PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between the number of teeth and frailty among Chinese older adults: A nationwide cross-sectional study
AUTHORS	Gu, Yaohua; Wu, Wenwen; Bai, Jinbing; Chen, Xuyu; Chen, Xiaoli; Yu, Liping; Zhang, Qing; Zou, Zhijie; Luo, Xianwu; Pei, Xianbo; Liu, Xin; Tan, Xiaodong

VERSION 1 – REVIEW

REVIEWER	Takamasa Komiyama Tohoku University Graduate School of Dentistry, Department of Aging and Geriatric Dentistry, Japan
REVIEW RETURNED	06-Mar-2019

GENERAL COMMENTS	This cross-sectional study examined whether the number of teeth in older Chinese adults is associated with frailty as evaluated by a frailty index. It seems to have important findings, but there are several concerns to be addressed before it is clear if it is worth publishing. Major comments 1. Participants themselves counted the number of their teeth. Since the mean age of the study sample was 84 years, one wonders if any of the participants had some degree of cognitive impairment, which would affect the accuracy of the data. The authors indicated that the numbers of teeth reported ranged from 0 to 36. They also stated that 30% of older Chinese adults have never visited a dentist at all. It is therefore difficult to judge the reliability of the self-reported numbers of teeth. The authors should address this issue. 2. The authors omit an explanation of the study design and the participants' response rate. The response rate affects the generalizability of the findings. Although the authors note that the strength of this study is its generalizability, that may not be the case if the response rate was low. The study design must be explained in more detail. In particular, the response rate must be stated. 3. In the results, the difference in the FI between those who were edentulous and those with 28 teeth was about 1. The authors should discuss the significance of this difference in relation to other variables or to previous studies. Specific comments 1. In the outcome variables, the authors should explain all chronic

	disease conditions and functional limitations. 2. In the outcome variables, nutritional status was not evaluated, although the authors mention malnutrition as a risk factor for frailty. The authors should explain why nutritional status was not included in the assessment of frailty. 2. In the statistical analysis, it is recommended that the authors confirm whether there was definite linearity between the number of teeth and the FI. Previous reports have indicated that the relationship between tooth loss and frailty may not be purely linear. 3. In the results section, the authors explained their findings using B, whereas it is my impression that β is more commonly used. Please confirm. 4. In Table 1, I can't understand how the p values were calculated for age, number of teeth, education years and total income of your household last year. In addition, the authors should define all abbreviations used in the table (also in Table 2). 5. In the first paragraph of the Discussion, although the authors state that "According to our results, more teeth are associated with a lower prevalence of frailty," it is unclear how they calculated the prevalence of frailty. 6. In the fourth paragraph of the Discussion ("In China, oral diseases are…"), I don't understand that this section discusses about which part of results of this study.

REVIEWER	Fu Hua Fudan University, China
REVIEW RETURNED	14-Mar-2019

GENERAL COMMENTS	On the whole, the article is still complete, but the quality is general, there are some personal views as follows: 1. In the summary section, the final indicators (B=-0.05, P=0.00) in the results are inconsistent with the indicators given in the results of the article (B=-0.04, P=0.00). 2. In the methodological section, 1) the introduction of the 38 indicators contained in the core indicators of the frailty index is somewhat too brief. 2) In the outcome variables part, 39 points of the scores do not correspond to 38 items. 3) More introduction of the statistical analysis in needed for the single factor analysis of continuous variables such as age and number of teeth and frailty score 4. Result section, 1) The results of Model 3 is suggested to describe the correlation between the number of teeth and the frailty scores in order to correct all confounding factors, rather than the results of model 1. 2) Although the number of teeth is correlated with the frailty scores in the model 3 showed in table 2, the correlation coefficient b is only-0.03, that is, for every tooth reduction, the frailty score increased by 0.05 points, which is obviously not practical importance; 3) The age, the number of teeth and other continuous variables and the frailty scores might be not linear relationship, the explanation of the results is less meaning. In summary, it is recommended to replace continuous variables with categorical variables for analysis. 5. Discussion section, 1) In 37th line on 8th page (According to our results, more teeth are associated with a lower prevalence of frailty)

