Author’s response to reviews

Title: HIV prevalence and factors associated with HIV infection among male injection drug users under 30: a cross-sectional study in Long An, Vietnam

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Author's response to reviews: see over
The BioMed Central Editorial Team
BMC Public Health

Dear Editors,

We would like to submit our revised manuscript entitled “HIV prevalence and factors associated with HIV infection among male injection drug users under 30: a cross-sectional study in Long An, Vietnam”. We have carefully considered all the comments and suggestions raised by reviewer 2, and have revised the manuscript accordingly. Our point-by-point responses were provided in separated sheets of paper. The changes we have made in the revised manuscript are underlined. The material has not been submitted for publication elsewhere and we wish it to be evaluated as a research paper for publication in “BMC Public Health” because the journal guarantees open access to all the readers in the world. The manuscript has been read and approved by all authors.

Sincerely yours,

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Dear Dr. Michael Clatts

We are very grateful for your incisive and important comments. We have incorporated your comments to the revised manuscript. Our responses and changes made in the revised manuscript are listed below point-by-point according to your comments.

P1. HCM City is not the capital.

[Authors’ response]
We apologize for the mistake. It was corrected in the revised manuscript (P5, L4 and P15, L3).

P7. It appears that low density settings were excluded, potentially skewing the types of subjects included in the study. Notably, the low density neighbourhoods might be more likely employed by IDU’s with a higher socio-economic status, noteworthy because the authors specifically note the potential significance of economic status in interpreting the results. While the use of this sampling approach is a reasonable approach to the problems of constructing at least broadly representative samples of out of treatment populations, these approaches are also vulnerable to exactly the kinds of undisclosed biases that seem to be operating here. This is not fatal, but it does require care and thought in interpreting the results. In explaining the sampling, the authors need to be more reflective about the potential biases, particularly in terms of socio-economic representation, that may be operant in sample construction and to be mindful of these issues in the subsequent interpretation of the data that is offered.

[Authors’ response]
We are grateful for your incisive and important comments. As the reviewer suggested, the study population may not be representative of the whole IDU population in the province because high-density communes were selected and snowball method was used to enroll participants. Since the additional purpose of selecting these hotspot communes was for the development and implementation of interventions, we have clarified these facts in the Method section of the revised manuscript. We also revised the results and discussion foregrounding this issue.

[Changes in the revised manuscript]
Abstract, Results, P3, L12:
The HIV prevalence among the studied IDUs was 32%.

Abstract, Conclusions, P3, L19:
About one-third of young IDUs aged less than 30 identified in the hotspot communes in Long An, Vietnam was found to be infected with HIV, and socio-demographic and injection-related factors might account for the infection risk.

Methods, Study area, P5, L6:
The province is also poor and characterized by its highly mobile population, FSWs and IDUs.

Methods, Geographical mapping and probability proportional to size (PPS) sampling, P5, L18:
An additional purpose of selecting these hotspot communes was for subsequent interventions. Thus, the target population of the present analysis can be described as IDUs who were identified in these hotspot communes, and they may not be representative of the whole IDU population in the province.

Discussion, P12, L2:
The major findings of the present study are that the prevalence of HIV among a relatively young IDU sample enrolled in the hotspot communes in Long An, Vietnam.

Discussion, P12, L18:
Because we sampled IDUs in the hotspot communes using the snowball method, they may not be representative of the whole IDU population in the province. Their socio-economic characteristics as well as the injection and sexual behaviors might have been similar reducing inter-individual variability in the variables. Although those aged 18 to 20 years seemed to be associated with higher HIV prevalence in the present sample, generalizability of the finding would be limited. Further studies are needed for better understanding of the risks associated with IDUs’ age on HIV infection.

Discussion, P13, L13:
Again, the present sample are not representative of the whole IDU population, so further studies using other sampling methods or with prospective design are needed to analyze the relation between the duration of injection drug use and HIV.

Discussion, P14, L1:
Because the population of the present study does not probably represent the variability in the studied variables which would have existed if the whole IDU population had been sampled, no firm speculation based on the statistical testing could be made.

