

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Changing trends of HIV, syphilis, HCV infections and behavioural factors among female sex workers in Chongqing, China: findings from six serial surveillance surveys
AUTHORS	Hu, Ling; Wu, Guohui; Lu, Rongrong; Zhu, Hua; Qiu, Hongfang; Jing, Dan; Ye, Mengliang

VERSION 1 - REVIEW

REVIEWER	Dr. Sheela Godbole MD ICMR-National AIDS Research Institute, 73, G Block MIDC Bhosari Pune India
REVIEW RETURNED	27-Feb-2020

GENERAL COMMENTS	<p>Review for BMJ Open Manuscript : 2019_036654</p> <p>Review Summary: The authors present trend data from 6 serial surveys between 2013-18 from southwest China. It is good to see data from China and as such would be a useful. However the paper has some limitations and would need some clarifications, further statistical analysis , considerable re-writing and another review before a decision regarding publication may be made. It is not fit to be published in the current format.</p> <p>Other than the feedback provided in the reviewing form some comments, suggestions and queries are outlined below.</p> <p>General :</p> <ul style="list-style-type: none">• Language needs close attention with many grammatical errors and editorial help for may be sought.• Authors use the term "infection rate" , however it is likley that they mean prevalence and it is suggessted that they review this and similar terminology before resubmission.• Please use full terminology in the first instance with abbreviations in parantheses, followed by use of abbreviations <p>Abstract- it is preferable that Cumulative 6 year prevalence is not reported particularly for this trend analysis.</p> <p>Introduction:</p> <ul style="list-style-type: none">• A more detailed review of the epidemic in China with specific references to difference between regions and provinces is suggessted, particularly with reference to the various drivers of the epidemic in China (IDU versus FSW). The Global scenario is less relevant for this paper.
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- Authors may include details about Chonqing (few sentences from page 4, under study sites may be moved to introduction), specifically the importance of this municipality vis-a vis the HIV and HCV in China.
- A few lines about female sex workers in Chonqing, how they operate and whether they migrate between municipalities and if so the rates may be provided. More information to contextualize sex work in China and Chonqing is required.
- FSW population size estimates may be provided disaggregated by tiers as defined in the paper, if available
- Treatment access HIV, HCV and Syphilis across the 6 year period may be described. Particularly as the HCV data are based on serology.

Methods:

- Study Sites - Description of Chonqing may be shifted to introduction (all the existing text in this section). If required a figure showing the seven surveillance sites may be included in this section.
- Participant Selection and Data Collection- Reference to operational manual/ paper describing methods may be provided if accessible online. Else may be provided as supplementary material.
- Was there a change in methods in 2017? Authors do mention changes in survey tool in 2016, however if there are others, please outline greater detail.
- Line 140- please explain this line. Which new drugs are referenced and what is “deliberate transmission of AIDS” ?
- Line number 121, last word ‘FSW’- do authors mean venues or FSW?

• Laboratory Testing:

- o Line 149- please revise sentence, a better term for the word ‘detected’ ?
- o Following need to be documented.
- o Were the test kits used consistent? Please mention names
- o How many laboratories were involved in testing? What systems for QC and QA were used?
- o Was DNA testing done for HCV?
- o Definition for Syphilis positivity may be provided- what titre of TRUST was considered reactive?

• Data Analysis/Statistical Methods:

- Line 160- please delete the word ‘changing’
- Data were collected in a cross sectional manner annually over 6 years. The sampling frame and sites where the data were collected were different each year and data about heterogeneity of this population across the years is not presented. The analysis of all 16791 participants surveyed over 6 years cumulatively, in table 1 is inappropriate. It is also inconsistent with the stated objective of analysing trends. Table 1 may be deleted or revised appropriately. At best the overall prevalence may be stated in the text. The Cochran –Armitage test in this table does not address trends over time.
- Nowhere in the paper do we see a clear delineation of the population (n) surveyed by year of survey
- How was the data for the variable ‘Consistent condom use’ defined / created ? Please clarify in methods
- The term multivariable analysis may be used instead of multivariate analysis
- Multivariable Logistic Regression- it is suggested that the model