	it is suggested to change the “prevalence” into “risk”. 2) The advantages of using FI in the second paragraph of the discussion section is suggested to move to the background section. 3) The fourth paragraph describes the causes of oral health problems of the elderly in China is not suitable here, because the purpose of this study does not explore the current situation of oral health in Chinese population. 6. There are some unsuitable language expression as followings: 1) unified format of the references; 2) in the background section, the reference 11 was cited two times, but the expressive meaning appears to be contradictory. (Notably, emerging research showed that frailty was significantly associated with oral health and functions, including tooth number, 11,12,13/ some studies did not find a significant association between number of teeth and frailty. 9, 11, 16, 17). 3) The first line of the result section ">65 years" should be "≥65 years", because of "range=65-113" in the 6th line of the result section.

REVIEWER	Cristiane da Mata University College Cork Ireland
REVIEW RETURNED	28-Mar-2019

GENERAL COMMENTS	The paper entitled “Association between number of teeth and frailty among Chinese older adults: A nationwide cross-sectional study” explores the association between number of teeth and frailty among Chinese senior individuals. It uses a large database from the Chinese Longitudinal Health Longevity Survey which included a comprehensive data collection from 1998 to 2014 (every 3 years=7 waves). The study has several strengths, including: use of a large database, large sample representative of the population, face-to-face interviews with participants were conducted, frailty scores generated based on 38 indicators of health deficits, including psychological cognitive and psychosocial markers (Frailty Index is a broad instrument). Some of the weaknesses include the study design (cross-sectional, no causal relationship can be determined), method of determining number of teeth (self-reported), time of tooth loss could not be determined (which in my view would change the interpretation of results). The manuscript is generally well written but some further changes could improve its clarity and quality. My main concern is how the authors have interpreted he results. They have found that there is an association between tooth loss and frailty. However, they discuss how tooth loss could contribute to frailty but not the other way around. I believe it is very important to explore the possibility of frailty contributing to tooth loss, which seems to be a strong possibility to me, with frail individuals not being able to perform some simple daily activities such as tooth-brushing. The major change that is needed is in the discussion, and authors should take into account the possibility of this association being inverse, i.e., frailty impacting on activities of daily living such as brushing, inability to leave the house and visit a dentist, etc… ultimately resulting in tooth loss. This is very important as it points out to the need of educating carers and family regarding how to care for their frail family member’s oral health in order to avoid tooth loss. The timing of the incidence of frailty, as well as tooth loss seem to me, to be extremely important in order to explain this relationship. If we do not know what comes first, it is hard to determine. Some of

	the studies cited, which have a longitudinal design, ended up with a very small sample of frail individuals to draw conclusions from. Additionally, the timing of events occurring does not seem to be known. I would like the authors to comment on this and probably include in their discussion. Additionally, I would like to suggest some minor changes as below: Abstract: Conclusions: third sentence should be: “specific mechanisms underlying how oral health is related to frailty”. Introduction 1) Page 4, line 4: please provide a reference for this Methods 1) First paragraph, line 4: It should read: “waves, from 1998 to 2014, in randomly selected older adults…” (delete a) 2) First paragraph, line 5: It should be : “ 85% of the Chinese population.” 3) Please comment on patients’consent and ethics. 4) Page 6, third line: It should read: This, the total score of these 38 items was 39. Results 1) First paragraph, line 5: It should read: number of teeth present was 9.58… The mean age of participants was… Discussion Page 11, line 2: It should read “Future studies” Page 11, line 20: It should read: frailty, future studies should…

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. Participants themselves counted the number of their teeth. Since the mean age of the study sample was 84 years, one wonders if any of the participants had some degree of cognitive impairment, which would affect the accuracy of the data. The authors indicated that the numbers of teeth reported ranged from 0 to 36. They also stated that 30% of older Chinese adults have never visited a dentist at all. It is therefore difficult to judge the reliability of the self-reported numbers of teeth. The authors should address this issue.
Response: Thank you for your valuable reminder. We indicated how the data of tooth number was collected in the survey, see Page 8. For those older adults who were not able to answer these questions due to cognitive, hearing or linguistic impairments, their closest relative or caregiver will be asked to answer them.

