Author’s response to reviews

Title: The effect of methamphetamine abuse on dental caries and periodontal diseases in an Eastern China city

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Title: The effect of methamphetamine abuse on dental caries and periodontal diseases in an Eastern China city

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Response to Editor’s Comments

[Point 1]: The study is not novel but the findings are important contribution to knowledge. It is however important that the authors use the correct non-stigmatising nomenclatures throughout the manuscript. The authors would need to review the entire manuscript to ensure the use of language are sensitive and non-stigmatising. For example the word is people who inject drugs (PWID) and not illegal drug users.
[Response]: According to your suggestion, the “illegal” has been deleted. Please see the revised manuscript Page 3 Line 4.

[Point 2]: The abstract alludes to having recruited ex-drug users, yet the methodology made no such allusion.

[Response]: Thank you for your suggestion, the word “former” has been added before the “drug users”. Please see the revised manuscript Page 6 Line 1, Line 2, Line 4.

[Point 3]: Abstract

• The methodology section should discuss what the dependent and independent variables of the studies were; and also discuss the analytical method to arrive at outcome variables measured for the study.

[Response]: According to your suggestion, the content of variables and analytical method were added. Please see the revised manuscript Page 3 Line 12-20.

[Point 4]: Second, systemic diseases is a broad term. It is important that the method section highlights the systemic diseases investigated so that the results make meaning to readers.

[Response]: Thank you for your suggestion. To make the results about systemic diseases meaningful to readers, we have rewritten the second paragraph in Background. Please see the revised manuscript Page 5 Line 21- Page 6 Line 3. In Abstract, limited by the word number, this content was not added. Furthermore, the sentence “The prevalence of systemic diseases was unremarkable in these former drug abusers.” was deleted in Abstract to avoid unnecessary misunderstanding.

[Point 5]: The authors wrote - prevalence of gingival bleeding in the former drug-addicted population. First, it was not made clear that prevalence of gingival bleeding was assessed in the study population in the methodology section. Second, he talks about drug-addicted population here yet the target population identified in the method section were drug users. Drug users is not synonymous with drug addiction. Please with clear with terminologies.

[Response]: According to your suggestion, we have replaced all the “drug-addicted population” with “drug users”. Please see the revised manuscript Page 3 Line 22, Page 10 Line 12 and Line 14, Page 13 Line 2 and Line 4. Additionally, the information of “prevalence of gingival bleeding” was added in both Abstract and Methods sections. Please see the revised manuscript Page 3 Line 15 and Page 8 Line 10.

[Point 6]: • The authors refer to ‘corresponding reference data’. The methodology did not in any way suggest that there would be a comparison with a reference population or data. This introduces a new set of variables with its bias and errors.

[Response]: Thank you for your good suggestion! The sentence “To analyze the relative severity of dental caries and periodontal diseases, the results of the present study were compared with the
corresponding data collected from the general population in Eastern China,”, and “To analyze the relative severity of dental caries and periodontal diseases, the results of the present study were compared with the corresponding data collected from the general population [16] [35-44 years of age group in East China in the third National Epidemiological Sampling Survey of Oral Health (NESSOH) in China.” have been added in Abstract and Methods sections. Please see the revised manuscript Page 3 Line 16-18 and Page 8 Line 1-5.

[Point 7]: •In the absence of an analysis plan, it is challenging to understand why the reference was a 3 years duration. Why not 5 years or 1 year. What is the age range of this study population? Knowing that there are age changes associated with periodontal diseases and caries, how was the confounding potential for age addressed in this study?

[Response]: Thank you for your good suggestion! To describe the basis for grouping clearly, a detailed statistical analysis plan was added in the Statistical Analysis section. Please see the revised manuscript Page 9 Line 5-9. The age range of this study population was 19-50 years old, which can be found in Page 9 Line 17.

Although there are age changes associated with periodontal diseases and caries, before carrying out statistical analysis in the present study, we have analyzed the age distribution of different groups by T-test. All the results showed that there was no age tendency 【for grouping based on the duration of drug abuse, t=1.852, p=0.066; for grouping based on brushing times, t=0.089, p=0.929; for grouping based on tooth brushing time, t=0.364, p=0.716】. Thus, the age distribution may not affect the conclusion in the present study significantly.

