patients received antiretroviral treatment since China implemented antiretroviral treatment for HIV/AIDS in 1999 [4], which could also contribute to a higher prevalence among older MSM as they just age with their infection.”

**Q10.** The first paragraph in the Discussion section makes very strong conclusions based on this meta-analysis. More emphasis should be put on the limitations, e.g. very small sample sizes of many studies and probably also bias in some studies. After revision of this paper, perhaps the conclusion might be additional, larger studies with random sampling might be needed?

**Response:** We understand and appreciate the concern expressed by the reviewer. We agree with reviewer and have modified the conclusion of the manuscript and added this into the limitation part of the study in the discussion part.

*Revised text: In the Discussion part (Page 10 Line 18)*

“Our meta-analysis also indicated that the trend of HIV prevalence among older MSM has substantially increased in the past decade.”

*In the Discussion part (Page 13 Line 20-21)*
“Small sample size may also restrict the statistical power in subgroup analyses, there are very small sample sizes of many studies and probably also bias in some studies.”

In the Conclusion part (Page 14 Line 10-13)

“Further large-scale epidemiological investigations, with standard sampling methods and adequate power, should be conducted to gain a more precise estimate of the status of the HIV and other sexually transmitted infection epidemics among older MSM in China.”

- Minor Essential Revisions

Q1. In Figure 1 in the box that starts with 3589, it should state NOT fulfilling the inclusion criteria.

Response: Thank you for your comments. We have revised the Figure 1 according to your suggestion.

Revised text:
Reviewer: Huachun Zou

- Minor Essential Revisions

**Q1.** Page 11, Line 1, please change “old MSM” to “older MSM”;

**Response:** Thank you very much for identifying this error. We have corrected the error in the revision.

*Revised text: In the Conclusion part (Page 11 Line 14)*

“HIV prevalence among older MSM in China is higher than older MSM in European countries such as Sweden (3.8%) and Germany (2.6%), but was much lower than those in four major cities in the United States (19%) [36, 37].”

**Q2.** Page 11, Line 20-21, you don’t really have to mention that the HIV epidemic in southwest China is driven by IDUs. This is a bit distracting and misleading.

**Response:** We thank the reviewer for their advice, and we revised the manuscript according to your useful suggestion.

*Revised text: In the Discussion part (Page 12 Line 9-10)*

“Subgroup analysis showed the highest HIV infection rate in southwest China (16.4%), which was consistent with prior studies [47,48].”

**Q3.** In the results section, please include data on syphilis prevalence in younger MSM.

**Response:** We have included this in the revision according to your valuable advice.

*Revised text: In the Results part (Page 9 Line 5-7)*

“The summary prevalence of syphilis infection among older MSM was marginal significantly higher than their younger counterparts (23.0% vs. 10.0%, Chi-square value=3.57, p=0.06).”

**Q4.** In the discussion section, authors probably want to discuss about HIV testing as increased HIV prevalence may be to some extent due to increase testing rate. HIV testing among Chinese MSM has been increasing over the decade (you can reference: Zou H, et al. HIV testing among men who have sex with men in China: a systematic review and meta-analysis. AIDS & Behavior, 2012). Do older MSM test for HIV and syphilis more often than their younger counterparts? (you can reference a few studies who were looking at HIV testing in Chinese MSM in
different age groups, for example: Zhang L, et al. Predictors of HIV testing among men who have sex with men in a large Chinese city, STD, 2013; Song Y, et al. HIV-testing behavior among young migrant men who have sex with men (MSM) in Beijing, China, AIDS Care, 2011

**Response:** We thank the reviewer for providing valuable advice. In accordance with the suggestion, we noted the influence of increased HIV testing rate in the discussion part.

Revised text: *In the Discussion part (Page 11 Line 6-8)*

“Secondly, HIV testing as increased HIV prevalence may be to some extent due to increase testing rate since HIV testing among Chinese MSM has been increasing over the decade [37]”

**Q5.** Authors may also want to discuss about aging in Chinese MSM. What problems will occur as MSM are growing older? There are quite some papers outside in this topic. These studies might be of some implication for older Chinese MSM.

**Response:** Thank you for your comments. We have added this into the discussion part.

Revised text: *In the Discussion part (Page 12 Line 11-15)*

“Older MSM living with HIV may bring more medical challenges. The elders are more vulnerable to side effects of antiretroviral drugs [49]. Aged people are facing problems of diabetes and heart disease, whereas research suggests that antiretroviral drugs contribute to high cholesterol levels and hamper insulin production, thus increasing the risk of health problems [50].”