2. The authors omit an explanation of the study design and the participants’ response rate. The response rate affects the generalizability of the findings. Although the authors note that the strength of this study is its generalizability, that may not be the case if the response rate was low. The study design must be explained in more detail. In particular, the response rate must be stated.
Response: We added the response rate of the participants in CLHLS, see Page 5 in the second paragraph.

3. In the results, the difference in the FI between those who were edentulous and those with 28 teeth was about 1. The authors should discuss the significance of this difference in relation to other variables or to previous studies.
Response: We edited the results section, see Page 9-12. And we edited the discussion section by discussing the significance of our results in relation to other variables and to previous studies, see Page 13-15.

4. In the outcome variables, the authors should explain all chronic disease conditions and functional limitations.
Response: We added explanation on all chronic disease conditions, functional limitation, activities of daily living and other health condition included in calculating Frailty Index. And we added Table 1 to illustrate the items clearly, see Page 7.

5. In the outcome variables, nutritional status was not evaluated, although the authors mention malnutrition as a risk factor for frailty. The authors should explain why nutritional status was not included in the assessment of frailty.
Response: Thank you for your comment. We added BMI as an indicator of nutritional status and we analyzed the data again by including BMI as one of the covariates, see Page 8. We also discussed how nutritional status could influence the association between tooth loss and frailty, see Page 15.

6. In the statistical analysis, it is recommended that the authors confirm whether there was definite linearity between the number of teeth and the FI. Previous reports have indicated that the relationship between tooth loss and frailty may not be purely linear.
Response: Thank you for the suggestion. We analyzed the data again using logistic regression to obtain more information if the relationship is not purely linear, see Pages 8 and 9. And we discussed the results in terms of the non-linear relationship, see Page 13-14.

7. In the results section, the authors explained their findings using B, whereas it is my impression that β is more commonly used. Please confirm.
Response: We re-analyzed the data using logistic regression model, so odds ratios were reported, see Page 11-12.

8. In Table 1, I can't understand how the p values were calculated for age, number of teeth, education years and total income of your household last year. In addition, the authors should define all abbreviations used in the table (also in Table 2).
Response: We revised the table and defined all the abbreviations used in the table, see Table 2 and 3. We added explanation on how the statistical analysis was performed, see Page 8 and 9.

9. In the first paragraph of the Discussion, although the authors state that "According to our results, more teeth are associated with a lower prevalence of frailty," it is unclear how they calculated the prevalence of frailty
Response: We re-analyzed the data and rewrite the discussion section, see Page 13. We also described how to define frailty according to FI, see Page 8 in the first line.

10. In the fourth paragraph of the Discussion ("In China, oral diseases are…"), I don't understand that this section discusses about which part of results of this study.
Response: We deleted that paragraph and rewrite the discussion section, see Page 12-16.

Reviewer 2
1. In the summary section, the final indicators (B=-0.05, P=0.00) in the results are inconsistent with the indicators given in the results of the article (B=-0.04, P=0.00).
Response: Thank you for the reminder. We re-analyzed the data and rewrite the abstracts and results section, see Page 2, 9-12.

2. In the methodological section, 1) the introduction of the 38 indicators contained in the core indicators of the frailty index is somewhat too brief. 2) More introduction of the statistical analysis is needed for the single factor analysis of continuous variables such as age and number of teeth and frailty score.

Response: 1) We added explanation on the 38 indicators and how the Frailty Index was calculated, and we also added Table 1, see Page 7. 2) We rewrite the statistical analysis section and explained the statistical analysis process, see Page 8 and 9.

3. Result section, 1) The results of Model 3 is suggested to describe the correlation between the number of teeth and the frailty scores in order to correct all confounding factors, rather than the results of model 1. 2) Although the number of teeth is correlated with the frailty scores in the model 3 showed in table 2, the correlation coefficient b is only -0.05, that is, for every tooth reduction, the frailty score increased by 0.05 points, which is obviously not practical importance; 3) The age, the number of teeth and other continuous variables and the frailty scores might be not linear relationship, the explanation of the results is less meaning. In summary, it is recommended to replace continuous variables with categorical variables for analysis.
Response:
1) We re-analyzed the data and reported the correlation between the number of teeth and the frailty scores using the final adjusted model, see Page 11 and Table3.
2) We re-analyzed the data using logistic regression and reported odds ratios for included variables, see Page 11 and Table 3.
3) We recoded the number of teeth and the Frailty Index as categorical variables for analysis, see Page 8.