	<p>should include a test for interactions</p> <ul style="list-style-type: none"> • <p>Results</p> <ul style="list-style-type: none"> o Tables- <ul style="list-style-type: none"> □ Tables need to be better formatted. It would help if the text Column 1 is not justified. Explanatory legends may be provided. □ Table 1- dissonance between text and table with respect to numbers 16791 versus 13791 in text. Revise to show demographic data by year □ There is no need to separately mark different values of 'p' with multiple asterixes in the tables. It is sufficient to denote any value below 0.05 with one asterix □ Provide two digits after decimal points for prevalence rates to help compare data with small differences. □ Table 3 needs better formatting. Please explain NA marked for column 6 and 7 row 5 o Figure 1- <ul style="list-style-type: none"> o The scales of the y-axes in each figure is different. It would be better not to present them side by side unless there is restriction on number of figures. o There should be a label below each figure specifying HIV, Syphilis and HCV o Please present error bars and trend lines for overall prevalence in the graphs. o Numbers of for FSW surveyed and numbers positive for each year may be included in the x-axis of each graph. o Text- <ul style="list-style-type: none"> o Socio-demographic characteristics- line 170- please check the numbers. o The socio-demographic characteristics may be presented by year. o Line 183-replace 'an' by a and add education/education level in the sentence in lines 184-186. o Line 213- sentence beginning ' But HCV..... ' is unclear may be revised o Line 219 – the words 'infection rate' may be replaced by prevalence <p>Discussion</p> <ul style="list-style-type: none"> o Please check grammar and language o Discussion may be better written o Line 253- pl provide a reference o Line 257- pl review the term 'average infection rate' o Line 264 – sentence beginning in this line may be revised . Do you mean practice consistent condom use ? o Lines 274-276 – reference 24 – sentence should be revised to make it clearer. Statements in lines 302-304 are not completely based on data from this analysis. May be revised. The comments for later arguments. They need to be referenced in the introduction/background first to provide a perspective.
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VERSION 1 – AUTHOR RESPONSE

Our responses are as follows:

General :

Comments 1. • Language needs close attention with many grammatical errors and editorial help for may be sought.

Response: Thanks for your kind comments. We have asked English-speaking colleagues to help us modify the language. If there are any remaining concerns that we did not address, we would be happy to revise again.

• Authors use the term “infection rate” , however it is likely that they mean prevalence and it is suggested that they review this and similar terminology before resubmission.

Response: Thanks for your kind comments. We have revised it.

• Please use full terminology in the first instance with abbreviations in parentheses, followed by use of abbreviations

Response: Thank you for this point. We had checked all acronyms to make sure they are spelled out the first time they are used.

(Page6 Line 168) “the National Center for AIDS Prevention and Control (NCAIDS)”

(Page21 Line 443) “Non-Governmental Organizations (NGOs)”

Abstract

Comments 1. It is preferable that Cumulative 6 year prevalence is not reported particularly for this trend analysis.

Response: Thanks for your comments. We have deleted it.

Introduction:

• A more detailed review of the epidemic in China with specific references to difference between regions and provinces is suggested, particularly with reference to the various drivers of the epidemic in China (IDU versus FSW). The Global scenario is less relevant for this paper.

Response: Thank you for your suggestions. We have deleted part of the Global scenario and added a more detailed review of the epidemic in China, with particular reference to the differences between regions and provinces, especially referring to the various drivers of the Chinese epidemic.

(Page4 Line 89-93) “Heterosexual sex has replaced intravenous drug use (IDU) and commercial blood/plasma collection as the primary transmission mode of HIV in China.¹¹ Among the newly reported HIV infections from January to October 2019, heterosexual transmission accounted for 73.7%, much higher than other transmission ways.¹²”

(Page5 Line 124-130) “According to China’s surveillance data, the average prevalence of HIV/syphilis/HCV among FSWs from 2010 to 2015 was estimated at 0.25%, 2.54% and 0.72%, respectively.²⁴ The prevalence varied from province to province and the southwest province had higher prevalence of STI.^{16 25} For example, although HIV prevalence among FSWs was lower than 0.05% in most provinces (such as, Heilongjiang, Hebei) in 2012, it exceeded 1% in the same year in Yunnan and Guangxi.¹⁶”

• Authors may include details about Chongqing (few sentences from page 4, under study sites may be moved to introduction), specifically the importance of this municipality vis-a vis the HIV and HCV in China.

Response: Thanks for your kind comments. We have shifted the description of Chongqing into introduction and emphasized its importance.

