Author's response to reviews

Title: Prevalence of human immunodeficiency virus 1 infection in the last decade among cross-border travelers who entered major land ports in the Yunnan Province, China

Authors:

Binghui Wang (binghuiwang@aliyun.com)
Yaobo Liang (ynkmlvb@163.com)
Yue Feng (fyky2005@163.com)
Yaping Li (lypciq@126.com)
Yajuan Wang (yajuanwang1990@163.com)
A-Mei Zhang (zam1980@yeah.net)
Zulqarnain Baloch (znbalooch@yahoo.com)
Li Liu (liuli2272@163.com)
Weihong Qin (qinwh19@sina.com)
Xueshan Xia (oliverxia2000@aliyun.com)

Version: 5 Date: 3 February 2015

Author's response to reviews: see over
Dear editor:

Thank you for your consideration on the possible publishing of our article in your journal, and please bring our thanks to these two reviews for their helpful comments and suggestions. According to the comments from editors and reviewers, we made a careful revision, and now resubmitting the revised paper to your journal.

The editor and reviewers have mentioned the limitations of our research. Actually, several date limitations is existed in previous version of this MS. In this revised version, a paragraph has been made to discuss the data limitations in detail. The major limitation of reviewers mentioned is that ‘7 main land ports were covered but not all 19 land ports’. We think this is a misunderstanding caused by our inappropriate description in previous manuscript. The cross-border travelers from the same prefecture are classified as a group actually. There are 8 prefectures bordering to Southeast Asian countries in Yunnan Province. Because of the lesser crossing border travelers and the irregular information, Nujiang Prefecture was excluded from this study. Finally, the entering travelers were recruited from 13 land ports located in the other 7 bordering prefectures, including 2 ports in Dehong, 1 in Baoshan, 2 in Lincang, 2 in Puer, 3 in Xishuangbanna, 2 in Honghe and 1 in Wenshan, respectively (the location of these ports was shown in the figure). Generally, there were about 80 million cross-border travelers through these 13 selected ports in Yunnan province annually. The total number of cross-border traveler through these 13 ports accounts for more than 90% of all entry-exit travelers. We think the HIV-1 prevalence among the recruited entering travelers could represent the situation of HIV-1 cross bordering transmission in Yunnan Province.

In addition, this manuscript has been sent to a professional language editing service (Editage) to ensure that the language is clear and free of errors.

Thank you for your consideration again. We look forward to your kind reply.
Sincerely,
First Author: Binghui Wang
Faculty of Life Science and Technology, Kunming University of Science and Technology
No. 727 Jing Ming Road, Chenggong District, Kunming, Yunnan, China
Tel: 86-13987140390; Fax: 86-871-65920570; E-mail: binghuiwang@aliyun.com
Corresponding Author:
Prof. Xueshan Xia, Faculty of Life Science and Technology, Kunming University of Science and Technology, Kunming, Yunnan 650500, China.
Tel: 86-871-65920756; Fax: 86-871-65920570; E-mail: oliverxia2000@aliyun.com

The below are the answers to reviewer’s questions & suggestions point to point:

**Reviewer: Wei Ma**

Reviewer's report:

Major Compulsory Revisions

1. Under study population and data collection of methods paragraph 1, kindly state the estimated average total number of cross-border travelers that enter the province through the selected ports annually. Also, what percentage of the total
annual cross-border travelers’ population does the sample size represent??

**Answer:** The local staff at land ports has been required to record the information and have the HIV-1 testing for one from every five-hundred travelers. We think the sampling is random through this unselected recruiting. There were about 80 million cross-border travelers on average through the selected 13 ports in Yunnan province annually. The recruited entering travelers accounted for 3.6‰ of the total cross-border travelers. The corresponding description has been added in the revised manuscript.

(line 97-100: Between January 2003 and December 2012, there were about 16 million entry travelers on average through the selected ports in Yunnan province annually. We randomly recruited 280,961 entry travelers (3.63‰) across the border in Yunnan Province, China.)

2. By what criteria did you define a “major land port”? Were the 7 land ports chosen specifically out of the rest purposively for any specific reasons or randomly?

**Answer:** We think this is a misunderstanding caused by our inappropriate description in previous manuscript. The cross-border travelers from the same prefecture are classified as a group actually. There are 8 prefectures bordering to Southeast Asian countries in Yunnan Province. Because of the lesser crossing border travelers and the irregular information, Nujiang Prefecture was excluded from this study. Finally, the entering travelers were recruited from 13 land ports located in the other 7 bordering prefectures, including 2 ports in Dehong, 1 in Baoshan, 2 in Lincang, 2 in Puer, 3 in Xishuangbanna, 2 in Honghe and 1 in Wenshan, respectively (the location of these ports was shown in the figure). Generally, there were about 80 million cross-border travelers through these 13 selected ports in Yunnan province annually. The total number of cross-border traveler through these 13 ports accounts for more than 90% of all entry-exit travelers. We think the HIV-1 prevalence among the recruited entering travelers could represent the situation of HIV-1 cross bordering transmission in Yunnan Province.
3. What were the inclusion and exclusion criteria applied to the random recruitment of potential participants? This information should be stated in your manuscript.