[Point 8]: •Measuring DT and DMFT is confounding since DT is also measured in DMFT.

[Response]: In our opinion, although DT, MT and FT interlap DMFT to some extent, different scores reflect different inner meanings. For example, DT reflects the severity of dental caries, and MT may be related with caries, periodontal disease and trauma, while FT reflects both medical level and whether patients pay much attention to their oral health. DMFT is an aggregative indicator. So, they can’t be mutually substituted.

[Point 9]: •The conclusion reflects bias. The authors never measured ‘bad oral hygiene habit’. One of the several oral hygiene habit I perceive was measured was frequency of tooth brushing. There was no scoring aggregate to determine oral hygiene was good or bad and so the conclusion on bad oral hygiene habit is spurious and unsubstantiated. The authors also conducted association analysis and not trend analysis and thus making conclusions that Long duration of drug abuse has a high damaging potential for oral health is spurious and unjustified from this study. The statement that Illicit drug abuse ……. resulted in significantly more common and more severe dental caries and periodontal diseases is also unjustified from this study. This conclusion needs to be completely re-written. The conclusion should focus on the outcome of the study with respect to the study objective.

[Response]: Thank you for your good suggestion! We have rewritten the conclusion- “The oral health status among former male meth users in Eastern China was poorer than general male
population. Prolonged drug abuse and lower frequency of tooth brushing may be the risk factors of their poor oral health”.

[Point 10]: Background

The background has a huge gap. The conceptual framework for this study was not developed. There is no detail on how the use of drugs can cause oral diseases (and there are mirages. The background did not focus on any specific oral disease of interest). It authors plan to investigate the oral health status of drug users. This study objective is not SMART. It is therefore difficult to assess if the study objective was achieved.

[Response]: Thank you for your good suggestion! We have rewritten the Background sections. In this part, how meth abuse cause oral diseases was added, and special meaning of the present study for China was also emphasized. Please see the revised manuscript Page 5 Line 4-6, Line 10-12, Line 15-17, and Page 6 Line 11-14.

[Point 11]: •Please provide a reference for the statement - Drug abuse increases social economic burden, crime rate, unemployment rate, and it incurs other social costs such as an increased threat to public safety.

[Response]: Thank you for your suggestion! Two related references has been added. Please see the revised manuscript Page 5 Line 4.

[Point 12]: •The authors notes - and so on [5-9]. Please list all. We do not write etc in a manuscript.

[Response]: Thank you for your suggestion! The “so on” has been replaced by “stomatognathic system”. Please see the revised manuscript Page 5 Line 20.

[Point 13]: •Please provide a reference for statement - Oral health problems are among the most prevalent diseases related to illicit drug addiction.

[Response]: Thank you for your suggestion! Two related references has been added. Please see the revised manuscript Page 6 Line 8.

[Point 14]: •Include in this section, details on the pathophysiology of oral diseases of interest associated with drug use. I am certain is not the illicit that makes the drug a problem but there are chemical induced reactions in the oral cavity. The background mentions oral health problems but does not highlight details on the severity of periodontal (and please be specific) diseases and caries associated with drug use. This is a big gap in this section.

[Response]: Thank you for your good suggestion! In this section, we have added the pathophysiology of caries and periodontal diseases in drug abusers. Please see the revised manuscript Page 6 Line 11-14.
The details on the severity of caries and periodontal diseases was put in Discussion section to help to analyze the present results.

[Point 15]: •The study also provides little justification for the study. Why is it important to understand the prevalence of oral health problems associated with drug use in the Chinese population? Why do you need to conduct this study and is there any reason why results of past studies cannot be extrapolated for use in China?

[Response]: Thank you for your good suggestion! Over the past two decades, drug abuse has also become an important social and public health issues in China, which has the largest population and imbalance of economic development around the country. The most important is, in the literature, there is little information about the oral health status of Chinese meth users, especially in economically developed Eastern China area, which affect seriously the anti-drug policy-making and professional oral health management for drug abusers. It is the main reason why we carried out the present study. We have added the above-mentioned information in Background section. Please see the revised manuscript Page 5 Line 4-6, Line 10-12, Line 15-17, Page 6 Line 16-17.

