

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Syphilis among mid-age female sex workers in China: A three-site cross-sectional study
AUTHORS	Liu, Hongjie; Dumenci, Levent; Morisky, Donald; Xu, Yongfang; Li, Xiaojing; Jiang, Baofa

VERSION 1 - REVIEW

REVIEWER	Bidhubhusan Mahapatra India
REVIEW RETURNED	28-Nov-2015

GENERAL COMMENTS	<p>The paper looks quite interesting given that most of the HIV research is focused on young sex workers and this one presents data on mid aged sex workers. However, I feel the authors have considered some important links while drawing conclusions. I have outlined my concerns below as major and minor concerns. I would appreciate if authors can address these concerns.</p> <p>Major concerns:</p> <ol style="list-style-type: none">1. The authors have started the introduction stating the old clients's syphilis is increasing rapidly and goes on to attribute this to sex with mid aged FSWs. I find it difficult to accept given that these clients may actually be working as a bridge population. These clients may be having sex with young FSWs and from there they may be getting infected and then they transmit the infection to middle aged FSWs. So, the entire premise of conceptualization that old males getting infected from middle aged FSWs is unsubstantiated. If authors can demonstrate that the high prevalence among old males is not due to sex with young FSWs, then only their argument is acceptable. Otherwise, they must rebuild their argument.2. Also, in the discussion, the start saying that the findings indicate a re-emerging epidemic. However, the result from the current research is not showing this. The authors need to present time series data to demonstrate this. As a result, I feel even the title of the paper is not right. It would be good to modify the title to reflect what the study shows.3. I am wondering, why the authors have not presented data from other research related to middle aged FSWs (though I am not very sure to what extent it is available on this topic). In the discussion also, authors have compared the current findings with that of young FSWs. I don't think this is a valid comparison.4. The authors have completely ignored any any ongoing HIV prevention program in the study area. I am sure that can influence the results a lot. To my surprise, even in the discussion, there is no concrete policy relevant recommendation. It would be good to include few recommendations.
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	<p>Minor concerns</p> <ol style="list-style-type: none"> 1. While data is collected in RDS, there is no need to present the overall (unweighted) percentages. They are highly misleading and should be avoided. 2. Please clarify which type of RDS estimates are you giving? Also, specify the version used for RDS analysis 3. How does the profile of FSWs compare with that of FSWs recruited through conventional sampling approach in the same area? It would be good to have some discussion around that. 4. What is "higher sex risk"? Do you mean to say "sex where risk is involved"? If so, then I would suggest use appropriate word. Currently, it is misleading. 5. The measures have not been defined adequately. Please define all the measures in the method section so that readers get clarity. Additionally, specify the items included to compute knowledge score. 6. What is non-appearance rate in each wave of recruitment as well as in overall. It is a good piece of information and must be included in while describing the recruitment. 7. Was any financial incentives given to participants for their travel to RDS center? If yes, please include in manuscript. 8. I noticed that some of the variables were entered as categorical in Table 3. But, in the next table they were made continuous. This is not the right approach. I suggest you stick to one approach. 9. On the analysis, just by entering the study site as a variable, I don't think it will reflect the cluster variation much. Why the authors did not fit a random effect model instead? 10. Finally, authors had sufficient sample size in each study site. Why they didn't conduct the analysis separately for each site. I feel that would have been much more informative to readers and policy makers.
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REVIEWER	Usha K Thamattoor St Johns Research Institute, Bnaglaore, India
REVIEW RETURNED	19-Jan-2016

GENERAL COMMENTS	<ol style="list-style-type: none"> 1. The definition of Mid-age FSWs is not clear. 2. Page 4, paragraph starting line 6: Purpose of this study is not introduced properly since earlier studies on general, older population is specified rather than FSWs. 3. Page 5, line 35: inclusion criteria seems to be confusing since FSWs with age>35 years are added while the authors speak of only mid-age FSWs 4. No reference mentioned supporting lines 18-23, page 15.
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VERSION 1 – AUTHOR RESPONSE

Responses to the reviewers' comments

We sincerely thank Drs. Mahapatra and Thamattoor for their constructive and insightful comments and have made changes in response to all of the comments in this revision. Changes are highlighted in red in the manuscript and are described below.