Conclusions, P17, L10-12:
In summary, being 18 to 20 years old, low educational level, sharing injection equipment or injection drug use in the other cities were associated with HIV seroprevalence among the studied IDUs in the hotspot communes in Long An, Vietnam.
P7. The paper states that the interviews were done in field settings. Was the HIV testing also done in the field settings. Also, was agreement to testing a de facto eligibility criteria? In other words, could subjects participate if they did not want to be tested? Again, this issue is relevant to understanding potential biases since the research was conducted under the aegis of the Ministry of Health and many IDU’s would be very cautious about interactions with agencies of the Vietnam government.

[Authors’ response]
We are grateful for your pertinent comment. Agreement to HIV testing was not among the eligibility criteria, and the HIV testing was not done in the field setting but in a laboratory. Among 300 IDUs interviewed, 284 agreed to take blood testing. And blood draw was performed by a trained laboratory technician after the interview only if the IDU had agreed. We ensured that participation and blood testing were solely on a voluntary basis, and that measures had been taken to assure confidentiality. In general, health care workers in Vietnam are trusted by the high risk populations because of the care and support they often provide. We have reconstructed the Methods section as follows.

[Changes in the revised manuscript]
Methods, Participants, P6, L8:
The aforementioned investigators conducted face to face interviews with the assistance of survey supporters. These investigators (interviewers) were trained not only for the interview skills but also regarding the psychological aspect of IDUs to gain their full trust in order to have them talk honestly and then provide effective counseling. As mentioned above, interviewers were local health staff who had a certain level of knowledge and skills, and health care workers in Vietnam are generally trusted by the high risk populations because of the care and support they often provide. In each cluster, ten IDUs were interviewed using the snowball technique. Briefly, the first interviewee was randomly selected by the survey supporters at each location. After the interview, the interviewer asked the interviewee to introduce or invite another participant from among the IDUs he knew. The interviews continued until ten IDUs were enrolled. As described later, participants were also asked for HIV testing after his interview although agreement to HIV testing was not among the eligibility criteria. Interviewees were informed verbally about the objectives of the study, and that the result would be kept strictly confidential. They were also provided written information that briefly described the objective and content of the study, and the contact information with their identification numbers, which could be used to request their HIV test results by phone. In total, 300 IDUs were
interviewed and 284 had their blood tested in the present survey. Although the ages of the contacted IDUs ranged from 14 to 49 years old, we excluded 36 subjects (13%) who were 30 years old or more, leaving 248 subjects eligible for the present analysis. Participation was solely on a voluntary basis, and measures were taken to assure confidentiality. The study protocol and informed consent procedure were approved by the Hanoi Medical University Ethics Committee.

**Methods, Interview process and pre- and post-test counseling, P6, L9:**
If the participants agreed to take blood testing for HIV invited after the interview, a trained laboratory technician performed the blood draw. In any cases, the interviewers gave pre-test counseling explaining the importance of knowing their HIV serostatus, emphatically assured them as to the confidentiality of the information, and thus encouraged the participants to obtain their test results. Out of the 300 IDUs interviewed, 284 agreed to take HIV blood tests.

**Methods, Laboratory method, P9, L8:**
The blood test was conducted in a laboratory at the Provincial Center for Preventive Medicine

*P7. The authors use a lot of sampling jargon, often without definition or references. Adding some citations regarding these kinds of sampling approaches may make the article more accessible for readers who may not be familiar with these approaches to research in out of treatment populations.*

**[Authors’ response]**
We are grateful to your comment. As the reviewer suggested, we have provided the information about the references for constructing the sampling frame in the revised manuscript. We have added one reference and adjusted the reference number accordingly.

**[Changes in the revised manuscript]**
**Methods, Geographical mapping and probability proportional to size (PPS) sampling, P6, L4:**
The mapping process and sampling procedures followed the behavioral surveillance surveys guideline published by Family Health International[14].

**References:**
Some general comments on analysis, interpretation, and discussion:

It is not clear what the rational is for collapsing the response categories related to needle sharing and condom use into two groups, always and never. These extremes do not really illuminate the complexities of these practices and their potential interaction, presumably important questions related to the development of interventions......a stated goal of the paper. Since the data was collected using a continuous measure, why isn’t it being analysed as a continuous variable(?), elaborating variability in practices across time, setting, and social context. It is not clear what the underlying theory or model that is being used to underpin the analysis. In some places, the analyses seem to be wholly driven by the biological data and this seems to be problematic given the concern raised above regarding the fact that the two sources of behavioural risk have been collapsed into all or nothing groups.