[Point 16]: Methodology

• This is a vulnerable population. It is important to describe in details the study recruitment process including how informed consent was administered.

[Response]: Thank you for your suggestion! One of our authors’ unit--Department of Stomatology, Chinese PLA 413 Hospital in Zhoushan, is the designated medical institution for the male Zhoushan Compulsory Detoxification Center. Almost every month there will be some drug abusers come to our department of stomatology to look for dental treatment. We are startled by their oral health condition. That is why we carried out the study.

Just as we described in Ethics approval and consent to participate, data collection for the present study only involved a standardized questionnaire and a traditional dental examination without any intervention affecting the health status. Furthermore, the dental examination will help participants learn about their oral health status. Therefore, all the participants were only asked to give an oral consent (without written informed consent) before the study. All the participants were very willing to accept the investigation. After investigation, we give all the participants personalized oral health care plan free.

[Point 17]: •Please discuss your sample size determination or if this was a convenient sample. This is important as we need to identify the study limitation if this study was not powered to determine was it is designed to determine.

[Response]: Thank you for your good suggestion! To be frankly, it is a convenient sample in the present study. In China, illicit drug abuse are illegal. Once found, the drug user will be sent to Compulsory Detoxification Center. So we can only find drug abusers in Compulsory Detoxification Center in China. We have discussed the study limitation in Discussion section. Please see the revised manuscript Page 15 Line 4-7.
[Point 18]: •What makes this a pilot study? A pilot study for what specific study? This is completely unclear.

[Response]: Thank you for your good suggestion! The word “pilot” has been deleted. Please see the revised manuscript Page 7 Line 5.

[Point 19]: •What details were collected when determining drug-use pattern?

[Response]: Thank you for your suggestion! When collecting the information of drug-use pattern in questionnaire, we asked all the participants to answer multiple-choice question (intravenous injection, inhalation, drink or other ways). We have added the information in Data collection and questionnaire. Please see the revised manuscript Page 7 Line 12-13.

[Point 20]: •What details were collected when determining degree of education?

[Response]: Thank you for your suggestion! When collecting the information of degree of education in questionnaire, we asked all the participants to answer multiple-choice question (elementary school, middle school, college or postgraduate). We have added the information in Data collection and questionnaire. Please see the revised manuscript Page 7 Line 13-14.

[Point 21]: •What details were collected when determining oral health habit?

[Response]: Thank you for your suggestion! When collecting the information of oral health habit in questionnaire, we asked all the participants to answer multiple-choice question (brushing teeth more than twice / once or never per day, brushing teeth for more than 2 minutes / 1-2 minutes / less than 1 minute per time, rinsing their mouths with tap water after every meal / every day / seldom / never). We have added the information in Data collection and questionnaire. Please see the revised manuscript Page 7 Line 14-16.

[Point 22]: •What details were collected when determining and systemic health condition? Why was this information extracted from the case note when the individuals were present and the details could have been collected first hand?

[Response]: Thank you for your suggestion! When collecting the information of systemic health condition, firstly we asked all the participants to answer multiple-choice question in questionnaire (if they have hepatitis, HIV, gastritis, heart disease, hypertension, or other diseases). All the participants will undergo medical examination regularly in the Compulsory Detoxification Center. To get precise information, the health condition determination will also refer to the medical examination report. We have added the related information in Data collection and questionnaire. Please see the revised manuscript Page 7 Line 17-19.

[Point 23]: •How was the questionnaire standardized – was this tool adapted from prior studies or was this tool developed specific for this study?
[Response]: Thank you for your suggestion! The dentists in our hospital (School of Stomatology, the Fourth Military Medical University) will organize and carry out oral health surveys more than 20 times, and will take part in National Epidemiological Sampling Survey of Oral Health (NESSOH) in China every time. So we have standardized questionnaires for different kinds of people. The questionnaire used in the present study was partly adapted from prior studies, for example the information about degree of education, oral health habit. For the specific information related with drug users, we discussed with the doctors in the Compulsory Detoxification Center, who is familiar with the real condition of the former drug users.

[Point 24]: •How were the four dentists standardized – any intra-examiner and inter-examiner reliability tests performed?

