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

Authors:

Thu Minh T Tran (thuminh1105@yahoo.com)
Hien N Tran (nthiennihe@vnn.vn)
Hiroshi Yatsuya (h828@med.nagoya-u.ac.jp)
Nobuyuki Hamajima (nhamajim@med.nagoya-u.ac.jp)
Akio Nishimura (nishimur@med.nagoya-u.ac.jp)
Katsuki Ito (katsuki@med.nagoya-u.ac.jp)

Version: 3 Date: 9 June 2006

Author's response to reviews: see over
9 June 2006

The BioMed Central Editorial Team
BMC Public Health

Dear Editors,

We would like to submit our revise 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 two reviewers, and have revised the manuscript accordingly. Our point-by-point responses were provided in separated sheets of paper. We have also changed the affiliation of one author (AN) since it had been changed after the initial submission. 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,

Submitting author
Dr. Hiroshi Yatsuya
Department of Public Health
Nagoya University Graduate School of Medicine
65 Tsurumai-cho, Showa-ku, Nagoya 466-8550
Japan
fax: 81-52-744-2131
tel: 81-52-744-2128
e-mail: h828@med.nagoya-u.ac.jp
Dear Dr. Andrei Kozlov

We are very grateful for your pertinent 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.

**General**

*This paper reports the results of an interesting and potentially important study of injection drug users (IDU) in Long An, Vietnam. There are limited data on HIV prevalence and risk behaviors of IDU from the Vietnam. The results provide clear evidence for the extent of the current HIV epidemic among IDU in Long An. The methods used in this study were appropriate. The results are clearly presented. The manuscript adheres to the relevant standards for reporting and data deposition. The writing is acceptable. At the same time there are several issues which should be clarified prior to publishing of this manuscript.*

[Authors’ response]

Thank you very much for your evaluation of our manuscript. Please see the changes we have made according to your suggestions as follows.

* The Methods section needs to be clarified in several points: population and sampling methods
  - The rationale for choosing Long An as a study area are not described.

[Authors’ response]

We are grateful for your important comment. We described population and sampling
methods in much more detail with newly created subheadings: Study area, Geographical mapping and probability proportionate cluster sampling, and Participants.

[Changes in the revised manuscript]

Methods, Study area, P6, L6:
Long An was chosen for the study because of its location and rapid increase in HIV prevalence. The province is also characterized by its highly mobile population. We selected 4 districts and the capital town as the study area within Long An because they are located along main roads and have borders with Ho Chi Minh City or Cambodia.

What were exactly the inclusion criteria for the study? How often people should be injecting in the previous month?

[Changes in the revised manuscript]

Methods, Geographical mapping and probability proportionate cluster sampling, P6, L13:
Male IDUs defined as men who used non-medically prescribed injection drugs a month previous to the survey, were included in the study no matter how often they had injected. There were no exclusion criteria. We confirmed whether the participant met this criterion at the time of interview.

- The rationale for not including women in the study are not described.

[Changes in the revised manuscript]

Methods, Geographical mapping and probability proportionate cluster sampling, P6, L16:
We did not include female IDUs in the present study because in-depth interviews earlier revealed them to be few in the province.
The characteristics of “hot spots” need to be described in more details.

[Authors’ response]

We are grateful for your incisive and important suggestion. Hotspot here refers to a commune with a high density of IDUs, drug dealers and mobile population. In the previous version of the manuscript, it had been confused with a cluster, which is the basic sampling unit, and was determined geographically in advance of the mapping. In this study, we first selected 4 districts and 1 town which have borders with Ho Chi Minh City or Cambodia. From 71 communes included in the selected area, 29 hotspot communes were identified by mapping. Using probability proportionate cluster sampling, we selected 30 clusters included in 19 hotspot communes. We have revised the manuscript accordingly.

[Changes in the revised manuscript]

**Methods, Geographical mapping and probability proportionate cluster sampling, P6, L17:**

We first mapped IDUs geographically based on the information from the survey supporters such as peer trainers of IDUs or FSWs, and officials from the Women’s or Youth Union or police station. A cluster, the basic sampling unit, was determined geographically in advance of the mapping. From 71 communes originally included in Long An Province, we further selected 29 hotspot communes that had a high density of IDUs, drug dealers and mobile population, places that could be considered hazardous for HIV transmission.

Where the interviews and blood testing took place?
Methods, Interview process and pre- and post-test counseling, P7, L16:
Interview and collection of blood sample were conducted wherever IDUs felt comfortable, e.g., in a corner of a park, on the street, in the place where they used injection drugs, in Karaoke bar, and in a friend’s house etc. A trained laboratory technician performed the blood draw before the interview.