[Authors’ response]
We are grateful to your pertinent comment. In the revised manuscript, we re-analyzed the data using the ordinal response categories of needle sharing and condom use. Because no HIV positive IDUs were in the category who had shared the needles almost every time, we combined every time and almost every time into one category.

Since multivariate logistic regression analyses incorporating both of the injection and sexual behaviors were difficult to perform practically as well as theoretically, we considered the logistic regression analysis as to the evaluation of the role of socio-demographic and injection-related factors while simultaneously controlling for possible confounding effects of age or other factors. And we did not examine variables related to sexual behaviors by logistic regression analyses in the present manuscript. The frequency of condom use with three types of sexual partners were presented separately in a new Table 5 according to HIV serostatus.

In the previous revision of the manuscript, we had created a variable in which a "yes" reply was assigned to those who had ever shared injection equipment and did not always use condoms. Be deleted this variable in response to adopting the original ordinal variables in the present analysis. We deleted the results and discussion related to this variable accordingly.

[Changes in the revised manuscript]
Abstract, Results, P3, L12:
Age range of 18-20 years old, low educational level, sharing injection equipment or injection drug use in the other cities were independently associated with HIV serostatus in the multivariate analysis.
Abstract, Results, P3, L15:
Among HIV seropositive IDUs who had sexual contact with primary (n=37), casual (n=6), and commercial (n=15) partners, only 5.4% (n=2), 33.3% (n=2), and 46.7% (n=7), respectively, responded that they had used condoms every time.

Methods, Variables, Factors related to injection, P8, L17:
The answer was assessed in 5 categories: never, sometimes, about half, almost every time, and every time. Because of the small number of participants who had responded almost every time (n=3) or every time (n=2), these two categories were combined.

Methods, Data management and statistical analysis, P9, L16:
We employed bivariate and multivariate logistic regression analyses with HIV serostatus as a dependent variable in order to evaluate the role of socio-demographic and injection-related factors while simultaneously controlling for possible confounding effects of age or other factors. Variables related to sexual behaviors were not examined by logistic regression analyses.

Results, P10, L22:
Once a day or more use of injection drugs, sometimes sharing of injection equipment or having used injection drugs in the other cities were associated with HIV seropositivity (age-adjusted OR: 1.70, 2.05 and 1.82, respectively).

Results, P11, L1:
Multivariate logistic regression analysis revealed that 18-20 years of age compared to the 14-17 group (OR: 3.30, P=0.034), and illiteracy/primary and secondly educational level compared to high school or more (OR: 2.37 and 2.07, P=0.045 and 0.044, respectively) were significantly associated with HIV serostatus (Table 3). Injection drug use in the other cities (OR: 1.69, P=0.089) and sometimes sharing injection equipments with others (OR: 1.91, P=0.082) were also associated with HIV serostatus with borderline significance.

Results, P11, L7:
The proportions of IDUs with multiple (2 or more) sexual partners were 41.7% (Table 4).

Results, P11, L10:
More than half (54.9%) of the IDUs who had sexual contacts with FSWs did not use condoms every time (Table 5). About one quarter of those who did not use condoms every time in their contacts with FSWs (28.6%, 8 out of 28) were HIV seropositive. Nearly all (94.1%) the IDUs reported that they did not use condoms every time in their contacts with their wives/girlfriends. Thirty-five out of 111 IDUs (31.5%) who did not use condoms every time with their wives/girlfriend were HIV seropositive.

Results, P11, L17:
Among 80 HIV seropositive IDUs, 5.0% (n=4) and 22.5% (n=18) had shared needles or syringes more than half the time, or at least sometimes, respectively in the previous month.
of the survey. Two out of four IDUs (50.0%) who had shared needles more than half times had never used condoms with their wife or girlfriend. Ten out of 18 IDUs (55.6%) who had sometimes shared needles had never used condoms with their wife or girlfriend. Similar, but less pronounced trend was observed among HIV negative IDUs (33.3% and 45.5%, respectively).