[Response]: To ensure the consistency of the examining results, 15 volunteers from dental students (grade III) in our school were chosen. After the training of the four dentists, all 15 volunteers were examined by every dentist, and the DMFT score and probing pocket depth were recorded. Two weeks later, the same examination was performed and recorded. During the 2 weeks, no dental treatment was carried out, and no oral health habit was changed. The intra-examiner agreement was to compare the examination results collected by the same dentist. The inter-examiner agreement was to compare the examination results collected by different dentists. One week later, the examination on the former drug users were conducted. The related information can be found in the revised manuscript Page 8 Line 11-14.

[Point 25]: •Please write out CPI at first use

[Response]: Thank you for your suggestion! We have written out the full name of CPI at the first use. Please see the revised manuscript Page 8 Line 2-3.

[Point 26]: •Please discuss in details how the examination for caries was performed – in a dental chair or not? The light source? Were the teeth cleaned or not? Was caries assessed before periodontal status? Were probes used to determine caries status? Too much information is currently missing

[Response]: Thank you for your good suggestion! We have added the related information. Please see the revised manuscript Page 8 Line 1-6.

[Point 27]: •Disease prevalence are calculated. For gingival bleeding and dental calculus, what you calculate for is the proportion of persons with gingival bleeding or with dental calculus.

[Response]: Yes, you are right.

[Point 28]: •In have a concern with the report of the authors. They note: After training of the examiners, the DMFT score and probing pocket depth were recorded and repeated within a 2-week interval by 4 dentists. Intra- and inter-examiner agreements for the oral examination were good, as indicated by kappa statistics of more than 0.8. If the probing pocket depth were recorded and repeated within a 2-week interval, it would be assumed that the participants for this standardization were treated during that period. It can also be assumed that
healing would take place in a few study participants over that 2 weeks duration. This implies that gingival bleeding would disappear and dental calculus would no longer be present. It therefore becomes completely challenging for me to understand how the authors got good Intra-examiner agreements after 2 weeks. Could the authors unravel this mystery.

[Response]: Thank you for your good suggestion! Before the oral health survey, we have thought of this problem. To avoid unnecessary misunderstanding, as we above respond to [Point 24], the DMFT score and probing pocket depth were recorded to verify the intra- and inter- examiner reliability. That means gingival bleeding and dental calculus were not involved in that segment. In the present survey, all the 4 dentists who conducted dental examination had independent dental clinic experience for more than 5 years, so they are experienced enough.

[Point 29]: •Data analysis section is completely inadequate. Please write up this section to allow a repeat of the analysis. 2 independent samples is not a non-parametric test. Please state VERY clearly, what prevalence(s) were determined, what tests of associations were done (identify the independent and dependent variables and the specific analysis tool used for the test of associations). Where the sample was divided, please discuss how this was done.

[Response]: Thank you for your good suggestion! We have rewritten the related information in Statistical analysis part. Please see the revised manuscript Page 8 Line 22-Page 9 Line 11.

[Point 30]: •The method did not discuss any comparison with a prior data as alluded to in the abstract.

[Response]: Thank you for your good suggestion! We have added the related information. Please see the revised manuscript Page 9 Line 1-5.

[Point 31]: Others

· The gaps in the methodology section are too major for the authors to make give meaningful results for the study. The authors are advised to revise the entire manuscript based on the feedback. This would help focus the study and help generate meaningful data.
[Response]: Thank you for your good suggestion! We have revised the entire manuscript based on your feedback.

[Point 32]: •Please refer to the STROBE to guide with the revision of this manuscript.

[Response]: Thank you for your suggestion! We have revised the manuscript according to STROBE.

[Point 33]: •The study has a large population of meth only users. Why not focus the study on this population so as to be able to make useful inferences? This way, the author can discuss about the pathophysiology of meth and periodontal disease and caries. The study can then be streamlined to caries and periodontal health status of people who use meth in China.
[Response]: Thank you for your good suggestion! According to your suggestion, we have focused the study on the meth only users and analyzed the results based on the new sample. Please see the revised manuscript.

[Point 34]: •Table 2 is challenging as the authors wrote they investigated systemic diseases but what they have here are symptoms. So this is completely unclear. The symptoms are also things that may have been happening at the point in time of the study enough to have disturbed oral health habits and predispose to the oral health conditions and not just the drug use. One major one is the mental health status. These confounders were not addressed in the analysis. All these introduce bias and makes the result non-dependable.

