Author's response to reviews

Title: Prospective cohort study of HIV incidence and molecular characteristics of HIV among men who have sex with men (MSM) in Yunnan Province, China

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Author’s response to reviews: see over
Prospective cohort study of HIV incidence and molecular characteristics of HIV among men who have sex with men (MSM) in Yunnan Province, China

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Response to comments to the first reviewer’s comments

Major Compulsory Revisions:
A. Method section.

Comment 1#
It would be helpful to clearly state in “Methods” the length of the follow-up period that was originally designed. From the authors’ description I may guess that the follow-up period seemed to be one year between June 2009 to March 2011, as long as the participants were not seroconverted or withdraw from the study.

Response 1#: We have changed the description according the reviewer’s comments, which can be seen below.

For the method part of the Abstract section: “An 18 months prospective followed up with a frequency of 3 month per visit were conducted among HIV seronegative MSM in Kunming city during 2009-2011.”.

For the Method section: “Between June 2009 and March 2011, Kunming MSM were recruited to attend an 18 months prospective follow-up with a frequency of three months per visit through a local MSM non-government organization (NGO).”

2. Given the dynamic nature of the cohort study design and an HIV testing every three months during the follow-up period, a Cox proportional hazard regression model, instead of a logistic regression model, should be used to determine risk factors for HIV seroconversion among this MSM group.

Response 2#: We have changed the statistical method in the method section and result section, which can be seen below. And the detailed statistical analysis result can be seen in table 2.

Method section: “Multivariate Cox proportional hazard regression model was used to determine the adjusted hazard ratio (aHR) for HIV seroconversion related factors”.

Result section: “Multivariate Cox hazard regression analysis showed that baseline syphilis infection (adjusted hazard ratio[aHR], 17.7, 95%CI, 3.6-86.4, P<0.001), occupation (male students vs. others [aHR, 5.7, 95%CI, 1.3-24.3, P=0.019], retirees vs. others [aHR, 4.1, 95%CI, 1.0-18.6, P=0.05]), bleeding experience after receptive anal intercourse in past 6 months (aHR, 7.6, 95%CI, 2.2-26.6, P=0.001), and ethnicity (ethnic minorities vs. Han) [aHR, 5.7, 95%CI, 1.5-21.5, P=0.01] were independent risk factors for HIV seroconversion among the recruited MSM cohort (table 2)

B. Results
1. For table 1, it might also be helpful to present and compare characteristics of those (about 30%
of the total cohort) lost to follow-up and those retained.

Response:
We have added these suggested characteristics comparison between those lost of follow-up MSM and retained MSM in the table 1. Additionally, we have added some discussion content in the limitation section, which was listed below.

“Secondly, some characteristics of those lost of follow-up and those retained in the cohort were statistically different, which may weak the generalizability of the study findings to total Kunming MSM.”

2. For table 2, it was “incidence” not “prevalence” should be reported, with a unit of person time. If the authors will use a Cox regression model instead of a logistic model, then HRs (hazard ratios) instead of ORs should be reported.

Response:
We have recalculated the unit of person years, hazard ratios, and we have adopted the suggested new statistical analysis method of Cox regression model, and these changes can be seen in the table 2.

3. The authors reported HIV-related risky behaviors such as sexual behaviors and illicit drug use among the study participants at the baseline survey, they should also reported occurrence of these behaviors during the follow-up period through the follow-up surveys since it were these behaviors that put the participants at risks of HIV seroconversion. There risky behaviors or exposures should be considered in an appropriate and pragmatic way in the multivariate analysis examining risk factors for HIV seroconversion during the follow-up period.

Response:
In the Cox hazard regression model, we have added two new representative HIV-related risky behaviors variable of “Failed to use condom with regular male sexual partners during receptive anal sex in the follow-up” and “Failed to use condom with regular male sexual partners during receptive anal sex in the follow-up, both of them occurred in the prospective cohort follow-up. While, both of them had marginally statistical correlation with the HIV incidence, and none of them kept in the last multivariate model.

Minor Essential Revisions

1. In Table 2, the % for each characteristic was redundant since it was already given in the overhead of the table.

Response: we have changed this redundant description in table 2.

2. The authors affirmed that they identified two HIV transmission pairs based on phylogenetic analysis and a later epidemiological survey. Although this
conclusion sounds acceptable, a sexual network (if available from the study) in which the two members of a transmission pair were involved would provide more robust evidence.

Response: we have added this suggested sexual network analysis, which can be seen in new added figure 2.

![Network diagram of 7 HIV seroconverted MSM and the detected HIV transmission pairs.](image)

**Fig. 2 Network diagram of 7 HIV seroconverted MSM and the detected HIV transmission pairs.**

The three triangles in the diagram represent main locations in which MSM seek homosexual partners (triangle A: Internet; triangle B: Bathing room/sauna/ massage room; triangle C: Bar/night club/tearoom). The five circles represent HIV antibody seroconverted MSM with the HIV-1 subtype of CRF01_AE and the two rectangles represent MSM with the HIV-1 subtype of CRF_07BC. Two HIV transmission pairs ([220287 vs. 220023] and [220141 vs. 220169]) were detected based on the phylogenetic analyses method. Their transmission relationship was confirmed by further conducted epidemiological survey.

3. There are some typos or grammatical errors in the text, e.g., “By phylogenetic comparison of virus sequence, we found two pair our HIV transmission pairs were found,” on line 352-353.