(Page5 Line 131-146) Chongqing, located in the southwest of China, is one of four Chinese municipalities directly controlled by the central government. It is geographically close to Yunnan and Guangxi and has large population contacts with Yunnan and Guangxi. It is the political and economic center of Western China and a city with obvious urban–rural dual structure and prosperous sex industry. A study using the network scale-up method estimated that FSWs accounted for 0.4% of women aged 15–49 years in Chongqing, and clients of FSWs represented 2% of men aged 15–49 years.²⁶ Although HIV prevalence among FSWs in Chongqing, 2012 was estimated at 0.25%, lower than that in other high-risk groups such as men who have sex with men (17.03%) and injecting drug users (7.35%).²⁷ But since 2007, heterosexual transmission has become the main way of HIV transmission in Chongqing.²⁸ Of the 6352 newly diagnosed HIV/AIDS cases reported in Chongqing, 2015, 75.08% were infected through heterosexual transmission.²⁸ Therefore, it is very important to understand the prevalence and trends of STIs among FSWs in Chongqing.

- A few lines about female sex workers in Chongqing, how they operate and whether they migrate between municipalities and if so the rates may be provided. More information to contextualize sex work in China and Chongqing is required.

Response: Thank you for your suggestions. We have added a lot of space to introduce sex work in China and Chongqing. However, we have not found relevant research on the flow of female sex workers in Chongqing.

(Page3 Line 81-85) "Since China's reform and opening up, sex industry has re-emerged due to economic growth, population migration, and changes in sexual attitudes.^{5 6} A large number of rural migrants moved to cities for better job opportunities. But those rural women found that the labor force was saturated or the wages were not high enough, and then sex work with quick financial return became an option.⁷"

- FSW population size estimates may be provided disaggregated by tiers as defined in the paper, if available

Response: Thank you for your suggestions. We searched the relevant literature, but we have not found a nationwide or Chongqing research on the estimated population size of FSW by tiers. So we introduced related researches in other cities in China.

(Page4 Line 107-109) "The size of different-tier FSWs may be related to the local economic level. In Jiangmen City, more than 60% of FSWs was high-tier FSW, while the proportion of low-tier FSWs was less than 10%;¹⁴ but in Jianshui County, the proportion of low-tier FSWs was close to 30%.¹⁵"

- Treatment access HIV, HCV and Syphilis across the 6 year period may be described. Particularly as the HCV data are based on serology.

Response: Thanks for your kind comments.

(Page5 Line 115-116) "The "Four Frees and One Care" policy helps treat AIDS patients with financial difficulties by providing free antiviral drugs."

Methods:

- Study Sites - Description of Chongqing may be shifted to introduction (all the existing text in this section). If required a figure showing the seven surveillance sites may be included in this section.

Response: Thanks for your comments. We have shifted the description of Chongqing into introduction and added a figure showing the seven surveillance sites.

- Participant Selection and Data Collection- Reference to operational manual/ paper describing methods may be provided if accessible online. Else may be provided as supplementary material.

Response: Thanks for your comments. We added a reference to the operational manual.

- Was there a change in methods in 2017? Authors do mention changes in survey tool in 2016, however if there are others, please outline greater detail.

Response: Thanks for your comments. There was not. Only 8 questions to assess HIV-related knowledge have been changed since 2016, other content has not changed. From 2013 to 2015, the eight questions are, 'Can a person infected with HIV be recognized by appearance?'; 'Can mosquito bites spread HIV/AIDS?'; 'Can eating together spread HIV/AIDS?'; 'Can you get AIDS by blood transfusion?'; 'Can you get HIV/AIDS by using shared syringes?'; 'Can HIV infected women transmit HIV to their children?'; 'Can condom use reduce the spread of HIV/AIDS?'; 'Can having sex with only one sex partner reduce the spread of HIV/AIDS?'. From 2016 to 2018, the eight questions are, 'Is AIDS an incurable and serious infectious disease?'; 'Is sexual transmission the main mode of AIDS transmission in China?'; 'Can a person infected with HIV be recognized by the appearance of the genitals?'; 'Can infection with other STDs increase the risk of HIV infection?'; 'Can consistent condom use reduce the risk of contracting and spreading AIDS?'; 'Will the use of new drugs (such as, methamphetamine, ecstasy, and ketamine) increase the risk of HIV infection?'; 'Should HIV testing and counseling be actively requested after the occurrence of high-risk behaviours (such as, sharing needles for drug use, unsafe sex)?'; 'Is there any legal liability for intentionally spreading AIDS?'