4. Discussion section, 1) In 37th line on 8th page (According to our results, more teeth are associated with a lower prevalence of frailty) it is suggested to change the “prevalence” into “risk”. 2) The advantages of using FI in the second paragraph of the discussion section is suggested to move to the background section. 3) The fourth paragraph describes the causes of oral health problems of the elderly in China is not suitable here, because the purpose of this study does not explore the current situation of oral health in Chinese population.
Response:
1) We changed the “prevalence” into “risk” and rewrite the discussion section, see Page 13.
2) We moved the paragraph of advantages of using FI to the background section, see Page 4 in the second paragraph.
3) We deleted that part.

5. There are some unsuitable language expression as followings: 1) unified format of the references; 2) in the background section, the reference 11 was cited two times, but the expressive meaning appears to be contradictory. (Notably, emerging research showed that frailty was significantly associated with oral health and functions, including tooth number, 11,12,13/ some studies did not find a significant association between number of teeth and frailty. 9, 11, 16, 17). 3) The first line of the result section ">65 years" should be "≥65 years", because of "range=65-113" in the 6th line of the result section.
Response:
1) We checked and modified the reference format, see Page 17.
2)We revised the sentence, see Page 4 in the second paragraph.
3) We changed ">65 years" to "≥65 years", see Page 9.

Reviewer 3
1. The major change that is needed is in the discussion, and authors should take into account the possibility of this association being inverse, i.e., frailty impacting on activities of daily living such as brushing, inability to leave the house and visit a dentist, etc… ultimately resulting in tooth loss. This is very important as it points out to the need of educating carers and family regarding how to care for their frail family member’s oral health in order to avoid tooth loss.
Response: Thank you for the reminder. We added how frailty might contribute to tooth loss in the discussion section, see Page 16.

2. Abstract: Conclusions: third sentence should be: “specific mechanisms underlying how oral health is related to frailty”.
Response: We revised the sentence accordingly, see Page 2.

3. Introduction: Page 4, line 4: please provide a reference for this.
Response: We provided a reference for the sentence, see Page 4.

4. Methods
1) First paragraph, line 4: It should read: “waves, from 1998 to 2014, in randomly selected older adults…” (delete a)
2) First paragraph, line 5: It should be: “85% of the Chinese population.”
3) Please comment on patients’ consent and ethics.
4) Page 6, third line: It should read: This, the total score of these 38 items was 39.
Response:
1) and 2) We changed the expression accordingly, see Page 5.
3) We added the patients’ consent and ethics. see Page 5 in the first and second paragraph.
4) We revised the expression accordingly, see Page 7.

5. Results: First paragraph, line 5: It should read: number of teeth present was 9.58… The mean age of participants was…
Response: We changed the sentence accordingly, see Page 9.

6. Discussion
Page 11, line 2: It should read “Future studies”
Page 11, line 20: It should read: frailty, future studies should…
Response to Reviewer 3 comment No. 6:
We rewrite the discussion section and modified similar grammar errors accordingly.

VERSION 2 – REVIEW

REVIEWER	Takamasa Komiyama Division of Aging and Geriatric Dentistry, Tohoku University Graduate School of Dentistry.
REVIEW RETURNED	20-May-2019

GENERAL COMMENTS	1. In Methods section, it is unclear how do the authors determine the cut-off score of frailty. It must be difficult for readers to understand where the cut-off score (0.21) come from. 2. In Discussion third paragraph (“Demographic factors are….”), it is unclear whether this section discusses the purpose of the present study.

REVIEWER	Cristiane da Mata University College Cork-Ireland
REVIEW RETURNED	04-Jun-2019

GENERAL COMMENTS	The manuscript has improved substantially. However, I would suggest some minor amendments Abstract: Conclusion: It should something like:" The presence of fewer teeth is significantly..." Introduction, last paragraph: Sentence starting with "Therefore"

	should be part of discussion. As part of the Introduction, that sentence should be replaced by: Therefore, the aim of this study was... " Page 8: Independent variable: Last sentence should read: "In the present study, to be in accordance with..." Page 9, second sentence should start: "A multiple logistic..." Page 9: Characteristics of participants, second sentence should be: The final analysis....older adults who had complete data". Page 9: Characteristics of participants, sentence starting with: For health behaviors should read: " For health behaviors, 66.3%...never smoked...never drank alcohol...did physical labor... Discussion, page 13, line 25 (" This finding might imply..."): Rewrite sentence, it does not read well. Page 15, line 10: It should read: "However, this hypothesis is not verified in population studies and is opposite to the findings of animal studies..." Page 15, line 17: It should be:There is a lack of studies on the relationship among...

