**Reviewer's report**

**Title:** Syndemics of syphilis, HCV infection, and methamphetamine use along the east coast of China

**Version:** 4  
**Date:** 6 December 2013

**Reviewer:** Geneviève van Liere

**Reviewer's report:**

Review

The authors successfully rewrote the introduction, methods and results. The current manuscript is more concise and clear. However, the discussion is still unstructured and needs to be further improved.

Unfortunately, a point-by-point response to the reviewer was still lacking, although I requested this three times. I had to search the entire manuscript to find sentences that had been removed or rewritten according to my comments. Because the quotes were missing, it was often not clear what the authors added and removed from the manuscript. For example comment 2.22, this sentence is not in the manuscript anymore, while the authors claim it was moved to the introduction. Moreover, a substantial part of comments were not (adequately) addressed or only partly addressed. For example comment 2.20. This gives the impression that the authors are indifferent towards the response. Quotes were only present in one comment (2.10), however the authors ignored the effect modification. Additionally, track changes was not used correctly. For example, it is impossible to find out what the authors have changed in the abstract. Altogether, this made the review process time consuming.

Previous comments not adequately addressed.

9. How did the recruitment took place? How many participants were recruited through which recruitment strategy? A flow chart could be informative to present recruitment.

It is still not clear how many participants were recruited through which recruitment strategy.

10. Recruitment criterium; participants should be willing to complete the study. This leads to a selection bias, and should be mentioned in the discussion. How many people were recruited/asked and how many agreed to participate in the study?

It is still not clear how many people were recruited/asked and how many agreed to participate in the study. The sentence ‘It could be another limitation that non-response or refusal of the participation was not collected.’ is unclear and grammatically incorrect. Information on study participation is an important measure of the quality of the study. For example, if 50 drug users were recruited...
and only 1 participated versus 50 recruited and 40 participated. If this information is missing, this should be acknowledged. Please rephrase into: ‘Second, information on study participation was lacking. Non-response could be substantial in this study because drug use is illegal in China. Moreover, the recruitment criterion to complete the study could have led to a selection bias. Therefore the results of this study are not fully generalizable to drug users in other settings or countries’

14. Did you test for confounding and effect modification?
Details on effect modification are missing.

Results

18. Generally, syphilis is a problem in a specific risk group for STDs; men who have sex with men. Do you have any information regarding sexual preference of the participants? Otherwise, this should be mentioned as a limitation in the Discussion.

Discussion

Major compulsory revisions

22. Drugs were not associated with syphilis infection. Only injecting drug use was independently associated with HCV infection, although it is not clear which type injected drug, probably heroin. This is a main result of the study and should be stated more clearly.

‘All participants are drug users, therefore, this study could not conclude whether or not the drugs were associated with syphilis infection. However, all syphilis cases (77) are methamphetamine users with 2 of them also ketamine and amphetamine users. Drug use is strongly associated with syphilis.’

This explanation seems contradictory. Indeed this study can not conclude whether drug use is associated with syphilis. However, syphilis prevalence in this study can be compared with syphilis prevalence in the general population or other risk groups to highlight the syndemics of drug use. Please add this in the discussion to make a better statement.

Can you distinguish between which type injected drug was associated with syphilis infection, in addition to comment #9.

23. Independent risk factors for syphilis were female sex, having commercial sex in the past 12 months, with less regular sex partners and co infection with HCV. No conclusions are made to target syphilis prevention in female sex workers, although this is the most vulnerable group for possible syphilis infection according to your results.
‘Our previous report (Liao et al. Sexually Transmitted Diseases, 2011) revealed an alarmingly high prevalence of methamphetamine use among FSWs. Methamphetamine users were more likely to be single, younger, inconsistent condom users, and have syphilis.’

This is the conclusion of another study, my question was about syphilis prevention which seems warranted regarding the results of this study.

24. Independent risk factors for HCV were injecting drug users and co-infection with syphilis. No recommendations for information/prevention programs were made. According to this study, needle sharing of injecting drug users could be a reasonable cause of the HCV infections.

25. The sentences ‘China has seen…of Shandong Province’ are well written and should be moved to the Introduction. It represents your study objective more concise than current sentences in the Introduction.

Please indicate if the sentences have been deleted or rephrased.

30. ‘Despite these limitations and possible biases, we feel the data highlight a prevention opportunity that cannot be ignored.’ Think about which prevention opportunities are supported by the results of this study and which prevention opportunities are supported by literature.

‘The current intervention efforts for substance abuse in China is still concentrated on heroin, which played an important role in China’s HIV/AIDS epidemic in the past decades, but so far no efforts have been made to tackle the new emerging challenge of club drug use. However, unprotected heterosexual contacts has been increasing proportionally in contribution of HIV transmission in China, and the club drug abuse could potentially fuel this trend in the nation without better-targeted, effective intervention efforts taking place in a timely fashion.’

This was still missing in the manuscript.