Answer: there is no exclusion criteria, sampling is completely random. The local staff of these land ports has been required to invite one for routine physical examinations and HIV-1 testing every five-hundred travelers. The corresponding description has been added in the revised manuscript.

(line 100-101): “The local staffs of land ports were required to invite one for routine physical examinations every five-hundred travelers.”

4. Under study population and data collection of methods paragraph 1 line 100

“Routine physical examinations were conducted” by the Entry-Exit Inspection and Quarantine personnel at each port, indicate examples of what types of medical tests were including in this physical examination.

Answer: Routine physical examinations include complete blood counting, blood chemistries, routine urine test and Detection of infectious pathogens (Hepatitis B virus, Hepatitis C virus, Syphilis, Malaria, Dengue virus and Typhoid fever virus). The corresponding description has been added in the revised manuscript.

(line 104-107): “Routine physical examinations include complete blood counting; blood chemistries etc. and the detection of infectious pathogens (Hepatitis B virus, Hepatitis C virus, Syphilis, Malaria, Dengue virus and Typhoid fever virus) were
conducted.”

5. Methods: study population and data collection: ‘Data on the social-demographic characteristics and risk behaviors for HIV infection were obtained from the enrolled participants via face-to-face interviews with trained staff by administering a structured questionnaire’. Please outline some examples of the questionnaire details to give readers an exact idea of what kind of questions were asked.

Answer: The questionnaire information of the interviewing was added in the txt, and a blank example of questionnaire was given as a support material to illustrate this (S1).

Line 107-111: Data on the social-demographic characteristics and risk behaviors for HIV infection were obtained from the enrolled participants via face-to-face interviewing with trained staff by administering a structured questionnaire (a blank example of questionnaire was given to illustrate this, S1).

6. Results: paragraph 1 “Of the 23 entry ports in the Yunnan Province, 19 land ports communicate via rail or road with Myanmar, Laos, and Vietnam. Between 2002 and 2012, we recruited 280,961 cross-border travelers from the major land ports of the Yunnan Province”; Are all 19 land ports also major land ports? If not, what is the difference between the major land ports and the other land ports?

Answer: The entering travelers were recruited from 13 land ports, including 3 ports in Dehong, 1 in Baoshan, 3 in Lincang, 2 in Puer, 2 in Xishuangbanna, 1 in Honghe and 1 in Wenshan, respectively. Generally, there were about 80 million cross-border travelers through these 13 selected ports in Yunnan province annually. The total number of cross-border traveler through these 13 ports accounts for more than 90% of all entry-exit travelers. We think the HIV-1 prevalence among the recruited entering travelers could represent the situation of HIV-1 cross bordering transmission in Yunnan Province. The corresponding interpretation was also given in Questions 2.
7. Under results paragraph 1, why were only cross-order travelers from major land ports recruited? Doesn’t the exemption of non-major land port cross-border travelers impact the study’s findings?

**Answer:** There are 19 land ports in Yunnan Province, and 13 of them were chosen in this study (shown in the figure). The cross-border travelers from the same prefecture are classified as a group. There are 8 prefectures bordering to Southeast Asian countries, 7 of them were chosen in this study. Because of the lesser crossing border travelers and the irregular information, Nujiang Prefecture was excluded from this study. The total number of cross-border traveler through these 13 ports accounts for more than 90% of all entry-exit travelers. We think the HIV-1 prevalence among the recruited entering travelers could represent the situation of HIV-1 cross bordering transmission in Yunnan Province.

8. Results: under Annual human immunodeficiency virus-1 infection rates among entry travelers in Yunnan. It’s better to show the trends of prevalence among different populations rather than proportions, because the readers do not know total numbers tested for each population. Same suggestion applies to figure 3.

**Answer:** The trend of yearly HIV-1 prevalence among the entering travelers was expressed logically by fitted trend line in Fig 2. According to this suggestion, Figure 3 had been optimized in order to more express the trend of prevalence among different groups clearly.

9. Results: last paragraph lines 175& 176 “However, the proportion of those aged 40–50 years showed an increasing trend, from 38.32% in 2003 to 27.21% in 2012” doesn’t sound correct since the data seems to be indicating a decrease rather than increase. In addition, it would be better if you have statistics to approve all trends you claimed.