- **How did participants get information about their HIV test results?**

Methods, Interview process and pre- and post-test counseling, P7, L20:
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.

- **How many participants (among 284) actually received their test results? What efforts were conducted by the study team to let know all the participants (especially, HIV positive) about their test result.**

Authors’ response
We are grateful for your important suggestions. Eighty percent of participants received their test results. The investigators were trained in advance of the survey how to gain IDUs’ trust. Assuming being trusted, the investigators emphasized the confidentiality of the information, and encouraged all the participants to receive their results. These measures were taken right after the interview for all the participants, thus no differential measures for the HIV-positive IDUs to receive their results had been employed. We
have revised the manuscript incorporating your suggestions.

[Changes in the revised manuscript]

Methods, Interview process and pre- and post-test counseling, P8, L1:
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.

Methods, Interview process and pre- and post-test counseling, P8, L4:
Out of the 300 IDUs interviewed, 284 agreed to take HIV blood tests. Among the 284 IDUs blood tested regardless of age, 227 (80%) received their test results.

- Did participants receive Pre- and Post- HIV test counseling? If “Yes”, who did provide it?

[Authors’ response]
We are grateful for your important suggestions. As mentioned earlier, all the participants received pre-test counseling and 80% received post-test counseling.

[Changes in the revised manuscript]

Methods, Interview process and pre- and post-test counseling, P8, L3:
Pre-test counseling was provided after the interview.

Methods, Interview process and pre- and post-test counseling, P8, L5:
The staff did not inform them of their test results without providing counseling. Post-test counseling was given when participants called in for the test results. IDUs with HIV negative test result received counseling by telephone or at the office. IDUs with positive test results were given brief counseling by phone, and then asked to come to the office to obtain their results with complete post-test counseling.
**Methods, Interview process and pre- and post-test counseling, P8, L10:**

The 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.

*Results/Discussion*

_The factor which is significantly associated with HIV infection such as injecting in other cities needs to be explained in more details._

Did the researchers find out the specific cities where participants have been traveling to? If “Yes”, what were HIV prevalence rates in those areas?

[Authors’ response]

We are grateful for your incisive and important comments. Most of the IDUs who gave affirmative answer to the question had gone to Ho Chi Minh City, where HIV prevalence among IDUs was reported to be highest in Vietnam (73.6%). We have revised the manuscript incorporating your suggestions.

[Changes in the revised manuscript]

**Discussion, P16, L3:**

Among those who had used injection drugs in other cities, 91.3% migrated to the capital, Ho Chi Minh City, where the prevalence of IDU is the highest in Vietnam (73.6%) according to the report from the AIDS division, Ministry of Health, Vietnam.

**Discussion, P16, L5:**

It could be that those mobile IDUs had spread HIV infection from city to city. Epidemiologically, migrants have been known to be vulnerable to HIV risk [23, 33].
Riskier sexual behaviors were reported in traveling individuals with HIV [34]. Migration is often related to IDUs socioeconomic status (SES), and economic distress may have affected the IDUs who gave an affirmative answer to this question. Such conditions usually accompany a situation with limited access to appropriate information on HIV. Moreover, mobile IDUs may have visited shooting galleries where transmission risk of HIV would be high [35]. Less availability of social support was also reported in migrant IDUs, and was presumably associated with their risk-taking behaviors [36]. At the same time, there may be sexual or addiction-related motives that have driven them to cities where a certain social network exists despite their knowledge of the risks involved.

* The title of the manuscript seems to be more adequate to study findings if the authors will change it to “HIV prevalence and Factors associated with HIV infection among male IDU in Long An, Vietnam”

[Authors’ response]

We agreed to your suggestions. We have changed the title of the manuscript as following. As the reviewer 2 suggested, we have limited the analysis to IDUs under the age of 30, this change have also been incorporated into the title.

[Changes in the revised manuscript]

Title, P1, L1:

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

* In the laboratory method section seems to be important to describe in more details
Testing Strategy III (for example, ELISA was conducted only for HIV positives in quick test or for all tests)

[Authors’ response]
We are grateful for your important comment. We have corrected the manuscript.

[Changes in the revised manuscript]

Methods, Laboratory method, P10, L11:
The blood test was conducted using Testing Strategy III from the Viet Nam Protocol of HIV testing, which included one quick test and two ELISA Screening tests to confirm HIV seropositivity. Those with positive results in all the three tests were considered as HIV seropositive.

* Not clear for what reasons in the results section the authors include information about statistically non significant association (A higher educational level seemed to be associated with a lower prevalence of HIV....)