[Response]: Thank you for your good suggestion! I agree with you at this point. “Irregular life style”, “Mental stress and anxiety”, ” Poor sleep” and “Irregular feces shape (dry or watery)” are all self-reported symptoms or conditions, and all of them were related to multi-factors. Additionally, these conditions are subjective and can’t be quantified, which may affect the accuracy of the results to some extent. So, we has been deleted the related information in the revised manuscript.

[Point 35]: •The way the age was dichotomized also is most unhelpful. It could be more appropriate to divide the study populations into adolescents, those in the reproductive age group and those older. This way, meaningful deductions can be made about the finding age wise.

[Response]: Thank you for your suggestion! We have ever thought of the problem. The age of the present sample ranged from 19-50 years old. The number of participants younger than 25 years old is 15, which is less than 10%. That means that almost all the participants were in the reproductive age group. So, it is hard to divide the present populations into adolescents, those in the reproductive age group and those older. In the present manuscript, we dichotomized the study population according to the median of the age distribution.

[Point 36]: •Also please prevent including discussions in the result section. This is currently all messed up right now.

[Response]: Thank you for your suggestion! We have revised the manuscript.

Response to Reviewer 1 (Juliana de Kassia Braga Fernandes)’s comment

[Point 1]: Methods: I suggest that you describe the way the sample is selected, whether it was random or for convenience.

[Response]: Thank you for your suggestion! Just as we respond to [Point 17], to be frankly, it is a convenient sample in the present study. In China, illicit drug abuse are illegal. Once found, the drug user will be sent to Compulsory Detoxification Center. So we can only find drug abusers in Compulsory Detoxification Center in China, and we can’t control the sample size freely. We have discussed the study limitation in Discussion section. Please see the revised manuscript Page 15 Line 4-7.
[Point 2]: I also suggest the power of the sample to show differences between the comparison groups.

[Response]: According to your suggestion, the power of the sample was added in Table 1. Please see the revised manuscript Page 23.

[Point 3]: It is important to mention whether there were oral hygiene guidelines during the study for the volunteers, which may influence the results.

[Response]: Thank you for your suggestion! In China, the former drug users in the Compulsory Detoxification Center were special population under strict administration. We have little chance to contact with them for long time. Only when they come out to look for dental treatment, we can tell them how to maintain their oral hygiene. So, to be frankly, there were no good and complete oral hygiene guidelines given to the whole population before the study. During the study, before dental examination, they were asked to rinse their mouth carefully.

[Point 4]: Necessary controls:

Although a reference population was used as a control, the age of this population is not comparable to all volunteers in the sample because of the difference between the ages.

[Response]: Thank you for your suggestion! In China, the National Epidemiological Sampling Survey of Oral Health (NESSOH) is the largest-scale and the most authoritative oral health survey in the whole country. In the third National Epidemiological Sampling Survey of Oral Health (NESSOH) of China, there were only four age-group populations under examination, including 5-years-old age group, 12-years-old age group, 35-44 years old age group and 65-74 years old age group. The 35-44 years old age group is the nearest one to the present sample (19-50 years), so the reference data from that age group were used as a control. We have discussed this limitation in Discussion section. Please see the revised manuscript Page 15 Line 10-14.

[Point 5]: In addition, the sample was divided into two groups depending on the variables described in the method and compared to each other, however the criteria for forming these groups were not described in the method.

[Response]: Thank you for your good suggestion! We have added the related information in Statistical analysis part. Please see the revised manuscript Page 9 Line 5-9.

[Point 6]: Conclusions:

The conclusion of the study needs to emphasize that this is a specific population with only men as participants, which makes any generalization difficult.

[Response]: Thank you for your good suggestion! We have revised the conclusion in Abstract and Conclusions section. Please see the revised manuscript Page 4 Line 7-8, and Page 15 Line 18-19.
[Point 7]: Statistics:

In the statistical analysis it is necessary to comment on the descriptive statistics and state which is the non-parametric test used.

[Response]: Thank you for your good suggestion! We have added the related information in Statistical analysis part. Please see the revised manuscript Page 8 Line 22- Page 9 Line 11.