**Discussion, P12, L2-8:**
The major findings of the present study are that the prevalence of HIV among a relatively young IDU sample enrolled in the hotspot communes in Long An, Vietnam is 32%, and that 18–20 years of age, low educational level, sharing injection equipment or injection drug use in the other cities were independently associated with HIV serostatus. More than 1 out of 4 HIV infected IDUs were found to have shared needles in the previous month of the survey. About half of the IDUs who had shared needles never used condoms at their sexual contacts with primary partners regardless of the HIV serostatus.

**Conclusions, P17, L10-12:**
In summary, being 18 to 20 years old, low educational level, sharing injection equipment or injection drug use in the other cities were associated with HIV seroprevalence among the studied IDUs in the hotspot communes in Long An, Vietnam.

_I continue to be under-whelmed by the “television watching” data. It is not clear how this variable fits into the model, what theoretical foundation exists for the use of this model, and what basis is there is for interpreting this data. Moreover, without far more detailed assessments of media exposure, its hard to see that there is a firm foundation for offering any kind of coherent interpretation of these data._

_[Authors’ response]_ We are grateful to your incisive and important comment, and agreed that much more detailed assessment of media exposure would be needed to unfold the associations between HIV serostatus, risk behaviors, socio-economic status and variables related to media exposure. We deleted TV watching and radio listening data and related discussion from the present analysis.

_[Changes in the revised manuscript]_  
**Introduction, P4, L20:**
We evaluated the association of socio-demographic factors as well as their injection and sexual behaviors with HIV seroprevalence.

_I am sympathetic to some of the arguments made in the discussion but many of them seem to have little or no foundation in the data that is being presented. For example, while it is_
no doubt true that greater coordination between ministries would be helpful, it is not clear how we get to this conclusion from the data that has been presented.

[Authors’ response]
We are grateful to your incisive and pertinent comment. We deleted the general statement in the discussion that had not been derived from the present study.

[Changes in the revised manuscript]
Discussion, P12, L8:
These results first suggest that current measures have not been sufficient to reduce risk behaviors and concurrent sustained HIV epidemic in Vietnam, and that more efforts to reduce transmission risks of HIV infected IDUs would be needed.

In many places I see that the authors have inserted some of my earlier comments or questions into the text of the manuscript itself. This is not an appropriate approach to developing this kind of presentation and it will be virtually unintelligible to most readers since they will not have the context in which my original comments were offered.

[Authors’ response]
According to your comment, we revised some of the sentences in the introduction and discussion.

[Changes in the revised manuscript]
Introduction, P4, L15:
, which warrants investigations in relation to socio-demographic factors and HIV infection risk.

Discussion, P13, L3:
The duration of injection drug use or the age when beginning injection drugs was not associated with HIV serostatus in the present study, although it would reflect cumulative injection risk for HIV infection.

Discussion, P13, L19:
, and most of the IDUs adopted the injection habit within a year (73.0%) or one to two years (17.3%). But we did not find any association between the duration of the transition period and HIV seroprevalence (data not shown).

Discussion, P16, L17:
, and future study must obtain a valid measure of SES in order to contribute to the development of effectively targeted prevention activities (deleted as well as to disentangle the web of causation from childhood to young adult.)
Conclusions, P17, L12:
Prevailing risky sexual behavior of this extremely marginalized population highlights the need to reduce their high transmission risks as a public health priority.

Other changes
Thirty clusters were randomly selected using proportionate probability sampling from 29 communes, but the selected clusters actually belong to 19 communes. Although we described in the previous manuscript that 30 communes were selected under 19 communes, they were randomly selected from 29 communes. We revised the methods accordingly to avoid confusions.

Abstract, Methods, P3, L7:
Thirty clusters were selected from 29 hotspot communes in Long An province by probability proportional to size (PPS) sampling method.

Methods, Geographical mapping and probability proportional to size (PPS) sampling, P5, L22:
Using a probability proportional to size (PPS) sampling method, 30 clusters from 29 hotspot communes where 791 IDUs had been mapped were randomly selected. Only clusters in a commune that included at least 15 IDUs were eligible to be sampled.