[Authors’ response]
We are grateful for your comment. We have deleted the statements from Results describing statistically non-significant (P>0.1) associations.

* The sentences “In the present study, 65,5% of IDUs started their injection drug use in the year 2000 or later.” And next one could be removed because sound confusing.

[Authors’ response]
We are grateful for your suggestion. We have deleted the sentence. As the reviewer 2 suggested, we have limited the analysis to IDUs under the age of 30, some of the figures presented in the manuscript have changed.
Results, P11, L20:

In the present study sample, 69.8% of IDUs started their injection drug use in the year 2000 or later (Table 2).
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.

**General**

_The potential significance of this paper is that it adds to the growing body of evidence about the rapid spread of HIV infection and other negative public health outcomes among heroin users in Vietnam. While heroin epidemics in neighboring countries within the Golden Triangle (including China and Thailand) have been extensively described, there is comparatively little information about this issue from Vietnam. Particularly important is the fact that the current epidemic is largely situated in youth and young adult populations. Consistent with other reports, the paper shows that HIV infection is spreading rapidly in Vietnam, fueled by both high risk injection practices associated with chronic heroin use as well as by co-morbid sexual risk (including low condom use with both regular and CSW sex partners). Combined, these factors portend the potential for a large and self-sustaining HIV epidemic in this country. The fact that the data show high rates of infection among relatively young adult IDUs highlights the urgent need for prevention activities. To the extent that this data may inform the development of such activities, it is potentially significant and therefore merits publication. There are a number of problems with the current manuscript that warrant reconsideration. First, the paper needs a thorough editing. There are numerous lapses in grammar, sentence structure, and overall flow which detract from easy comprehension of the material. The_
various sections are not entirely coherent. For example, some of the material in the discussion section should appear earlier in the paper and used to foreground the substantive issues considered in the paper.

[Authors’ response]

Thank you very much for your pertinent and important comments and evaluation of the potentiality of our manuscript. We had the manuscript English-proved by an America-born English editor. We have reconsidered the manuscript entirely as to incorporate your general comments into the revised manuscript to clarify the aim of the present study in Background, Discussion, and Conclusion. We have also repeatedly stated that this study should serve for better understanding of IDUs’ transmission risk within and from IDUs in order to develop effective targeted HIV prevention activities.

[Changes in the revised manuscript]

Abstract, Background, P3, L2:

Sufficient targeted HIV prevention activities aiming at reducing HIV transmission within and from an extremely marginalized population of injection drug users (IDUs) must urgently and efficiently be implemented in Vietnam. This study was conducted to facilitate the development of such activities by describing transmission risks of young IDUs and evaluating factors in association with HIV infection.

Abstract, Conclusions, P3, L21:

Socioeconomic status and the severity of addiction might account for the risk clustering and the associations with HIV, which warrant detailed assessment of drug and sex initiation and their chronological changes in relation to socioeconomic status. Prevailing risky sexual behavior of this extremely marginalized population highlights the need to reduce their high transmission risks as a public health priority.
Background, P5, L9:
…., assessment of the behavioral risks of IDUs for both themselves and other population including women and children is highly important, and urgently needed especially in Vietnam, where there is little information about this issue compared to other countries located near the Gold Triangle, one of the places producing the largest amount of drugs in the world [9, 10]

Background, P5, L14:
…., which warrants investigations as to how and why socio-demographic factors may be related to HIV infection risk.

Background, P5, L18:
…., which also highlights the urgent need for prevention activities in young IDUs.

Background, P5, L18:
This study was conducted to facilitate the development of such targeted HIV prevention activities aiming at reducing HIV transmission within and from IDUs based on harm-reduction strategies.

Discussion, P13, L12:
These results first suggest that current measures have not been sufficient to reduce risk behaviors and concurrent sustained HIV epidemic, and that more and more co-ordination between the ministries and the agencies involved in HIV/AIDS and drug programs is needed, to create policies for a supportive environment for changing both drug use and HIV risk behaviors.

Discussion, P15, L20:
The present results should be used to enhance or modify the development of such measures as to monitor risk behaviors in hidden populations and to improve preventive
strategies to reduce transmission risk as a public health priority not only in Vietnam but in other countries as well.

**Conclusions, P19, L3:**

…, prevailing risky sexual behavior of this extremely marginalized population highlights the need to reduce their high transmission risks as a public health priority. These findings also indicate the importance of addressing these issues through various media including behavior education, supplying clean needles and syringes, condom distribution, and encouragement of HIV testing [7, 38, 39] as an efficient way to reach out to these hidden populations.