Additional comments

Introduction

However, in recent years, China has seen an upsurge in club drug use in recent years, especially methamphetamine, which is quickly replacing heroin to become the most widespread illicit drug across the nation.
Statistical analyses.
1. ‘The prevalence rates were calculated using demographic characteristics, drug use and sexual behaviors, and utilization of HIV-related prevention services’

2. What kind of univariate and multivariable analyses was performed; logistic of lineair.

3. What procedure was used for the multivariable model (e.g. backward stepwise).

Results
4. ‘Of 805 eligible participants, 82.8% were male; 28.0% single, 70.2% currently married or cohabitating;’
Did you exclude participants who did not completed the survey (how many)?

5. ‘about 66.8% correctly answered at least 6 out of 8 questions on HIV transmission,’
Delete the word ‘about’.

6. ‘only 16.1% received HIV-related intervention in the past 12 months;’
Delete the word ‘only’. Results should be interpreted in the discussion.

7. ‘while only 52.6% knew their HIV test result (Table 1).’
Delete the word ‘only’. Results should be interpreted in the discussion.

8. ‘Of the participants, 96.6% (778) were methamphetamine users, 6.3% (51) ketamine users, 4.5% (36) MAMD users, 4.0% (32) amphetamine users and 3.2% (26) heroin users.’
Please add n=, for example (n=778) in the manuscript.

9. What is the difference between heroine use and injecting drugs? This is not clear in the manuscript. Which drugs are injected? This is important for HIV, HCV and syphilis infection.

10. ‘Of the participants, 98.8% reported ever having sex with regular sex partners,’
In addition to reviewer #1, the definition of regular sex partner is still missing. It seems likely to me that a person can only have 1 regular sex partner.

11. ‘Of the participants, 0.2% were infected with HIV, 9.6% with syphilis and 3.7% with HCV. 1.4% (11) were infected with both syphilis and HCV. ‘
Please add n=, for example (n=778) in the manuscript.

12. In the introduction the focus of the paper is on HIV/STD transmission. However, a multivariable model for HIV correlates was lacking. This should be added.
13. Move ‘unprotected sex’ to drug use and sexual behaviors.

14. Combine prevalence and correlates of HIV, syphilis and HCV into one paragraph.

15. Use the same sequence of variables in methods, results and discussion. For example in the discussion HIV was mentioned first and the next sentence starts with MA use.

‘This is the first to report on the assessment of the syndemetics of HIV, syphilis, HCV, and MA use among drug users in China. This study found alarmingly high rates of MA use (96.6%), syphilis (9.6%), and HCV infection (3.7%) among drug users in the two cities along the east coast of China with historically low HIV prevalence.’

16. Add HIV prevalence to the above sentences.

17. Shortly describe the other predictors besides ‘Syphilis and HCV infection predicted each other.’.

18. This sentence belongs in the introduction.

‘MA use quickly replaced heroin as the most widespread abused drug in China[8]. However, research on club drugs and its impact on HIV/other STDs including syphilis and HCV remains scarce in China.’

19. Move this section to the introduction after ‘across the nation’…

‘In recent years, Shandong is one of the provinces confronting the rapid emerging club drug use. One of the cities along the east coast has been named the “ice city”, for its common use of club drugs, especially among young people. MA and other club drugs are often used in entertainment venue settings, such as hotels, Bars, KTV and tea houses. Club drugs were perceived as a pastime, an entertainment additive without any stigma attached to it, rather than the highly stigmatized traditional substance abuse. Methamphetamine can be smoked, snorted, injected or orally ingested. These drugs meet the psychological characteristics of young people, e.g., curiosity, wonder, and excitemen[t19, 20].’

20. This is not a conclusion of this study: ‘There is a general lack of knowledge about the harmful impact of club drugs, as shown by a study in which 44.3% of the respondents considered club drug use as being of little or no harm at all [12]. Most young people in Thailand perceived MA as controllable and does not cause negative consequences [21]; therefore, the misperception toward club drugs could also fuel the epidemic of club drug abuse.’

Start with discussing the results of this study.

21. What STD, please be clear you only tested for HIV, syphilis and HCV.

‘It is even more worrisome that club drug users will take a potential role in the epidemiologic bridge of HIV/STD transmission to their regular sex partners[23].’
22. Do not repeat results in the discussion; interpret the results. For example: ‘This study showed that 98.8% reported ever having sex with regular sex partners, with 74.7% never using condoms in the past 12 months and 92.7% not using a condom in the last sexual encounter.’

23. ‘and the prevention infrastructure has not been strategized to tackle the newly emerging challenge of club drug abuse.’

What kind of prevention do the authors recommend? This is missing in the discussion.

24. Move the limitations to the end of the discussion.

25. ‘Further research is needed’ is a vague statement. Be more specific; what kind of research, which important information is still missing?

26. Table 1
‘Subtotals do not add up to 100% for some variables because of missing values’
Response to reviewer #1; ‘Because the variables “types of drugs” and “injected drug use” were multi-choice variables, the percentages will not add up to 100%.’

This should also be added to the table, or described in methods.

27. Table 2.
OR and 95% CI are described in table 2, therefore remove OR and 95% CI from text in results and refer to table 2.