Responses to Dr. Mahapatra's comments

Major concerns:

1. The authors have started the introduction stating the old clients' syphilis is increasing rapidly and goes on to attribute this to sex with mid aged FSWs. I find it difficult to accept given that these clients may actually be working as a bridge population. These clients may be having sex with young FSWs and from there they may be getting infected and then they transmit the infection to middle aged FSWs. So, the entire premise of conceptualization that old males getting infected from middle aged FSWs is unsubstantiated. If authors can demonstrate that the high prevalence among old males is not due to sex with young FSWs, then only their argument is acceptable. Otherwise, they must rebuild their argument.

We have provided additional rationales for selecting mid-age female sex workers as our study population. The selection was based on the epidemics of HIV/STIs and the findings from our previous studies in China. The epidemics of STIs and HIV have spread among older adults in China. The majority of HIV/STI-infected older cases reported having had commercial sex with sex workers, especially those over 35 years old in China. The findings from our qualitative studies conducted at the same study sites and results from this quantitative study document that the majority of mid-age FSWs' clients were over 40 years old and there were more clients who were older than mid-age FSWs (42%) than clients who were younger than FSWs (13%). Relevant evidence has been cited in this revision.

2. Also, in the discussion, the start saying that the findings indicate a re-emerging epidemic. However, the result from the current research is not showing this. The authors need to present time series data to demonstrate this. As a result, I feel even the title of the paper is not right. It would be good to modify the title to reflect what the study shows.

We concurred this comment. The term of 're-emerging epidemic' has been removed from the revision. The title has been changed accordingly.

3. I am wondering, why the authors have not presented data from other research related to middle aged FSWs (though I am not very sure to what extent it is available on this topic). In the discussion also, authors have compared the current findings with that of young FSWs. I don't think this is a valid comparison.

As HIV/STI epidemics among mid-age FSWs is a new issue in China, there are few studies conducted among this population. Nevertheless, we have tried our best to cite the findings from our qualitative studies and studies conducted by others. While we did not understand the reasons why the comparison between younger and mid-age FSWs was not valid, we have provided some caveats when we made the comparison. Based on the results of the comparison, we believe that STI intervention in China should be given to not only young FSWs, but also mid-age FSWs who had been ignored.

4. The authors have completely ignored any ongoing HIV prevention program in the study area. I am sure that can influence the results a lot. To my surprise, even in the discussion, there is no concrete policy relevant recommendation. It would be good to include few recommendations.

We have added recommendations for STI intervention in this vulnerable population. We have performed thorough literature search and could not find any report of HIV intervention program among mid-age FSWs. If there were some on-going intervention programs given to mid-age population that would influence our results, the bias would be towards the null, meaning the prevalence of both active and prevalent syphilis should be higher than it was reported in our study.

Minor concerns

1. While data is collected in RDS, there is no need to present the overall (unweighted) percentages. They are highly misleading and should be avoided.

The overall percentages have been removed. Instead, we have reported the RDS-adjusted proportions.

2. Please clarify which type of RDS estimates are you giving? Also, specify the version used for RDS

analysis.

It has been added with a citation.

3. How does the profile of FSWs compare with that of FSWs recruited through conventional sampling approach in the same area? It would be good to have some discussion around that.

The major reason to use RDS was that a certain proportion of mid-age FSWs were not venue-based FSWs, according to our qualitative studies conducted at the three study sites. It was also confirmed in this quantitative study. Thus, the venue-based sampling or other conventional sampling could not cover FSWs who worked on streets or public parks. As few studies have been conducted among mid-age FSWs, we could not find publications reporting results generated from conventional sampling. Instead, we assessed the quality of the RDS sampling. The Results of this assessment have been reported in this manuscript.

4. What is "higher sex risk"? Do you mean to say "sex where risk is involved"? If so, then I would suggest use appropriate word. Currently, it is misleading.

It has been changed accordingly. "high-risk" was defined by the response to being susceptible to syphilis infection, including inconsistent condom use, number of clients, drug use.

5. The measures have not been defined adequately. Please define all the measures in the method section so that readers get clarity. Additionally, specify the items included to compute knowledge score.

Additional information about measures have been provided, including example items for STI knowledge.

6. What is non-appearance rate in each wave of recruitment as well as in overall. It is a good piece of information and must be included in while describing the recruitment.