*A number of the measures that are used in the analysis are not adequately described. The time frames are not always clear. It is not clear how SES was assessed.*

[Authors’ response]

We divided Methods section with several subheadings into "Study area", "Geographical mapping and probability proportionate cluster sampling", "Participants", "Interview process and pre- and post-test counseling", "Variables", "Laboratory method", and "Data management and statistical analysis". We revised them with adequate descriptions for each part taking account of time frames. We obtained socio-demographic information such as martial status, people with whom they were living, or educational level, but not economic status. We have pointed out this fact as one of the limitations of the present study in the Discussion.

[Changes in the revised manuscript]

**Methods, Study area, P6, L8:**

We selected 4 districts and the capital town as the study area within Long An because
they are located along main roads and have borders with Ho Chi Minh City or Cambodia.

Methods, Geographical mapping and probability proportionate cluster sampling, P6, L20:

From 71 communes originally included in Long An Province, we further selected 29 hotspot communes that had a high density of IDUs, drug dealers and mobile population, places that could be considered hazardous for HIV transmission. We then mapped IDUs geographically based on the information from the survey supporters…

Methods, Participants, P7, L7:

In each cluster, the aforementioned investigators interviewed ten IDUs face to face using the snowball technique with the assistance of survey supporters.

Discussion, P18, L1:

Second, we did not obtain detailed information on the participant SES, nor did we inquire as to the reason why the IDUs had gone to other cities and used injection drugs there. As mentioned in the earlier discussion of this issue, SES, both at the individual, family or community level, would have had a significant impact on the behavior risks, and future study must obtain valid measure of SES in order to contribute to the development of effectively targeted prevention activities as well as to disentangle the web of causation from childhood to young adult.

The authors are clearly attempting to disentangle age and onset of risk but the discussion is not entirely clear and the data itself may not fully support this effort. For example, it would seem that age and person years of injection risk are the key variables of interest, but it is not clear if this is really what is being examined in the model. There
is no discussion of the fact that many IDU’s begin as heroin smokers and that the early
course of habitual heroin use may be marked by substantial movement back and forth
between these two modes of administration. This introduces substantial "noise" into the
kind of analysis that is put forward in the paper. In short, the authors seem to be having
some difficulty in adequately disentangling age, period, and cohort factors in the data,
or at least this is not clear in the presentation.

[Authors’ response]
We are grateful for your incisive comments. As you suggested, current age, the year and
age of initiation and cumulative duration of injection are key factors determining
injection risk of HIV infection. Of these variables, only age was associated with HIV in
the present study. And because the present sample is relatively skewed in terms of these
variables, we could not evaluate the inter-relationships among them. We have pointed
out this fact in the Discussion. In terms of the issue related to acquiring injection habit,
we have calculated mean age (year) at which IDUs started using drugs or injection
drugs. But we did not obtain detailed information regarding this issue, therefore we
have indicated the fact incorporating your suggestion. Furthermore, frequency of
injection drug use was incorporated into the analysis, but detailed assessment of drug
use history including its chronological change in intensity had not been performed, we
have discussed this issue. We have added four references in Discussion (reference no.
14, 18, 22, and 23).

[Changes in the revised manuscript]

Methods, Variables, Factors related to injection, P9, L10:
Their injection frequency in the previous month was assessed and grouped into two
categories (once a day or more or others).

**Results, P11, L21:**
The mean ages when IDUs began using drugs or injection drugs were 19.0 and 19.4 years old, respectively.

**Results, P12, L3:**
Once a day or more use of injection drugs, sharing injection equipment or having used injection drugs in the other cities were associated with HIV seropositivity (age-adjusted OR: 1.70, 1.93 and 1.82, respectively).

**Results, P12, L18:**
Multivariate logistic regression analysis revealed that 18-20 years of age compared to 14-17 group, (OR: 3.24, P=0.041), once a day or more use of injection drugs (OR: 1.80, P=0.057), and once a week or more TV watching (OR: 0.49, P=0.047) were associated with HIV serostatus (Table 4).

**Discussion, P13, L5:**
The major findings of the present study are that the prevalence of HIV among a relatively young IDU sample in Long An Province in Vietnam is 32%, and that 18-20 years of age, infrequent (less than once a week) TV watching, and frequent (once a day or more) use of injection drugs were independently associated with HIV.

**Discussion, P13, L10:**
Consistent with the previous reports [14], frequent use of injection drugs was associated with HIV,

**Discussion, P14, 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
person-years of injection risk for HIV infection [4, 18, 19].