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1. In Methods section, it is unclear how do the authors determine the cut-off score of frailty. It must be difficult for readers to understand where the cut-off score (0.21) come from.

Response: Thank you for the comments. We explained the cut-off score of FI and indicated the reference.

2. In Discussion third paragraph (“Demographic factors are….”), it is unclear whether this section discusses the purpose of the present study.

Response: We edited the sentence and shortened the paragraph. In this section we discussed how the study design and data analysis might influence the findings.

Reviewer: 3

1. Abstract: Conclusion: It should something like:" The presence of fewer teeth is significantly..."

Response: Thank you for the comments. We edited the sentence accordingly.

2. Introduction, last paragraph: Sentence starting with "Therefore" should be part of discussion. As part of the Introduction, that sentence should be replaced by: Therefore, the aim of this study was... "

Response: The sentence has been edited.

3. Page 8: Independent variable: Last sentence should read: "In the present study, to be in accordance with..."

Response: The sentence has been edited.

4. Page 9, second sentence should start: "A multiple logistic..."

Page 9: Characteristics of participants, second sentence should be: The final analysis....older adults who had complete data".

Page 9: Characteristics of participants, sentence starting with: For health behaviors should read: " For health behaviors, 66.3%...never smoked...never drank alcohol...did physical labor...

Response: Thank you for the corrections. We revised all of these sentences.

5. Discussion, page 13, line 25 (" This finding might imply..."): Rewrite sentence, it does not read well.

Response: The sentence has been edited.

6. Page 15, line 10: It should read: "However, this hypothesis is not verified in population studies and is opposite to the findings of animal studies..."

Page 15, line 17: It should be: There is a lack of studies on the relationship among...

Response: We revised the sentences accordingly.

VERSION 3 – REVIEW

REVIEWER	Takamasa Komiyama Tohoku University, Japan
REVIEW RETURNED	20-Aug-2019

GENERAL COMMENTS	None

REVIEWER	Cristiane da Mata University College Cork Ireland
REVIEW RETURNED	04-Sep-2019

GENERAL COMMENTS	The manuscript has improved substantially. Some minor suggestions are as following: 1) Page 2, Primary and secondary outcome measures, line 8: Replace "employing" with "using". 2) Introduction, First paragraph, line 7: Poised should be replaced with a more widely used term. Line 9: Replace "person" with "individual". 3) Should the term "frailty phenotype" be written in capital letters the same as "Frailty Index"? Correct it throughout the manuscript. 4) Page 28, first line: It should read "present", instead of "presence". 5) The term Univariate logistic regression should be singular. "A univariate logistic regression was used". Please correct it throughout. 6) Discussion, 10th line, sentence starting with" To the best of our knowledge" should be in the beginning of the section, maybe after the first sentence.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 3
1) Page 2, Primary and secondary outcome measures, line 8: Replace "employing" with "using".
Response: Thank you for the correction. We edited the sentence accordingly.
2) Introduction, First paragraph, line 7: Poised should be replaced with a more widely used term. Line 9: Replace "person" with "individual".
Response: We edited the sentences accordingly.
3) Should the term "frailty phenotype" be written in capital letters the same as "Frailty Index"? Correct it throughout the manuscript.
Response: We edited the words throughout the manuscript.
4) Page 28, first line: It should read "present", instead of "presence".
Response: We corrected the word.
5) The term Univariate logistic regression should be singular. "A univariate logistic regression was used". Please correct it throughout.
Response: We corrected the words throughout the manuscript.
6) Discussion, 10th line, sentence starting with" To the best of our knowledge" should be in the beginning of the section, maybe after the first sentence.
Response: We changed the place of the sentence accordingly.