- Line 140- please explain this line. Which new drugs are referenced and what is "deliberate transmission of AIDS" ?

Response: Thanks for your comments. New-type drugs refer to a category of recreational drugs emerging in recent years, as distinguished from opium and heroin. New-type drugs including methamphetamine, ecstasy, and ketamine. The two related items are, ' Will the use of new drugs (such as, methamphetamine, ecstasy, and ketamine) increase the risk of HIV infection? '; 'Is there any legal liability for intentionally spreading AIDS? '.

- Line number 121, last word 'FSW'- do authors mean venues or FSW?

Response: It mean "FSWs". Thanks for your comments.

- Laboratory Testing:

- o Line 149- please revise sentence, a better term for the word 'detected' ?

Response: Thanks for your comments. We have revised it.

"In all surveys, venous blood samples were tested for HIV, syphilis, and HCV by trained laboratory technician."

Following need to be documented.

- o Were the test kits used consistent? Please mention names

Response: Thanks for your comments. The HIV and HCV testing kits were produced by Yingke Xinchuang Technology Company, Beijing Wantai Pharmaceutical Company in China, and Abbott Laboratories in the USA. The syphilis testing kits were produced by Beijing Jinhao Pharmaceutical Company in China and Fuji Industrial CO. LTD in Japan.

- o How many laboratories were involved in testing? What systems for QC and QA were used?

Response: Thanks for your comments. We added "Quality Assurance" in the manuscript.

"Quality Assurance

All investigators were strictly trained before the survey to ensure that they were familiar with the questionnaire structure and mastered the unified investigation standards and requirements. After the investigation, the investigator carefully reviewed the questionnaire and promptly corrected the missing items, wrong items, and logical errors. Experts from the Chongqing Center for Disease Control and Prevention went to the investigation site for guidance and inspection to ensure the quality. All laboratory tests were conducted at designated and certified laboratory at local CDC or hospitals."

- o Was DNA testing done for HCV?

Response: DNA testing for HCV was not done.

- o Definition for Syphilis positivity may be provided- what titre of TRUST was considered reactive?

Response: Thanks for your comments. The test kit is unified. The quality and validity of the test kits meet the requirements of the regulations, and the operation was strictly in accordance with the instructions of the kit.

- Data Analysis/Statistical Methods:

- Line 160- please delete the word 'changing'

Response: Thank you for this point. We have deleted it.

- Data were collected in a cross sectional manner annually over 6 years. The sampling frame and sites where the data were collected were different each year and data about heterogeneity of this population across the years is not presented. The analysis of all 16791 participants surveyed over 6 years cumulatively, in table 1 is inappropriate. It is also inconsistent with the stated objective of analysing trends. Table 1 may be deleted or revised appropriately. At best the overall prevalence may be stated in the text. The Cochran –Armitage test in this table does not address trends over time.

Response: Thanks for your comments. The original Table 1 has been deleted and replaced by the demographic characteristics of the population by year of survey. The overall prevalence was stated in the text.

- Nowhere in the paper do we see a clear delineation of the population (n) surveyed by year of survey

Response: Thank you very much for this important point. Table 1 depicted all participants' demographic characteristics stratified by year of survey.

- How was the data for the variable 'Consistent condom use' defined / created ? Please clarify in methods

Response: Thanks for your kind comments. Consistent condom use (CCU) in the past month, in this study, was defined as always using a condom during commercial intercourse. Participants were

asked how often they had used condoms when they had sex with their clients in the last month, with options being "never", "usually", and "always". Only choosing "always" would be considered as CCU.

- The term multivariable analysis may be used instead of multivariate analysis

Response: Thank you for this point. As you pointed out, we have revised it.

- Multivariable Logistic Regression- it is suggested that the model should include a test for interactions

Response: Thanks for your comments. According to your suggestion, we have tested the interactions of these factors. In order to test the interactions of the factors included in the model, every two factors were constructed as an interaction term. The effect due to interaction was assessed by adding the interaction term (as independent variable) in the same model, as well as their individual terms. But we found that these interaction terms were not statistically significant ($p > 0.05$).