**Discussion, P14, L14:**

In addition, the adoption of injection reportedly occurred within a year on average [22], and a short transition period was reported to be an HIV risk [23]. We also found that the mean ages of IDUs when they started using drugs were only slightly lower than when they became injectors (19.0 vs. 19.4 years old, respectively). Although we could not evaluate the inter-relationships among acquiring the habit, duration of injection, and cumulative injection risk in the present dataset, the fact that many IDUs begin as heroin smokers and that the early course of habitual heroin use may be marked by substantial movement back and forth between these two modes of administration warrants further investigation regarding the determinants of injection initiation for a better understanding of their risk perception and for more effective HIV prevention.

**Discussion, P17, L14:**

In terms of drug use-related inquiries, individual and contextual level factors related to injection initiation, chronological change in the level or pattern of drug use together with that of sexual activities, and characteristics of the drug use network should be assessed in future studies from both epidemiological and preventive points of view.

**Conclusions, P18, L20:**

In summary, being 18 to 20 years old, frequent injection drug use, and no habitual TV watching were associated with HIV seroprevalence.

*It might have been helpful to limit the analysis to a narrow age range within the overall data set. For example, limiting the analysis to IDU’s under the age of 30, while reducing the sample available for the analyses, might eliminate some of the "noise" that*
seems to be confounding the model and yield a more straightforward picture of the risk trajectories of interest.

[Authors’ response]

According to your suggestion, we have limited the analysis to IDUs under the age of 30, which excluded 36 subjects from the earlier sample.

[Changes in the revised manuscript]

Title, P1, L1:
HIV prevalence and factors associated with HIV infection among male injection drug users under 30: a cross-sectional study in Long An, Vietnam

Abstract, Methods, P3, L9:
The cross-sectional association of factors obtained during direct structured interviews to 248 male IDUs aged 14 to 29 years old and with their HIV test results were examined.

Abstract, Results, P3, L12:
The HIV prevalence among the IDUs was 32%.

Methods, Participants, P7, L12:
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.

Results, P11, L11:
The prevalence of the HIV infection was 80 (32%) among the 248 IDUs aged 29 years old or less.

This applies to the overall age of the sample, but also to some of the subgroups included in the sub-analysis. For example, age 10 to 20 spans a broad spectrum of time, both
historical and developmental, and is probably too complex a grouping to be useful.

As with upward age boundary, it might have been more useful to exclude age outliers so as to reduce the overall noise that inclusion of these cases introduces in the analysis of the data.

[Authors’ response]

According to your incisive suggestion, we have revised the manuscript using new age-category: 14-17, 18-20, 21-24, and 25-29 years old. We have also changed their initiation age-category: 10-17, 18-20, 21-24, and 25-29 years old. Subtle change in the category, for example, 18-19, 20-24, did not substantially change the results.

[Changes in the revised manuscript]

Methods, Variables Socio-demographic factors, P8, L21:

…, and the participants were categorized into those aged 14-17, 18-20, 21-24, and 25-29 years old.

Methods, Variables Factors related to injection, P9, L8:

Their initiation age was categorized into 4 groups (10-17, 18-20, 21-24, and 25-29 years old) for the analyses.

Results, P11, L14:

The proportion of the IDUs aged 17 years or younger, 18 to 20 years, 21 to 24 years and 25 to 29 years was 11.3%, 33.5%, 38.3%, and 16.9%, respectively.

Results, P11, L22:

The proportions of IDUs who started injection drugs at ages 10-17, 18-20, 21-24, and 25-29 were 27.4%, 41.5%, 24.2%, and 6.8%, respectively.

Results, P12, L18:

Multivariate logistic regression analysis revealed that 18-20 years of age compared to
14-17 group, (OR: 3.24, P=0.041), once a day or more use of injection drugs (OR: 1.80, P=0.057), and once a week or more TV watching (OR: 0.49, P=0.047) were associated with HIV serostatus (Table 4).

**Discussion, P13, L17:**

Males aged 18 to 20 years old had a significantly higher HIV seroprevalence in the IDUs, and the association was independent of other factors.

*I am not an expert on logistic regression but I am not sure that this kind of data is best examined with this kind of approach. The kind of analysis that is being attempted here appears to be somewhat different (albeit more interesting and potentially useful!) than that which was originally intended in constructing the measure, with the result that I am not entirely sure that a regression model is the best way to approach or present the data, particularly in the absence of a theoretical model. A paired T-test model might be more straightforward approach to the presentation. At the very least, however, a more straightforward statement of the regression model is needed.*

[Authors’ response]

As the reviewer suggested, we have revised the tables by showing the proportions of each factor according to HIV serostatus. Differences in the proportions were tested by $\chi^2$ tests. Continuous variables were tested unpaired Student t-test. Because no within individual comparison could be performed, we did not employ paired t-test. Bivariate and multivariate logistic regression analyses were conducted in order to evaluate the role of certain factors while simultaneously controlling for possible confounding effects of age or other factors. The model was not constructed for predicting individual estimates of risk. In addition, since there were a strong correlation between the ages of
the IDUs at the time of the survey and when they started injection (Pearson’s $r=0.75, P<0.001$), we did not perform age-adjusted logistic regression analysis against the injection initiation age to avoid collinearity that might have occurred.