Response:

We have changed these grammar mistakes, which was described below.

By phylogenetic comparison of virus sequence, we found two HIV transmission pairs.
Response to the second reviewer's comments

Minor Essential Revisions:
1. Page 3, abstract section, 'which HIV incidence epidemic and molecular characteristics of new infected Yunnan MSM were not evaluated before' should be revised to 'while HIV incidence epidemic and molecular characteristics of new infected Yunnan MSM were not evaluated before'.
   Response: We have revised this sentence according to reviewer's suggestion.

2. Page 3, abstract section, 'Fifteen MSM seroconverted to syphilis' should be revised to 'fifteen MSM seroconverted to syphilis'.
   Response: we have revised the incorrect word in the abstract section.

3. Page 3, abstract section, 'Two pairs of HIV transmission pair detected among seroconverted minority ethnic MSM' should be revised to 'Two HIV transmission pairs were detected among seroconverted minority ethnic MSM'.
   Response: we have revised this sentence in the abstract section.

4. Page 3, abstract section, conclusion: the authors concluded that 'Yunnan province needs to strengthen syphilis screening among MSM' in fact the HIV incidence was also moderately high, so it should stress both of HIV and syphilis screening program among local MSM population.
   Response: we have revised this description, which can be seen below.
   Yunnan province needs to strengthen both HIV and syphilis screening among MSM population.

5. Page 7, introduction section, the authors stated that previous 'prospective surveys were mainly conducted during 2006-2007, and they cannot reflect current HIV incidence epidemic among China MSM'. While in the last paragraph of the introduction section, the authors failed to tell the study period of this study. It is very necessary for the authors to add such description in this manuscript.
   Response: In the beginning of the method section, we have added related description, which can be seen below.
   Between June 2009 and March 2011, Kunming MSM werewas recruited to attend an 18 month prospective follow-up through a local MSM non-government organization (NGO).

6. Method section: the authors described that 'each participant was compensated with 100 Renminbi (RMB) [about 16 United States Dollar (USD)] for his participation', while it is confusing that whether participants were totally given 100 RMB during the follow-up, or be given 100 RMB at each visit time point?
   Response: we have changed this sentence, which can be seen below.
   Each participant was compensated with 100 RenMinBi (RMB) [about 16 United States Dollar (USD)] for each round of attending this follow-up.
7. Result section: for the paragraph of 'Migrant status of MSM participants' the word of 'Yunan' should be changed to 'Yunnan'.

Response:
We have revised this word from “Yunan” to “Yunnan”.

8. Result section: for the paragraph of 'HIV subtyping and primary drug resistance genotyping', the description of 'By phylogenetic comparison of virus sequence, we found two pair our HIV transmission pairs were found' was grammatically incorrect, and should be revised.

Response: we have changed this sentence, which can be seen below.
By phylogenetic comparison of virus sequence, we found two HIV transmission pairs.

9. Discussion section, the authors discussed that baseline syphilis infection significantly increased HIV seroconversion risk in the third paragraph. While, there is one minor grammar mistake. For example, 'This information can also help decrease HIV infection rate and transmission risk among in this population'. And it is should be revised.

Response: we have changed this sentence, which can be seen below.

This information can also help decrease HIV acquisition rate and transmission risk among this population.
Editorial requirements:

Competing interests

A competing interest exists when your interpretation of data or presentation of information may be influenced by your personal or financial relationship with other people or organizations. Authors must disclose any financial competing interests; they should also reveal any non-financial competing interests that may cause them embarrassment were they to become public after the publication of the manuscript.

Authors are required to complete a declaration of competing interests. All competing interests that are declared will be listed at the end of published articles. Where an author gives no competing interests, the listing will read 'The author(s) declare that they have no competing interests'.

Response: we have moved the 'Declaration of interest' from the front of the manuscript to the end of it, which can be seen below.

Declaration of interest:

This study was supported by the Mega-projects of national science research for the 12th Five-Year Plan (2012ZX10001-006); China-Gates Foundation Cooperation Programme; and National Nature Science Foundation of China (81001291). The funding organization had no role in the development of study design or in the collection, analysis, and interpretation of data. The authors declare that they have no competing interests.

Authors' contributions

In order to give appropriate credit to each author of a paper, the individual contributions of authors to the manuscript should be specified in this section.

An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. To qualify as an author one should 1) have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; and 3) have given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

We suggest the following kind of format (please use initials to refer to each author's contribution):

AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair who provided only general support.

Response: we have described the 'Authors' contributions' from the front of the manuscript to the end of it, which can be seen below.
Authors' contributions: Conceived and designed the experiments: JJX LL HS participated in the design of the study. MHA XXH MHJ YLM MZ performed the study and experiments. JJX MHA analyzed the data; QHH ZXC JZ YJJ WQG contributed reagents/materials/analysis tools; JJX HS LL wrote and revised the manuscript.

Requesting consent statement:

Please state in the Methods section whether written informed consent for participation in the study was obtained from participants or, where participants are children, a parent or guardian.

Response: In the method section, we described the consent statement and participants’ age criteria as follows.

MSM individuals were interviewed and their eligibility was confirmed through screening questionnaires and HIV testing after they provide written informed consent to the study. The eligible criteria for the cohort entry criteria were: 1) serological negativity for both HIV antibodies and NAAT, 2) at least 18 years of age.