**Answer:** There is indeed a mistake. The sentence had been replaced by “However, the proportion of those aged 40–50 years showed an increasing trend, from 9.35% in
Answer: We removed duplicate content, and the further discussion has been carried on these findings. The previous description was replaced with “In view of the age-specific HIV-1 prevalence, the major age group of HIV-1 infected travelers was 21–40 years (76.20%). The proportion of individuals aged 21–30 years increased annually. Although Jia et al. reported a decreasing tendency in the HIV-1 infection rate among those aged 31–40 years in the general population of Yunnan in 2010 [12], this was not observed in the current study population. This difference may be caused by the different study subjects; they focused on the general population. Drivers was accounted for the major occupation of the HIV-1 infected entry travelers due to the occupation limitations of entry personals in this study. Therefore, HIV monitoring on this sub-population is particularly necessary.”

(line 221-229)
such as the hepatitis C and B viruses is well documented to be very specific in Yunnan compared to other regions of China [28-30]. …… further understand cross-border HIV-1 transmission’. This paragraph doesn’t seem to have any bearing on the study topic what so ever and hence should be exempted.

**Answer:** we suggest to keep it. The diverse epidemiological characters of these blood-borne viral disease highlights the importance for monitoring the HIV-1 epidemic among cross-border travelers in this region. The appropriate modification has been given to make it more concise. “The epidemic of a variety of blood-borne viruses such as the hepatitis C and B viruses is well documented to be very specific in Yunnan compared to other regions of China [28-30].” has been changed to “The epidemic of a variety of blood-borne viruses was proven to be influenced by the transmitted strains from the Southeast Asian countries [28-30]. Cross-border travelers are the bridge population between China and Southeast Asian countries.”(Line 254-256)

12. Kindly include a paragraph on the various limitations observed during the study in the discussion section. For example, only a very small part of HIV-infected travelers had information on route of transmission, education, etc.

**Answer:** This study exactly faces several date limitations. It is our negligence that the date limitations of the study have not been discussed in our manuscripts. A paragraph has been added to discuss the limitations in detail in order to make up for such mistake. “Although the HIV-1 prevalence among these recruited 280,961 cross-border travelers who entered at major land ports in last decades were described, there are still several limitations need to be complemented. Firstly, there are 8 border prefectures in Yunnan; because of the lesser crossing border travelers and the irregular information, Nujiang Prefecture was excluded from this study. Secondly, the characteristics of HIV-1 prevalence among this recruited population was needed to be further confirmed due to the lack of detailed information for unwilling of some participants. Nevertheless, the monitoring on HIV-1 prevalence among this bridge population in last decades is
vital for understanding on the HIV-1 cross-bordering transmission.” (line 262-270)

13. In Table 1 Occupation total was reported for 2447, however, your total number of infected persons was 2380, so why the difference in totals? In addition, please use another word for “worker” as an occupation.

Answer: It is a real mistake; the data statistics is wrong. The corresponding error has been corrected in txt.

14. Reference 8: please indicate date you accessed because it is not available now.


Minor Essential Revisions

1. Background: paragraph 3 line 77 “Yunnan has the largest population of cross-border travelers after the Xinjiang Province, with most of these being from Southeast Asia” should rather be “Yunnan has the largest population of cross-border travelers after Xinjiang Province, with most of these travelers originating from Southeast Asia”. In addition, Xinjiang is not a “Province” in China.

Answer: This mistake had been modified, and “Xinjiang Province” had been replaced by “Xinjiang Autonomous Region”. (line 77)

2. Results: paragraph 1 line 134 “The annual recruited population (range, 31,749–45,495) did not differ significant between the sampling years” should be “The annual recruited population (range, 31,749–45,495) did not differ significantly
between the sampling years”.

**Answer:** This error has been corrected. “significant” in the previous sentence has been replaced by “significantly” (line 145)

3. Discussion: paragraph 5 lines 236 “The population of cross-border travelers at the Dehong port is larger than that at all other ports of the Yunnan Province” should be “The population of cross-border travelers at the Dehong port is larger than that of at all other ports of the Yunnan Province.”

**Answer:** It has been modified. “than that at all other ports of the Yunnan Province” in the previous sentence has been replaced by “than that of at all other ports of the Yunnan Province.” (line 245)

Discretionary Revisions

1. Can the phrase ‘iatrogenic infection’ be replaced by any other synonym that is easy to comprehend?

**Answer:** This is a technical term, it is difficult to find a common word to replace it.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

**Answer:** This manuscript has been sent to a professional language editing service (Editage) to ensure that the language is clear and free of errors.