[Changes in the revised manuscript]

Methods, Data management and statistical analysis, P10, L17:
Differences in proportions between HIV positive and negative IDUs were tested by $\chi^2$ tests. Continuous variables were compared by Student $t$-tests. We employed bivariate and multivariate logistic regression analyses with HIV serostatus as a dependent variable in order to evaluate the role of certain factors while simultaneously controlling for possible confounding effects of age or other factors. The model was not constructed for predicting individual estimates of risk.

Methods, Data management and statistical analysis, P11, L2:
Bivariate logistic regression against the injection initiation age was not performed to avoid collinearity that might have occurred if age had been adjusted due to a strong correlation between the ages of the IDUs at the time of the survey and when they started injection (Pearson’s $r=0.75, P<0.001$).

There are clear limitations to the data and the authors acknowledge some of these limitations in the latter sections of the paper. However, a more substantive discussion would give better direction to the next generation of IDU studies that are needed in Vietnam and would enhance the contribution that the paper might make to the literature.

[Authors’ response]
We are very grateful for your incisive and important comment. As you suggested, we
have revised the manuscript by discussing more substantive issues in order to encourage future IDU studies. We have added two reference (reference no. 37 and 38).

[Changes in the revised manuscript]

Discussion, P13, L12:
These results first suggest that current measures have not been sufficient to reduce risk behaviors and concurrent sustained HIV epidemic, and that more and more co-ordination between the ministries and the agencies involved in HIV/AIDS and drug programs is needed, to create policies for a supportive environment for changing both drug use and HIV risk behaviors.

Discussion, P17, L5:
About one-third of IDUs (n=80), all of whom identified themselves as never married, did not answer to the questions dealing with their sexual behavior. Although we obtained similar results from sensitivity analyses conducted as if these people had had either no or five or more sexual partners, caution is needed due to possible misclassification of the variable.

Discussion, P17, L9:
In addition, we did not include any inquiries related to concurrency in partnership or homosexuality because we have paid less attention to the latter issue in Vietnam [37]. It is imaginable that disclosure of this issue may also be limited, and thus we have probably been underestimating the actual situation. Further investigations with an appropriate assessment of these issues are needed possibly using some device to guarantee complete privacy.

Discussion, P17, L14:
In terms of drug use-related inquiries, individual and contextual level factors related to
injection initiation, chronological change in the level or pattern of drug use together
with that of sexual activities, and characteristics of the drug use network should be
assessed in future studies from both epidemiological and preventive points of view [38].

**Discussion, P17, L18:**
The number of needles exchanged in the area could be used as a surrogate measure of
needle sharing.

**Discussion, P18, L1:**
Second, we did not obtain detailed information on the participant SES, nor did we
inquire as to the reason why the IDUs had gone to other cities and had used injection
drugs there. As mentioned in the earlier discussion of this issue, SES, both at the
individual, family or community level, would have had a significant impact on the
behavior risks, and future study must obtain valid measure of SES in order to contribute
to the development of effectively targeted prevention activities as well as to disentangle
the web of causation from childhood to young adult.

**Discussion, P18, L8:**
In future studies, not just general knowledge about HIV/AIDS of the IDUs but what has
been causing barriers for behavior modification should be investigated. Health beliefs of
IDUs should also be evaluated. Other psychiatric disorders including depression,
post-traumatic disorders, and childhood abuse should be associated with their risk
behaviors. In addition, other quantifiable assessments of drug use such as blood or urine
test may well be combined.

**Discussion, P18, L16:**
Ideally, prospective observation or interventional studies should also be conducted.
On the face of it, TV watching appears to be a somewhat trivial association and the readers need to expand upon the way that this and related variables might inform our understanding of how and why SES impact behavioral risk.

[Authors’ response]
As the reviewer suggested, there would probably be unmeasured confounding factors especially in the socioeconomic domain that could explain at least some part of the present findings related to TV or radio. We have revised the manuscript accordingly.

[Changes in the revised manuscript]

Discussion, P16, L21:
These associations may be trivial because there are other unmeasured confounding factors especially in the socioeconomic domain that could explain the possible effect of TV or radio. However, since there is a possibility that information disseminated through the media could have kept the IDUs from risky behaviors [13], the role of information media in possibly modifying behaviors should be studied more extensively.