Results

o Tables-

- ♣ Tables need to be better formatted. It would help if the text Column 1 is not justified. Explanatory legends may be provided.

Response: Thanks for your comments. We have revised it.

- ♣ Table 1- dissonance between text and table with respect to numbers 16791 versus 13791 in text.

Revise to show demographic data by year

Response: Thank you for catching this error. We have revised it. Table 1 depicted all participants' demographic characteristics stratified by year of survey.

(Page9 Line 237) "This study included 16791 of 16810 participants recruited between 2013 and 2018."

- ♣ There is no need to separately mark different values of 'p' with multiple asterixes in the tables. It is sufficient to denote any value below 0.05 with one asterix

Response: Thanks for your comments. We have revised it.

- ♣ Provide two digits after decimal points for prevalence rates to help compare data with small differences.

Response: Thanks for your comments. We have revised it.

- ♣ Table 3 needs better formatting. Please explain NA marked for column 6 and 7 row 5

Response: Thanks for your comments. We have revised it.

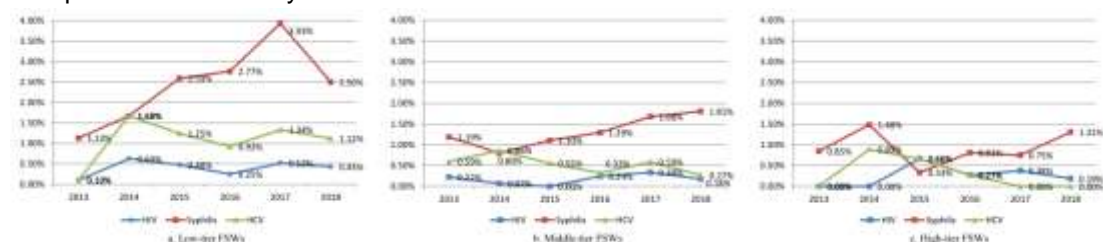
o Figure 1-

o The scales of the y-axes in each figure is different. It would be better not to present them side by side unless there is restriction on number of figures.

Response: Thank you for catching this error. We have revised it.

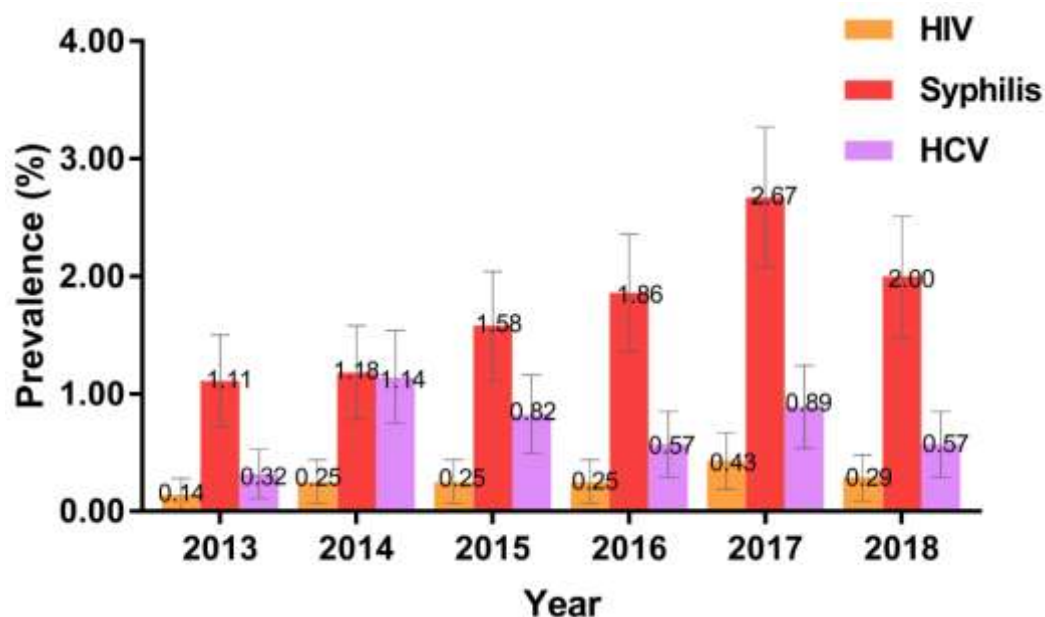
o There should be a label below each figure specifying HIV, Syphilis and HCV

Response: Thanks for your comments. We have revised it.



o Please present error bars and trend lines for overall prevalence in the graphs.