While this information is important, unfortunately, we did not have such data available. Instead, we have provided detailed information on the assessment of the quality of the RDS sampling (assessment of convergence or equilibrium). This assessment indicates the RDS sampling reached the convergence of RDS compositions and the RDS sample included a broad cross-section of the hidden population. Nevertheless, we have added the non-appearance as one additional limitation in this revision.

7. Was any financial incentives given to participants for their travel to RDS center? If yes, please include in manuscript.

Information about incentives have been added.

8. I noticed that some of the variables were entered as categorical in Table 3. But, in the next table they were made continuous. This is not the right approach. I suggest you stick to one approach.

In table 3, we have purposely used the categorical form for some continuous variables (e.g., age, duration of sex work, number of clients in the past 7 days, HIV/STI knowledge). The categorical form provides detailed information about the distributions of categorical variables (the proportion of subjects at each level of categorical variables). They were entered in the models as continuous variables for the purpose of equating statistical power.

9. On the analysis, just by entering the study site as a variable, I don't think it will reflect the cluster variation much. Why the authors did not fit a random effect model instead?

We tried to fit a random effect model. However, because the number of site (level-two variable) was small (only three sites), the model failed. Entering the level-two variables with a limited size has been commonly used in multilevel analysis. We have cited an influential reference book in which the same approach was described and recommended.

10. Finally, authors had sufficient sample size in each study site. Why they didn't conduct the analysis separately for each site. I feel that would have been much more informative to readers and policy makers.

We have previously tried. However, because the number of syphilis cases (the outcome variable of the model) in each site was small, the separated model failed. In addition, there would be a huge table reporting separate findings from each site.

Responses to Dr. Thamattoor's comments

1. The definition of Mid-age FSWs is not clear.
We have made it clearer.

2. Page 4, paragraph starting line 6: Purpose of this study is not introduced properly since earlier studies on general, older population is specified rather than FSWs.
We have accordingly revised this paragraph.

3. Page 5, line 35: inclusion criteria seems to be confusing since FSWs with age>35 years are added while the authors speak of only mid-age FSWs.
We have accordingly made it clearer.

4. No reference mentioned supporting lines 18-23, page 15.
We thank the reviewer for this careful review. Citations have been added here.

VERSION 2 – REVIEW

REVIEWER	Bidhubhusan Mahapatra India
REVIEW RETURNED	18-Mar-2016

GENERAL COMMENTS	<p>The revised draft looks quite improved and many of the concerns that I indicated earlier have been addressed. However, when I read the improved version, few more questions came to my mind particularly in the discussion section.</p> <p>1. Page 12, Line #14: The authors suggest that the low HIV prevalence may indicate the HIV epidemic has just started spreading.... I don't think this is a valid conclusion the study finding provides. It could have been simply due to the fact that middle aged FSWs have historically low prevalence. You need to show a trend data to draw any conclusion on this. The low prevalence could be due to the fact that the study participants entered sex work only in their mid 30s and have been in sex work ranging from 1 year to 6 years. This may not be a sufficient time for sex workers to acquire HIV infection. Several studies have shown this. Therefore, author may like to review this statement and draw a more valid conclusion based on the study finding. Moreover, the study aimed to find level and correlates of syphilis. Authors should draw their primary conclusions in that respect rather in relation to HIV.</p> <p>2. Surprisingly, the degree of risk perception varies across sites to a great extent. But at the same time, the knowledge on HIV score hardly varies. How do you explain this?</p> <p>3. In page 13, authors indicate that they expected rural FSWs to</p>
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	<p>have higher syphilis levels than urban ones. Can you explain why did you expect so? Also, now that contrasting results were noticed, what could be the possible reason? This can be really helpful to readers.</p> <p>4. Authors could not find any relationship between duration in sex work and syphilis. Did you check the rate of condom use by duration of sex work and if this was something to do with this insignificant relationship?</p> <p>5. Authors have indicated that intervention should take into consideration unique features of mid-age FSWs...But, the factors suggested holds more for young FSWs. For example, young FSWs are less likely to have negotiation power for same sex. Also, it would help for program implementer if authors can really give an example on how the suggested component can be designed more specifically for mid-aged FSWs? Most of the HIV interventions do consider these factors while designing their programs. What additional they need to do to better outreach mid-aged FSWs?</p> <p>6. Page 14, Line 54: Authors indicate many HIV/STI intervention activities have been conducted.... It would be good to include a citation here on the ongoing programs. Also, it would be good to throw some light on what are nature of interventions.</p> <p>7. In the conclusion provided in abstract, I suggest avoiding comparison to young FSWs.</p>
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VERSION 2 – AUTHOR RESPONSE

Responses to the reviewer's comments

We thank Dr. Mahapatra for his useful comments. We have further revised this manuscript according to his comments.

The revised draft looks quite improved and many of the concerns that I indicated earlier have been addressed. However, when I read the improved version, few more questions came to my mind particularly in the discussion section.

1. Page 12, Line #14: The authors suggest that the low HIV prevalence may indicate the HIV epidemic has just started spreading.... I don't think this is a valid conclusion the study finding provides. It could have been simply due to the fact that middle aged FSWs have historically low prevalence. You need to show a trend data to draw any conclusion on this. The low prevalence could be due to the fact that the study participants entered sex work only in their mid 30s and have been in sex work ranging from 1 year to 6 years. This may not be a sufficient time for sex workers to acquire HIV infection. Several studies have shown this. Therefore, author may like to review this statement and draw a more valid conclusion based on the study finding. Moreover, the study aimed to find level and correlates of syphilis. Authors should draw their primary conclusions in that respect rather in relation to HIV.

We have deleted that conclusion and revised it based the reviewer's comments.

2. Surprisingly, the degree of risk perception varies across sites to a great extent. But at the same time, the knowledge on HIV score hardly varies. How do you explain this?

According to the theories of behavioral changes, adequate knowledge is a necessary factor, but not a sufficient factor for behavioral changes. It is the reason that interventions targeting for behavioral

changes need to be driven by theories of behavioral changes (e.g., Theory of Planned Behavior). We have revised it.

3. In page 13, authors indicate that they expected rural FSWs to have higher syphilis levels than urban ones. Can you explain why did you expect so? Also, now that contrasting results were noticed, what could be the possible reason? This can be really helpful to readers.

Almost all reported findings worldwide (including those reported from China) have documented that migrants, especially, rural-to-urban migrants, were more likely to engage in risky sexual behaviors for STIs and had high prevalence of them than non-migrants. This is where our expectation came from. We have added the potential reasons:

“We compared sexual risk behaviors (condom use and number of clients), HIV/STI knowledge, and duration of sex work between the two groups and did not find substantial differences. Further studies are needed to explore this finding.”

4. Authors could not find any relationship between duration in sex work and syphilis. Did you check the rate of condom use by duration of sex work and if this was something to do with this insignificant relationship?

Yes, we did. The association between consistent condom use and duration of sex work was very small and not significant. It has been added to the revision.

5. Authors have indicated that intervention should take into consideration unique features of mid-age FSWs...But, the factors suggested holds more for young FSWs. For example, young FSWs are less likely to have negotiation power for same sex. Also, it would help for program implementer if authors can really give an example on how the suggested component can be designed more specifically for mid-aged FSWs? Most of the HIV interventions do consider these factors while designing their programs. What additional they need to do to better outreach mid-aged FSWs?

We actually stated that mid-age FSWs had a lower power to negotiate for safer sex, compared to young FSWs. We have briefly listed suggestions for the development of interventions targeting mid-age FSWs.

“Intervention should take into consideration the unique features of mid-age FSWs (family burden, low power to negotiate condom use, sex with older clients with erectile dysfunction), target mid-age FSWs from both urban areas and rural areas. Effective interventions should be implemented geographic areas with higher HIV/STI epidemics as well as areas with small-scale epidemics.”

6. Page 14, Line 54: Authors indicate many HIV/STI intervention activities have been conducted.... It would be good to include a citation here on the ongoing programs. Also, it would be good to throw some light on what are nature of interventions.

Because Nanning is located in the most HIV-affected area in China, the national or local health authorities have invested lot of many for HIV/STI intervention activities in the city. However, those activities are not research-oriented. We could not find any reports published in journals. As a result, we could not provide detailed information on those interventions and could not cite references here.

7. In the conclusion provided in abstract, I suggest avoiding comparison to young FSWs.

We have deleted that comparison.

VERSION 3 - REVIEW

REVIEWER	Bidhubhusan Mahapatra India
REVIEW RETURNED	08-Apr-2016

GENERAL COMMENTS	I see very good improvement in the paper. More insight into the policy recommendation would have been useful. But, I leave it for the editor to take a call on this now.
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