Similarly, more detailed consideration of the import of movement between cities, which is likely to be related to economic migration, may have on behavioral risk. These issues are especially import in considering targeted prevention activities, but they are not adequately elaborated in the discussion to be really useful.

[Authors’ response]
We are grateful for your incisive suggestion. We have revised the manuscript describing the possible existence of economic distress that had used injection drugs in other cities, and as to how the socioeconomic status impact behavioral risk. We have added two references (reference no. 35 and 36).
Among those who had used injection drugs in other cities, 91.3% migrated to the capital, Ho Chi Minh City, where the prevalence of IDU is the highest in Vietnam (73.6%) according to the report from the AIDS division, Ministry of Health, Vietnam. It could be that those mobile IDUs had spread HIV infection from city to city. Epidemiologically, migrants have been known to be vulnerable to HIV risk [23, 33]. Riskier sexual behaviors were reported in traveling individuals with HIV [34]. Migration is often related to IDUs socioeconomic status (SES), and economic distress may have affected the IDUs who gave an affirmative answer to this question. Such conditions usually accompany a situation with limited access to appropriate information on HIV. Moreover, mobile IDUs may have visited shooting galleries where transmission risk of HIV would be high [35]. Less availability of social support was also reported in migrant IDUs, and was presumably associated with their risk-taking behaviors [36]. At the same time, there may be sexual or addiction-related motives that have driven them to cities where a certain social network exists despite their knowledge of the risks involved.

*Clearly, longitudinal work is needed but it would be helpful if the paper could give some direction to how those studies should proceed in relation to sampling and measurement, and indeed better direction to what the core questions should be for understanding effects over time. For example, the authors acknowledge that it is sometimes difficult to obtain reliable assessments of behavioral risk among IDUs in Vietnam due to substantial social desirability. Some discussion of how this relates to particular variables and what alternative approaches (e.g., in measurement, sampling, design,*
construct development, etc.) would be helpful. Similarly, there are clear problems with self-reported needle sharing and some creative thinking about how to enhance measurement of this issue would be useful.

[Authors’ response]

We are grateful for your important comments and suggestions. As you suggested, there is substantial social desirability which might have seriously affected the present findings. For example, about one-third of IDUs did not answer to the questions dealing with their sexual behavior. We did not include questions related to concurrency in partnership or homosexuality. In addition, despite their knowledge of the risks involved, IDUs might have been keeping their risk behaviors, and have answered their own desirability. We have discussed these issues in Discussion, and also raised some alternative approaches to obtain valid measure of these variables. Finally, in terms of the core questions to be used to understand the effects over time, we still think those would be sharing of needles and use of condoms.

[Changes in the revised manuscript]

Discussion, P17, L5:

About one-third of IDUs (n=80), all of whom identified themselves as never married, did not answer to the questions dealing with their sexual behavior. Although we obtained similar results from sensitivity analyses conducted as if these people had had either no or five or more sexual partners, caution is needed due to possible misclassification of the variable.

Discussion, P17, L9:

In addition, we did not include any inquiries related to concurrency in partnership or homosexuality because we have paid less attention to the latter issue in Vietnam [37]. It
is imaginable that disclosure of this issue may also be limited, and thus we have probably been underestimating the actual situation.

**Discussion, P17, L12:**

Further investigations with an appropriate assessment of these issues are needed possibly using some device to guarantee complete privacy.

**Discussion, P17, L14:**

In terms of drug use-related inquiries, individual and contextual level factors related to injection initiation, chronological change in the level or pattern of drug use together with that of sexual activities, and characteristics of the drug use network should be assessed in future studies from both epidemiological and preventive points of view.

**Discussion, P17, L18:**

The number of needles exchanged in the area could be used as a surrogate measure of needle sharing.

**Discussion, P18, L8:**

In future studies, not just general knowledge about HIV/AIDS of the IDUs but what has been causing barriers for behavior modification should be investigated. Health beliefs of IDUs should also be evaluated. Other psychiatric disorders including depression, post-traumatic disorders, and childhood abuse should be associated with their risk behaviors.

**Discussion, P18, L11:**

In addition, other quantifiable assessments of drug use such as blood or urine test may well be combined.

*And finally, some direction about the interaction between drug and sexual risk would be*
most welcome.

[Authors’ response]

We are grateful for your incisive suggestion. In addition to discussing the issue in
Discussion, we have incorporated your suggestion into the present study. We have
created a new variable in which a "yes" reply was assigned to those who shared
injection equipment and did not regularly use condoms. We presented the association of
this new variable with HIV serostatus in another table (Table 3) with other results
related to sexual behavior. We have found that clustering of sharing needles and
unprotected sex behaviors were associated with frequent use of injection drugs,
injection in other cities, and infrequent radio listening, which implied that SES and the
severity of addiction may account for these findings. In the last place, we agree with
your suggestion that detailed assessment of drug and sex initiation and their
chronological changes in relation to individual and contextual level SES are especially
needed.

[Changes in the revised manuscript]

Methods, Variables, Clustering of risk behaviors, P10, L5:

Clustering of risk behaviors: Because targeted HIV prevention activities among IDUs
emphasize the importance of using clean needles and condoms, we created a new
variable in which a "yes" reply was assigned to those who shared injection equipment
and did not regularly use condoms. Those who failed to respond to the question on
regular condom use were considered as a "no" reply regarding this variable.

Methods, Data management and statistical analysis, P11, L6:

We also performed another multivariate logistic regression analysis taking clustering of
risk behaviors as a dependent variable and other variables as independent variables.
Results, P12, L15:
Clustering of sexual and injection risk behaviors of IDUs not regularly using condoms and sharing injection equipment was significantly associated with HIV seropositivity (age-adjusted OR: 2.32, P=0.035).

Results, P12, L21:
Another multivariate logistic regression analysis evaluating the association of IDUs’ socio-demographic and injection characteristics with clustering of risk behaviors revealed once a week or more radio listening (OR: 0.39, P=0.053), once a day or more use of injection drugs (OR: 2.69, P=0.032), and having used injection drugs in other cities (OR: 2.78, P=0.013) as significant or nearly significant factors.

Discussion, P13, L8:
We also found that clustering of sharing needles and unprotected sex behaviors were associated with frequent use of injection drugs, injection in other cities, and infrequent radio listening.

Discussion, P16, L11:
Moreover, mobile IDUs may have visited shooting galleries where transmission risk of HIV would be high [35]. Less availability of social support was also reported in migrant IDUs, and was presumably associated with their risk-taking behaviors [36]. At the same time, there may be sexual or addiction-related motives that have driven them to cities where a certain social network exists despite their knowledge of the risks involved.

Conclusions, P18, L21:
The use of injection drugs once a day or more and in other cities were associated with the clustering of two risk behaviors of sharing needles and no condom use.
In short, the potential strength of this paper comes from the experience of the research group from which it is coming and the opportunity that the data afford us all in beginning to understand how the HIV epidemic is unfolding in Vietnam. More substantive comment on what has been learned, not just from the data itself but more broadly from the research effort more generally, would enhance the contribution that this paper could make to the emerging literature on HIV in Vietnam.

[Authors’ response]

We are especially grateful for your evaluation of the potentiality of our manuscript. We have revised the manuscript by describing the survey methods in much more detail in order to facilitate further investigations that should overcome the shortcomings of the present study. We have stated substantive limitations contained in the present study in Discussion and future directions of IDU studies.

[Changes in the revised manuscript]

Discussion, P14, L19:

…, the fact that many IDUs begin as heroin smokers and that the early course of habitual heroin use may be marked by substantial movement back and forth between these two modes of administration warrants further investigation regarding the determinants of injection initiation for a better understanding of their risk perception and for more effective HIV prevention.

Discussion, P17, L12:

Further investigations with an appropriate assessment of these issues are needed possibly using some device to guarantee complete privacy.

Discussion, P17, L14:

In terms of drug use-related inquiries, individual and contextual level factors related to
injection initiation, chronological change in the level or pattern of drug use together with that of sexual activities, and characteristics of the drug use network should be assessed in future studies from both epidemiological and preventive points of view.

**Discussion, P17, L18:**
The number of needles exchanged in the area could be used as a surrogate measure of needle sharing.

**Discussion, P18, L4:**
…, and future study must obtain valid measure of SES in order to contribute to the development of effectively targeted prevention activities as well as to disentangle the web of causation from childhood to young adult.

**Discussion, P18, L8:**
In future studies, not just general knowledge about HIV/AIDS of the IDUs but what has been causing barriers for behavior modification should be investigated. Health beliefs of IDUs should also be evaluated. Other psychiatric disorders including depression, post-traumatic disorders, and childhood abuse should be associated with their risk behaviors.

**Discussion, P18, L11:**
In addition, other quantifiable assessments of drug use such as blood or urine test may well be combined.

**Discussion, P18, L16:**
Ideally, prospective observation or interventional studies should also be conducted.

**Conclusions, P19, L1:**
…, which warrant detailed assessment of drug and sex initiation and their chronological changes in relation to individual and contextual level SES.