Response: Thanks for your comments. We have revised it.



o Numbers of for FSW surveyed and numbers positive for each year may be included in the x-axis of each graph.

Response: Thanks for your comments. We have revised it.

o Text-

o Socio-demographic characteristics- line 170- please check the numbers.

Response: Thank you for catching this error. We have revised it.

“This study included 16791 of 16810 participants recruited between 2013 and 2018.”

o The socio-demographic characteristics may be presented by year.

Response: Thank you very much for this important point. We have revised it. Table 1 depicted all participants' demographic characteristics stratified by year of survey.

o Line 183-replace 'an' by a and add education/education level in the sentence in lines 184-186.

Response: Thank you for catching this error. And this sentence was deleted in the revised manuscript.

o Line 213- sentence beginning ' But HCV..... ' is unclear may be revised

Response: Thanks for your comments. And this sentence was deleted in the revised manuscript.

o Line 219 – the words 'infection rate' may be replaced by prevalence

Response: Thank you very much for this important point. We have revised it.

Discussion

o Please check grammar and language

Response: Thanks for your kind comments. We have asked English-speaking colleagues to help us modify the language. If there are any remaining concerns that we did not address, we would be happy to revise again.

o Discussion may be better written

Response: Thanks for your kind comments. The discussion has been rewritten quite a bit. For examples:

(Page19 Line357-364) And the prevalence of HIV among FSWs in Chongqing is at a relatively high level in China, which is higher than that in most provinces such as Beijing,³¹ Liaoning,³² and Hainan,³³ and lower than in Sichuan,³⁴ Yunnan,³⁵ and Guangxi.³⁶ HCV prevalence was fluctuated between 2013 to 2018 with the six-year average prevalence of 0.72%, but no significant trend was found. This result is in agreement with previous study conducted in Guangxi.³⁶ However, a previous study using national data reported that from 2008 to 2012, the overall HIV and HCV prevalence among FSWs in mainland China showed a decreasing trend;¹⁶ the differences may due to differences in scope of study area and study period.

(Page20 Line413-426) There was no significant increase or decrease trend in drug use among FSWs. The average prevalence of drug use was 3.3%, while the national prevalence among FSWs was

reported at 1.2%.¹⁶ The prevalence of injecting drug use seems to be declining, at 0.4% in 2018. Injecting drug use may exacerbate unsafe sexual behaviors and structural risks, leading to increased risk of HIV and other STI.^{45 46} In 2017, the detection rate of HIV, syphilis and HCV among drug users in Chongqing was respectively 5.4%, 5.9% and 44.9%, which was much higher than that of the general population.⁴⁷ Compared with FSWs and injecting drug users, FSWs who inject drugs exposed to both sexual and blood transmission routes are at a higher risk of contracting HIV and syphilis.^{36 48} Similar to previous study, results showed a strong association between injecting drug use and HCV infection,⁴⁹ and the sharing of needles may be the main and underlying route of HCV transmission. Drugs and prostitution are involved relevant laws and ethics, so HIV prevention programs and outreach for FSWs may require more thinking and attention to the individual's external risk environment and risk factors.

o Line 253- pl provide a reference

Response: Thanks for your comments. We have revised it.

o Line 257- pl review the term 'average infection rate'

Response: Thanks for your comments. We have revised it.

(Page19 Line354)“Our study showed that HIV prevalence among FSWs in Chongqing was relatively stable with an annual average HIV prevalence at 0.27% from 2013 to 2018.”

o Line 264 – sentence beginning in this line may be revised . Do you mean practice consistent condom use ?

Response: Thank you very much. We have revised it.

(Page20 Line399-401) “We also found that more and more FSWs practiced consistent condom use, but in 2018 only half of FSWs reported the consistent use of condoms in the last month.”

o Lines 274-276 – reference 24 – sentence should be revised to make it clearer. Statements in lines 302-304 are not completely based on data from this analysis. May be revised. The comments for later arguments. They need to be referenced in the introduction/background first to provide a perspective.

Response: Thank you for this point. As you pointed out, we have deleted it.