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.
Reviewer's report

Title: Prevalence of human immunodeficiency virus 1 infection in the last decade among cross-border travelers who entered major land ports in the Yunnan Province, China

Version: 4 Date: 12 January 2015

Reviewer: Weiming Tang

Reviewer's report:

Major Compulsory Revisions

1. The author mentioned that the participants were randomly selected. How? This was not mentioned in the method part. I doubt that this is just a convenience samples;

   **Answer:** Sampling is completely random. The local staff of land ports has been required to invite one for routine physical examinations and HIV-1 testing every five-hundred travelers. The corresponding description has been added in the revised manuscript.
   (line 100-101): “The local staffs of land ports were required to invite one for routine physical examinations every five-hundred travelers.”

2. The author demonstrated that the HIV prevalence was decreased over time. I will not agree with this until author do the trend analysis.

   **Answer:** Due to the highly active antiretroviral therapy and effective prevention measures, HIV-1 infection rates is declining undoubtedly. According to 2013 Report on the Global AIDS Epidemic from UNAIDS, it was showed that “There were 2.3 (1.9–2.7) million new HIV infections globally, showing a 33% decline in the number of new infections from 3.4 (3.1–3.7) million in 2001.” Our result also presented a decreasing trend of HIV-1 infection rate over the past 10 years among the recruited entry travelers (it was expressed logically by fitted trend line in Fig 3.), although infection rate in 2006 and 2012 looks irregular.

3. The author should further stratify the participants into several groups, for example,
come from which country, since the HIV epidemic is different between countries and countries in southeast Asia.

**Answer:** Unfortunately, HIV-1 Infection rates of different population can’t be obtained accurately due to the lack of detailed information of whole cross-border travelers. Here, we use the proportion distribution of HIV-1 positive cases in different population to reflect infectious characteristics indirectly. The difference of HIV-1 infection rates definitely exist among the cross-border travelers who from different Southeast Asian countries. In spite of this, it is a good suggestion for our further investigation.

4. Do this study have any limitation? I did not see it in the discussion part, so for strength.

**Answer:** There is still several date limitations in this study. A paragraph has been added to discuss the limitations in detail in order to make up for this mistake.

(line 262-270): “Although the HIV-1 prevalence among these recruited 280,961 cross-border travelers who entered at major land ports in last decades were described, there are still several limitations need to be complemented. Firstly, there are 8 border prefectures in Yunnan; because of the lesser crossing border travelers and the irregular information, Nujiang Prefecture was excluded from this study. Secondly, the characteristics of HIV-1 prevalence among this recruited population was needed to be further confirmed due to the lack of detailed information for unwilling of some participants. Nevertheless, the monitoring on HIV-1 prevalence among this bridge population in last decades is vital for understanding on the HIV-1 cross-bordering transmission.”

**Minor Essential Revisions**

1. Non-consistent number of decimals, suggest to keep one decimal;

**Answer:** It has been modified. To make it more correct, all the value in this manuscripts has been changed to keep two decimal.
2, line 200, what is the reference for this? One of the epicenters?

**Answer:** Two references have been added. Exactly, Southeast Asia was considered as one of the epicenters. (line 209-211)


3, do not repeat results in discussion part.

**Answer:** We removed duplicate content (such as “However, the proportion of those aged 21–30 years declined from 38.32% in 2003 to 27.21% in 2012. In contrast, the proportion of those aged 41–50 years increased from 9.35% in 2003 to 27.21% in 2012.”).

4, delete line 245-248, not related information.

**Answer:** we suggest to keep it. The diverse epidemiological characters of these blood-borne viral disease highlights the importance for monitoring the HIV-1 epidemic among cross-border travelers in this region. The appropriate modification has been given to make it more concise. “The epidemic of a variety of blood-borne viruses such as the hepatitis C and B viruses is well documented to be very specific in Yunnan compared to other regions of China [28-30].” has been changed to “The epidemic of a variety of blood-borne viruses was proven to be influenced by the transmitted strains from the Southeast Asian countries [28-30]. Cross-border travelers are the bridge population between China and Southeast Asian countries.” (Line 254-256)

5, the statistical analysis part is too simple
**Answer:** Yes, we agree with you. The previous paragraph was changed to “All recruited individuals were categorized according to sampling year, ports' location, age and occupation. The statistical analysis was conducted using the SPSS, version 12.0 software package (SPSS Inc., Chicago, IL, USA). Characteristics were compared between the groups using $\chi^2$ tests, and results with $P$ values of $<0.05$ were considered statistically significant.” (line 126-130)

6, how the different variables were measured?
**Answer:** Detailed information of all recruited individuals is used for statistical analysis. All recruited individuals were categorized according sampling year and entering prefectures to analyze the yearly changing trend of HIV-1 infection and difference of HIV-1 prevalence among travelers who entry in different prefectures. A sentence has been added in “Statistical analysis” part: “All recruited individuals were categorized according to sampling year, ports' location, age and occupation. The statistical analysis was conducted using the SPSS, version 12.0 software package (SPSS Inc., Chicago, IL, USA).” (line 126-128)

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests