PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Areca nut consumption with and without tobacco among the adult population: a nationally representative study from India
AUTHORS	Singh, Prashant Kumar; Yadav, Amit; Singh, Lucky; Mazumdar, Sumit; Sinha, Dhirendra; Straif, Kurt; Singh, Shalini

VERSION 1 – REVIEW

REVIEWER	Clara André Instituto Politécnico de Santarém Escola Superior de Saúde de Santarém Portugal
REVIEW RETURNED	03-Oct-2020

GENERAL COMMENTS	The overall article is well written and a very important subject nowadays. Regarding the references, they could be more up-to-date, despite being adequate.

REVIEWER	Otto Ruokolainen Finnish Institute for Health and Welfare, Finland
REVIEW RETURNED	02-Nov-2020

GENERAL COMMENTS	Review for 'Areca nut use among the adult population in India: a nationally representative cross-sectional study' (bmjopen-2020-043987) by Sing et al. submitted to BMJ Open. Thank you for the opportunity to review this manuscript. The manuscript describes the prevalence and determinants of areca nut use with and without tobacco in India. The authors utilize a large and nationally representative cross-sectional study (GATS) from India and include several background factors to examine the correlates of different types of areca nut use. Overall, I find the study interesting but I have some remarks on the paper which hopefully help the authors to strengthen it. Throughout, the manuscript would benefit of a more careful language revision as some sentences were quite hard to follow and there were quite many typos as well. Also, currently it is unclear if some presented results/differences between groups were formally tested or not. Below are my comments point-by-point. Abstract • First sentence: Would 'substance use' be more appropriate than 'substance abuse'? Since the authors refer also for example to caffeine, I would prefer 'substance use' (also nicotine could be 'used' instead of 'abused' in terms of NRT). It could be more neutral, while in the main body text, health harms of areca nut use could be provided (as the authors have). Also, later in the manuscript the authors refer to 'consuming' areca nuts (see for

	example Results in the Abstract); it might be good idea to use the same concepts throughout the manuscript. • Participants: Please, provide response rate. • Results: “When compared to females, males were more prone...”: Could this be reformulated as: “When compared to females, males were more prone to use consume areca nut (with tobacco: RR...; without tobacco: RR....). I think it would be more easy to read. • Conclusion: “Areca nut is not explicitly covered by the WHO FCTC”. I wonder, why should it be? Of course, as the authors state in the introduction, areca nut use could be seen as form of smokeless tobacco use when including tobacco, but why should areca nut use when not containing tobacco be covered by WHO FCTC? This sentence could be reformulated. • Conclusion, second sentence: “...in the country”. In which country? (In India) Strength and Limitations of this study • This section appear to me more like highlights etc. instead of strenghts and limiations. • Third bullet: Do the millions after each states refer to estimated number of areca nut users? • Fourth bullet: “...significantly determines...”. In my opinion, this is rather too causal language and should be rephrased. For example: ”... affilition were significantly associated with areca nut use in India”. • Fifth bullet: Why is the age limit seen as a limitation (or is it)? When the authors look into to different determinants of areca nut use such as education, occupation, and marital status, I think it is more relevant to include older participants than under 15-year-olds. Funding statement • On page 15 of the manuscript, different information on the funders are provided 8”Indian Council of Medical Research, New Delhi”). Which one is correct? Introduction • Since all the international readers might not be familiar with areca nut and its different types, I suggest more information on this is provided in Introduction. Some of these are covered later in the manuscript but I think it would be beneficial to include more explicit notions already in the Introduction that there areca nut is being used in different/several forms (betel, gutka, pan masala?), possibly including also tobacco (this is written out in lines 52–54 but I think more explicit notion would be beneficial). What else do these products contain than areca nut and tobacco? Refer to, for example, how smokeless tobacco or electronic cigarettes are being described in articles. • Page 5, line 25: How many studies/participants did this meta-analysis include? • Page 5, line 27: “Furthermore, studies have documented that areca nut use adversely affects all organs of the human body”. Is there really evidence that areca nut use affects all organs of the body? In the cited reference (number 6, Garg et al. 2014), this is being stated: “Areca nut affects almost all organs of the human body”. Maybe this sentence could be rephrased based on the cited reference?. • Page 5, lines 30–36: “Studies also found...” This sentence is, in my opinion, rather hard to follow. • Page 5: line 37: “Children start...” I am not sure if this sentence is necessary. Do the authors intend to state that areca nut use is being started at an early age and could be started with different kinds of areca nut products? If this is so, the sentence could be revised.

	• Page 5, Line 51: “SLT”. Please, define this abbreviation since not all readers might know which does this refer to. • Page 5: lines 51–56: I am not sure I followed this sentence. Maybe it could be rewritten? • Page 6, line 3, “Existing studies on areca nut lack representativeness”. Based on the provided search terms, I think the authors have looked into prior research in India. If this is true, it could be included in the sentence. Another question is, should the authors conduct a more broad search of prior studies to account for studies outside India as well (since the authors state in the Introduction that areca nut is being used in many Asia-Pacific countries, China and Taiwan)? • Page 6, line 25: “...consumption remains at the top”. Do the authors mean that areca nut use is highly prevalent/common etc. in India? Methods and Materials • Page 6, line 54: Is there some other response rate available than “household and individual response rate”? Are these two the same? For this section, I would like to have read something, even shortly, about how households were selected. • Dependent variables: If I understood correctly, areca nut use without tobacco and areca nut use with tobacco was assessed differently (pan masala and betel quid withouth tobacco: “Do you use..”, but for example betel quid with tobacco: On average, how many times a day...”).What is the rationale for this? Also, response options for these questions could be presented. Currently, it is unclear whether this has been a multiple choice or an open question. Could the authors compute a variable with different levels of areca nut use? The difference between these classes could be interesting to examine, for example in table 5. • Page 6, line 42: Could this be “(i) areca nut use only without tobacco, (ii) arca nut use only with tobacco” to highlight the exclusive use of such product? Same applies to line 50: “Areca nut use only without tobacco...” • Page 7, line 3, “Areca nut of any type”: I understood that areca nut use might include also tobacco, for which this class sounds to me that it should be “Any type of areca nut use only without tobacco”. I am sorry if I missed something. • Page 8, line 15: Both forms: ...”at the same time”. If the authors mean “dual use”, this could be inserted (the products are not used in practice at the same time). • Page 8, lines 24–25: For which the citations numbers 14–18 refer to? • Page 8, line 30: “(i) no education”. In tables, the class is named “No formal education”. Please, use analogous terms. • Page 8: More details of the conducted PCA would be beneficial. Why was PCA conducted instead of just computing the sumvariables (if such variables were used)? How many variables were there originally and how many constructs got computed based on the iterations? Which PCA method was applied? See also citation number 9 on reference list is incomplete. • Page 9, line: 10: “Do you think tobacco leads to addiction”. So this question was for tobacco, not spesifically for smokeless tobacco. If so, the composite variable is not exclusively on the “poor health impact of smokeless tobacco use”. • Page 9, lines 19–22: Please use a uniform term for caste/social group. Also, it would be interesting to know what type of and what level of socioeconomic disadvantage in education, health, etc. led to certain classification. • Page 9, line 29: “UT:” Please write out this abbreviation.

	• Page 9, line 36: Please write out the abbreviation χ^2. What did the authors exactly test with this test? The association between areca nut use and background variables ('independent variables')? Looking at Table 4 and its footnote, it is not self-evident what the authors have calculated. Also, the p-values are missing from the Table 4 altogether (or some explicit mention on the footnotes about the p-values). • Page 9 line51: What is the rationale for using multinomial logit regression over conducting three different binary logistic regression models? • Page 9, lines 51–55: Please, revise the name of the classes accordingly (for example, 'areca nut use with tobacco' --> 'areca nut use only with tobacco'). Consider also if the 'dual user' should be changed to 'areca nut use bot with and without tobacco'. • Page 9, line 55: In the text, the abbreviation for relative risk ratio is presented as 'RR' while in the Tables it is presented as 'RRR'. • Page 10, line 4: Please add a citation to the GATS India report. • Page 10: In the text Stata 15 is being referred to but in the reference list, Stata 13 is being referred to. Also, where pweights or some other weights utilized ("Appropriate adjustement for sampling weights was considered")? Results • Overall, it should be stated more clearly if some presented differences were statistically tested. For example, page 11, lines 40: "Consumption of areca nut in any form was gigher among males as compared to females" • It might be good to give some background information on the regional characteristics/disparities etc. in the introduction. Currently, pretty much emphasis is put on the regional areca nut use prevalences but these differences or their interpretation/meaning tell little to international readers. • Page 10, line 34, "Of the 74037 sample": Would 74037 respondents be more appropriate? • Page 10, line 37: Does" illiterate" mean the same as "no formal education2 (as in the Suppl Table 1)? Please use one term exclusively. • Page 10, line 49: Men used gutka the most. Please include if this was statisitcally tested or postulated otherwise (e.g. loooking at whether 95% CIs overlapped). • Page 11, line 9, Regional and socioeconomic disparity in areca nut, Include the term "use" in the section heading. The section includes also age, marital status which are not regional nor socioeconomic factors. Should the heading be "Demographic and regional differences" etc.? Also, the next section is "Determinants of areca nut use" but I think this section also considers determinants of areca nut use. • Page 11, line 46: "All forms of areca nut use was higher..." Please add, higher than in which group? Also, add if this was formally tested or not. • Page 11, line 46: To me, this result seems invalid: in table 4, among the 19–23 year-olds, the prevalence of areca nut use without tobacco is 14.8% • Page 11, line 47: The reader might wonder why is the result for widowed/separated/divorced presented but not for other groups? • Page 12, line 11–12, "Regression results suggest that the likelihood of areca nut use in both forms were positively associated with increase in age". With the current study design, would this be the other way around? So that increase in age results in the higher likelihood of areca nut use?

	• Page 12, lines 23: ‘”dual use was declining with increase...”. Could it be stated more accurately that the probability of areca nut use declined etc.? • Table 4: Please providide explanation of the conducted statistical test and p-values. • Table 5: It might be good idea to switch the position of the columns “p-value” and “95% CI”. Also add what is the reference category in the analysis. • Suppl Table 1: Please, write out “SLT” • Suppl Table 2: Would it be better to move the column “Areca Nut of Any Type” to the far right? If that is a more comprehensive class than “Gutka, Areca Nut-Tobacco Lime Mixture, or Mawa”. I am sorry if I have understood something incorrectly. • Suppl Table 3 & 4: These tables have the same title but different contents. It should be stated in the title that Suppl table 3 desribes urban/rural differences while Suppl table 4 describes gender differences. Again, were the differences formally tested? Discussion • Overall, I would like to have read more implications/possible explanation regarding the proposed results (“Why is this so?”). Currently, the discussion is rather descriptive. Also, more discussion on the interplay between tobacco control and areca nut use control would be welcomed. • Page 12, lines 37, “making areca nut a much bigger public health challenge”. Bigger public health challenge than what? Also, is the areca nut in itself or its use the problem? • Page 12, line 40: “Moreover, nearly 10% consumed areca nut with tobacco”. It must be stated that of the areca nut users, 10% consumed it with tobacco (rather than 10% of the population used it with tobacco as it currently leads to interpret). • Page 12, line 44–47, regulation of areca nut products. This would be important background information for the readers already in the Introdution: what is the current state of legislation considering areca nut and its use. • Page 13, lines 6–8, “As far as other SES determinants..:”. Age, gender, marital status, and religion are not determinants of socioeconomic position/SES. Please see for example Galobardes et al. 2006 https://dx.doi.org/10.1136/jech.2004.023531 • Page 13, line 25, “..and elsewhere[11]”. Where actually? This could be stated. • Page 13, lines 27–29: “in 11 states, areca nut use was higher among women as compared to men”. I find it rather inconvenient to present altogether new results in the Discussion section. Would this results be stated somewhere in the Results section as well (or to revise the last sentence in the first paragraph of the section Regional and socioeconomic disparity”? Again, include also the notion if this difference was formally tested. • Page 13, lines 34–36, “were highly addicted and less aware about the cessation methods.” It is unclear for me in which results does this refer to? Was dependence measured? • Page 14, line 41: “often start at younger age”. Why is this a limitation? When examining determinants of areca nut use – not areca nut use initiation – I don’t view this as a limitation. • Page 15, line 15: “... in the country”. In which country? Would urgent policy interventions be applicable to one country only?

REVIEWER	Rooban Thavarajah 1. Department of Oral & Maxillofacial Pathology, Ragas Dental College and Hospital, 2/102 East Coast Road, uthandi, Chennai-600119, India

	2. Marundeeeswara Oral Pathology Services and Analytics, Shollinganallur, Chennai 600119, India
REVIEW RETURNED	07-Nov-2020

GENERAL COMMENTS	The research work titled "Areca nut use among the adult population in India: a nationally representative cross-sectional study" is the need of the hour as the use of smokeless tobacco, particularly those with areca nut is being increasingly used by the young Indians. About 2 decades back it was estimated that about 600 million use globally, areca nut in some form. Since then, this reference by Gupta PC was used as the standard reference for across most of the areca nut literature. In 2015, Thavarajah R et al., estimated the Pan Masala and Gutka users across India using NFHS data. The overall areca nut consumption in India as well as number of people projected to regularly chew areca nut was not reported. This present work attempts to address the same. Areca containing products poses severe public health challenge and its aftermath, a terrible socio-economic-health burden. Such a burden warrants policy alterations to combat the areca use epidemic. For this to happen, the epidemiology of areca nut consumption across India needs to be studied. This study moves in that direction. As outlined in the reference 1, the areca nut use across India has not been documented and this GATS 2016-2017 data might be one of the best available way to have a robust estimate. This robustness needs to be stressed and the value of this exercise cannot be ignored. Authors have clearly justified the need of the study and answered partly to a direction suggested by the Thavarajah R, Ranganathan K, Joshua E, Rao UK. Areca nut use disorder: A dynamic model map. Indian J Dent Res 2019;30:612-21. In this regard, this article could add valuable insights to existing body of literature. As such the introduction part has no major issues barring minor language and typographical corrections. The methodology part is clear, reproducible - However, as it is a secondary data analysis, the readers should be warned of the limitations of study design, extra-polation and limitations of India specific GATS survey - Perhaps the limitation paragraph in discussion could be expanded. In results section- the proportion of any areca nut use in India can be projected as a choropleth map to show the high geographical variation for ease of understanding to ordinary reader and perhaps which could be used liberally by policy makers in future. The authors may consider highlighting the following facts in discussion - The calibration of different forms of Areca nut across a socio-economic-religio-culturally diverse country such as India in GATS was not performed as that was not the primary intention of GATS. The nomenclature of various areca nut products in geographically diverse location intrinsically could be a source of concern and there by cloud the results - For example, Khaini, ("HANS") a smokeless tobacco product, has probably no or very little of areca nut shaving but been considered as areca nut product by several investigators. This diversity in areca nut-tobacco products could have bio-psycho-social ramifications when translated/accounted for policy based decisions. The issue of health effects difference between traditional chewing practice and newer ones, (as per the study of ICAR-CPCRI, Arecanut Research and Development Foundation, Directorate of Arecanut and Spices Development in the Indian Journal of Arecanut, Spices and Medicinal Plants (Vol 22-I) by C T Jose, S Keshava Bhat, K P Chandran, S Jayashekara and Ananda Gowda) has to be considered.

	Authors need to include the fact that a substantial part of this data has been covered in the publication - Arora M, Shrivastava S, Mishra VK, Mathur MR. Use of Betel Quid in India from 2009 to 2017: An Epidemiological Analysis of the Global Adult Tobacco Survey (GATS). Subst Use Misuse. 2020;55(9):1465-1471. doi: 10.1080/10826084.2020.1726393. As this particular work was carried in a chronoenvironment, the peculiar habit dynamics have been captured. Authors of the present work failed to consider and include in discussion this work. In the present study and that of Arora M study, it was observed that Areca /Betel Quid use was higher in certain parts of the country. This variation has got huge policy level ramifications, as betel quid has a great socio-religious and cultural sanction. Areca nut Cessation programs in such parts of India would bank on social determinants and level of awareness to formulate their microlevel policies. Also, past UP/Lucknow based population level screening has revealed that a substantial part of the pan masala chewing population suffers with oral precancerous states. Considering all this facts, the conclusions of the study has huge public health ramifications. Hence the result of the study including determinants has to be interpreted in caution. There is no second thought that the projected numbers of Areca nut chewers or the role of determinants – However, these are robust estimates. These data would help to refining an exhaustive but pertinent Areca nut usage screening survey. Probably such a survey would yield the much needed accurate answers for the research questions. The reports of use of pan masala and gutka in males/females/urban-slums has been previously reported using a nationally representative sample - this work and its conclusion has also not been considered in discussion. Though they do not represent the entire areca nut using population at that point of time, those data have captured most of the reported trend, at least a decade ago. These articles could greatly contribute to the discussion as findings of social determinants could be compared. The RRR of various Areca nut product, as compared to north India, for other parts have increased RRR. The reason behind this phenomenon, as compared to NFHS data, would be interesting to compare and explore the reasons for the difference. The health effects of the areca nut are cumulative. With substantial part of the 223.79 million users across India would be casual users (not confirming to dependence/ addiction/ use disorders definitions), it would be prudent to include in future directions that the GATS studies regarding intensity, frequency and duration of areca nut products consumption included as the public health burden due to Areca nut could be computed.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comment: The overall article is well written and a very important subject nowadays.
Regarding the references, they could be more up-to-date, despite being adequate.
Response: We have added updated references in the revised document, as mentioned below.
• Gupta PC, Ray CS, Papke RL, et al. Perspectives on areca nut with some global implications: Symposium report. Transl Res Oral Oncol 2018;3:2057178X18814068.

• Mehrtash H, Duncan K, Parascandola M, et al. Defining a global research and policy agenda for betel quid and areca nut. Lancet Oncol 2017;18:e767–75.
• Singh PK, Yadav A, Lal P, et al. Dual Burden of Smoked and Smokeless Tobacco Use in India, 2009–2017: A Repeated Cross-Sectional Analysis Based on Global Adult Tobacco Survey. Nicotine Tob Res Published Online First: 2020. doi:10.1093/ntr/ntaa033
• Bandyopadhyay A, Irfan M. Educational and Wealth Inequalities in Smokeless Tobacco Use: An Analysis of Rural-Urban Areas of Bangladesh and India. Subst Abus Res Treat 2019;13:1178221818825074.

Reviewer: 2

Abstract
Comment: First sentence: Would 'substance use' be more appropriate than 'substance abuse'? Since the authors refer also for example to caffeine, I would prefer 'substance use' (also nicotine could be 'used' instead of 'abused' in terms of NRT). It could be more neutral, while in the main body text, health harms of areca nut use could be provided (as the authors have). Also, later in the manuscript the authors refer to 'consuming' areca nuts (see for example Results in the Abstract); it might be good idea to use the same concepts throughout the manuscript.
Response: The suggestion has been incorporated in the revised manuscript.

Comment: Participants: Please, provide response rate.
Response: The suggestion has been incorporated in the revised manuscript. Please refer to the 'participants' section of the abstract.
Results: Comment: "When compared to females, males were more prone...": Could this be reformulated as: "When compared to females, males were more prone to use consume areca nut (with tobacco: RR...; without tobacco: RR....). I think it would be more easy to read.
Response: The suggestion has been incorporated in the revised manuscript. Please refer to the result section of the abstract.

Conclusion: Comment: "Areca nut is not explicitly covered by the WHO FCTC". I wonder, why should it be? Of course, as the authors state in the introduction, areca nut use could be seen as a form of smokeless tobacco use when including tobacco, but why should areca nut use when not containing tobacco be covered by WHO FCTC? This sentence could be reformulated.
Response: We do not intend to say that Areca nut should be included in FCTC. We have suggested that since Areca nut is not covered under FCTC, tobacco control efforts would not cover Areca nut consumption without tobacco which is now the dominant form of Areca nut use in India. We have revised our conclusions to make this point clearer.

Comment: Conclusion, second sentence: "...in the country". In which country? (In India)
Response: Yes, it should be India. The suggestion has been incorporated in the revised manuscript

Strength and Limitations of this study
Comment: This section appear to me more like highlights etc. instead of strengths and limitations.
Fourth bullet: "...significantly determines...". In my opinion, this is rather too causal language and should be rephrased. For example: "... affilition were significantly associated with areca nut use in India".
Fifth bullet: Why is the age limit seen as a limitation (or is it)? When the authors look into to different determinants of areca nut use such as education, occupation, and marital status, I think it is more relevant to include older participants than under 15-year-olds.
Response: We have revised thissection of the manuscript and addressed your suggestions, please see the Strengths and Limitations section.

Comment: On page 15 of the manuscript, different information on the funders are provided 8"Indian Council of Medical Research, New Delhi"). Which one is correct?
Response: We have resolved this issue. No funding was received for this study.

Introduction
Comment: Since all the international readers might not be familiar with areca nut and its different types, I suggest more information on this is provided in Introduction. Some of these are covered later in the manuscript but I think it would be beneficial to include more explicit notions already in the Introduction that there areca nut is being used in different/several forms (betel, gutka, pan masala?), possibly including also tobacco (this is written out in lines 52–54 but I think more explicit notion would be beneficial). What else do these products contain than areca nut and tobacco? Refer to, for example, how smokeless tobacco or electronic cigarettes are being described in articles.
Response: Thank you for your suggestion. We have added the following in the first paragraph of the introduction.
It is not only known in several, sometimes local names, but also used in several forms e.g. pan masala, gutkha, mawa, dohra, Kharra, betel etc. with or without tobacco. Some forms of consumption may also include other constituents, such as betel leaf, slaked lime and various spices.

Comment: Page 5, line 25: How many studies/participants did this meta-analysis include?
Response: This meta-analysis was based on 50 studies and this has been included in the revised draft.

Comment: Page 5, line 27: "Furthermore, studies have documented that areca nut use adversely affects all organs of the human body". Is there really evidence that areca nut use affects all organs of the body? In the cited reference (number 6, Garg et al. 2014), this is being stated: "Areca nut affects almost all organs of the human body". Maybe this sentence could be rephrased based on the cited reference?.
Response: We have rephrased the sentence as suggested and now it reads…. "A global systematic review based on 62 studies concluded that consumption of areca nut affects almost all organs of the human body, including the brain, heart, lungs, gastrointestinal tract and reproductive organs; and causes or aggravates pre-existing conditions such as neuronal injury, myocardial infarction, cardiac arrhythmias, hepatotoxicity, asthma, central obesity, type II diabetes, hyperlipidemia, metabolic syndrome[8]."

Comment: Page 5, lines 30–36: "Studies also found..." This sentence is, in my opinion, rather hard to follow.
Response: We have modified the sentence in the revised document.
"Previous studies observed that areca nut dependency among users [9] and its withdrawal effects [10] were similar to those observed among nicotine users [10]."

Comment: Page 5: line 37: "Children start..." I am not sure if this sentence is necessary. Do the authors intend to state that areca nut use is being started at an early age and could be started with different kinds of areca nut products? If this is so, the sentence could be revised.
Response: We have revised the sentence as below.
"It is also a gateway product in children who start using different kinds of areca nut products at an early age."

Comment: Page 5, Line 51: "SLT". Please, define this abbreviation since not all readers might know which does this refer to.
Response: We have defined the abbreviation in the revised manuscript – smokeless tobacco (SLT).

Comment: Page 5: lines 51–56: I am not sure I followed this sentence. Maybe it could be rewritten?
Response: We have modified the sentence in the revised document.
“Alhough tobacco control policies are applicable to areca nut products which contain tobacco a considerable number of people now consume areca nut without tobacco, which poses greater public health challenges in controlling and regulating the substance [13].”

Comment: Page 6, line 3, “Existing studies on areca nut lack representativeness”. Based on the provided search terms, I think the authors have looked into prior research in India. If this is true, it could be included in the sentence. Another question is, should the authors conduct a more broad search of prior studies to account for studies outside India as well (since the authors state in the Introduction that areca nut is being used in many Asia-Pacific countries, China and Taiwan)?
Response: The focus of our study is on Areca nut consumption in India, the country with the largest number and most diverse habits of Areca nut users worldwide. We have revised the sentence accordingly:“A comprehensive search of the literature revealed that
studies on areca nut use in India lack representativeness.

Comment: Page 6, line 25: “...consumption remains at the top”. Do the authors mean that areca nut use is highly prevalent/common etc. in India?
Response: We have modified the sentence in the revised document.
“While India’s share to overall areca nut production and consumption remains at the top in the world,…”

Methods and Materials
Comment: Page 6, line 54: Is there some other response rate available than “household and individual response rate”? Are these two the same? For this section, I would like to have read something, even shortly, about how households were selected.
Response: We have added the response rate and sampling design in the revised manuscript. Please refer to the ‘Study design and participants’ section.
The household response rate and person-level response rate were 96.7 percent and 96.0 percent respectively resulting in an overall response rate of 92.9 percent.

Comment: Dependent variables: If I understood correctly, areca nut use without tobacco and areca nut use with tobacco was assessed differently (pan masala and betel quid withouth tobacco: “Do you use..”, but for example betel quid with tobacco: On average, how many times a day...”).What is the rationale for this? Also, response options for these questions could be presented. Currently, it is unclear whether this has been a multiple choice or an open question.
Response: We have provided the response options for all questions in the revised manuscript. We have also removed the questions related to the frequency of areca nut as it was not used for constructing the dependent variables of this study. Please refer to the ‘Dependent variable’ section.

Comment: Page 7, line 42: Could this be “(i) areca nut use only without tobacco, (ii) arca nut use only with tobacco” to highlight the exclusive use of such product? Same applies to line 50: “Areca nut use only without tobacco...”
Response: We have modified the manuscript as suggested.

Comment: Page 8, line 3, “Areca nut of any type”: I understood that areca nut use might include also tobacco, for which this class sounds to me that it should be “Any type of areca nut use only without tobacco”. I am sorry if I missed something.
Response: We have revised it as ‘Areca nut of any type only without tobacco’.

Comment: Page 8, line 15: Both forms: ...”at the same time”. If the authors mean “dual use”, this could be inserted (the products are not used in practice at the same time).
Response: We have modified it as ‘dual use’

Comment: Page 8, lines 24–25: For which the citations numbers 14–18 refer to?
Response: We have modified the sentence and now it clearly shows that these citations are linked with the inclusion of key socioeconomic and demographic characteristic. Please refer to the “Independent variables” section.

Comment: Page 8, line 30: “(i) no education”. In tables, the class is named “No formal education”. Please, use analogous terms.
Response: We have made the terminology consistent throughout the manuscript.

Comment: Page 8: More details of the conducted PCA would be beneficial. Why was PCA conducted instead of just computing the sumvariables (if such variables were used)? See also citation number 9 on reference list is incomplete.
Response: We have included description about why a PCA was conducted and also updated the citations.
“A wealth index was calculated based on availability of electricity, flush toilet, radio, television, fixed telephone or cell phone, refrigerator, washing machine, moped/scooter/motorcycle and car using PCA (Principle Component Analysis) methodology[29]. There are various ways to assign weighting values to the indicator variables. Ad hoc weights, such as assigning “1” for a bicycle, “3” for a motorcycle, and “5” for a car or truck, work to a certain extent, but they are arbitrary and are difficult to assign when the wealth ordering is not readily apparent. For this reason, Filmer and Pritchett recommended using principal components analysis (PCA) to assign the indicator weights, the procedure that is used for the wealth index[30]. This procedure first standardizes the indicator variables (calculating zscores); then the factor coefficient scores (factor loadings) are calculated; and finally, for each household, the indicator values are multiplied by the loadings and summed to produce the household’s index value. In this process, only the first of the factors produced is used to represent the wealth index. The resulting sum is itself a standardized score with a mean of zero and a standard deviation of one[29]. Individuals were divided into five wealth quintiles based on their household score ranges from 1 being poorest to 5 being wealthiest, with each category representing 20 percent of the score[29].”
Reference
29. Rutstein SO, Johnson K. The DHS wealth index . DHS Comp. Reports No. 6. . 2004.http://dhsprogram.com/pubs/pdf/CR6/CR6.pdf
30. Filmer D, Pritchett LH. Estimating wealth effects without expenditure data—or tears: an application to educational enrollments in states of India. Demography 2001;38:115–32.

Comment: Page 9, line: 10: “Do you think tobacco leads to addiction”. So this question was for tobacco, not spesifically for smokeless tobacco. If so, the composite variable is not exclusively on the “poor health impact of smokeless tobacco use”.
Response: In the GATS questionnaire, this question - “Do you think tobacco leads to addiction” was asked in both sections – those who were smokers and those who said they chew smokeless tobacco. For better understanding and avoiding any confusion we have modified it as “Do you think smokeless tobacco leads to addiction”.

Comment: Page 9, lines 19–22: Please use a uniform term for caste/social group. Also, it would be interesting to know what type of and what level of socioeconomic disadvantage in education, health, etc. led to certain classification.
Response: We have made this terminology consistent throughout the manuscript. We have also added a few lines on disadvantages in health and education.

“Caste (social group) was categorised based on individual’s self-reporting as Scheduled Castes (SCs), Scheduled Tribes (STs), Other Backward Classes (OBCs) and others. This broad categorization of caste is based on their socioeconomic disadvantage in education, health, nutrition, and employment by federal government. For instance, a study has shown that as compared to other caste, children (age 2-5 years) and adolescents (age 6-18 years) belonging to scheduled tribes had the greatest risk of mortality (OR = 1.94, 95% CI = 1.47, 2.57), followed by those from scheduled castes (OR = 1.35, 95% CI = 1.05, 1.74) and other backward classes (OR = 1.33, 95% CI = 1.05,1.67) [17]. Other studies have also shown lower enrolment and completion of education among scheduled castes and scheduled tribes due to various factors [31,32].”

Comment: Page 9, line 29: “UT:” Please write out this abbreviation.
Response: We have already defined this abbreviation in the second line of the “study design and participant” section.

Comment: Page 9, line 36: Please write out the abbreviation χ^2. What did the authors exactly test with this test? The association between areca nut use and background variables (‘independent variables’)? Looking at Table 4 and its footnote, it is not self-evident what the authors have calculated. Also, the p-values are missing from the Table 4 altogether (or some explicit mention on the footnotes about the p-values).
Response: Please refer to the ‘Analytical Strategy’ of the revised manuscript and table 4 with added information related to the chi-squared test and p-values for better clarity. Chi-squared ( ) tests were performed to examine whether variations in areca nut consumption across independent variables were statistically significant.

Comment: Page 9 line51: What is the rationale for using multinomial logit regression over conducting three different binary logistic regression models?
Response: Binary logistic regression models can only be used with the ‘binary response’. However, in this study the outcome variable has four categories and therefore we used multinomial regression analysis:
(i) ‘non areca nut user’ (reference category)
(ii) ‘areca nut use with tobacco’,
(iii) areca nut use without tobacco’ and
(iv) ‘dual user’
We have extensively reviewed various cross-sectional studies, which used multinomial regression models for the outcome variables which has more than two categories and found that many studies have opted for the same considering the nature of the outcome variables and survey design (cross-sectional) Please refer to the below mentioned few highly cited studies for quick reference:

1. Ketteler, M., Bongartz, P., Westenfeld, R., Wildberger, J. E., Mahnken, A. H., Böhm, R., ... & Floege, J. (2003). Association of low fetuin-A (AHSG) concentrations in serum with cardiovascular mortality in patients on dialysis: a cross-sectional study. The Lancet, 361(9360), 827-833.
2. Forero, R., McLellan, L., Rissel, C., & Bauman, A. (1999). Bullying behaviour and psychosocial health among school students in New South Wales, Australia: cross sectional survey. BMJ, 319(7206), 344-348.
3. Haan, M., Kaplan, G. A., & Camacho, T. (1987). Poverty and health prospective evidence from the alameda county study. American Journal of Epidemiology, 125(6), 989-998.
4. Akhtar, P. C., Haw, S. J., Currie, D. B., Zachary, R., & Currie, C. E. (2009). Smoking restrictions in the home and secondhand smoke exposure among primary schoolchildren before and after introduction of the Scottish smoke-free legislation. Tobacco Control, 18(5), 409-415. PMID: 19671536
5. Chau, J. Y., van der Ploeg, H. P., Merom, D., Chey, T., & Bauman, A. E. (2012). Cross-sectional associations between occupational and leisure-time sitting, physical activity and obesity in working adults. Preventive Medicine, 54(3-4), 195-200.

6. Rognli, E. B., Bramness, J. G., Skurtveit, S., & Bukten, A. (2017). Substance use and sociodemographic background as risk factors for lifetime psychotic experiences in a non-clinical sample. Journal of Substance Abuse Treatment, 74, 42-47. PMID: 28132699
7. Gubelmann, C., Heinzer, R., Haba-Rubio, J., Vollenweider, P., & Marques-Vidal, P. (2018). Physical activity is associated with higher sleep efficiency in the general population: the CoLaus study. Sleep, 41(7), zsy070. PMID: 29617980
8. O'Connell, M. A., Leahy-Warren, P., Kenny, L. C., O'Neill, S. M., & Khashan, A. S. (2019). The prevalence and risk factors of fear of childbirth among pregnant women: A cross-sectional study in Ireland. Acta obstetricia et gynecologica Scandinavica. https://doi.org/10.1111/aogs.13599 PMID: 30821844
9. Schmidt, C. O., & Kohlmann, T. (2008). When to use the odds ratio or the relative risk?. International journal of public health, 53(3), 165-167.
10. Lee, J. (1994). Odds ratio or relative risk for cross-sectional data?. International Journal of Epidemiology, 23(1), 201-203.

Comment: Page 9, lines 51–55: Please, revise the name of the classes accordingly (for example, ‘areca nut use with tobacco’ --> ‘areca nut use only with tobacco’). Consider also if the ‘dual user’ should be changed to ‘areca nut use bot with and without tobacco’.
Response: We have revised the classes as per the suggestion in the revised ‘Analytical Strategy’ section of the manuscript. As per suggestion of this reviewer above, we are now consistently using “dual use”,

Comment: Page 9, line 55: In the text, the abbreviation for relative risk ratio is presented as ‘RR’ while in the Tables it is presented as ‘RRR’.
Response: It should be RRR. We have corrected the text.

Comment: Page 10, line 4: Please add a citation to the GATS India report.
Response: We have added the citation to the revised manuscript.

Comment: Page 10: In the text Stata 15 is being referred to but in the reference list, Stata 13 is being referred to. Also, where pweights or some other weights utilized (“Appropriate adjustement for sampling weights was considered”)?
Response: We have corrected the reference to STATA version 15and rephrased the sentence as: “The analysis was adjusted for sampling weights and multistage sampling design using syv command in STATA. Analysis was carried out in STATA 15 version”.

Results

Comment: Overall, it should be stated more clearly if some presented differences were statistically tested. For example, page 11, lines 40: “Consumption of areca nut in any form was higher among males as compared to females”
Response: Please refer to Table 1 which shows statistical differences between men and women and separately for urban and rural areas,, differences in areca nut use between men and women by state is shown in the descriptive statistics.

Comment: It might be good to give some background information on the regional characteristics/disparities etc. in the introduction. Currently, pretty much emphasis is put on the regional areca nut use prevalences but these differences or their interpretation/meaning tell little to international readers.
Response: We have added a paragraph in the Introduction section on regional disparity as suggested. Please refer to the 4th paragraph of Introduction section.

“India, with a population of over 1.30 billion, exhibits one of the highest socioeconomic and demographic heterogeneities ever experienced anywhere in the world at the regional level[14]. There is a considerable evidence of marked regional inequities in tobacco use[15], health and healthcare [16]and mortality outcomes [17]in India. These differences are primarily the outcome of differences in community-level development, population composition, state health expenditure, poverty levels, status of women, and availability, accessibility and affordability of maternal and child health care services and their utilization [18–20]. For instance, less than 1% women aged (15-49) had no formal schooling in Kerala (a state of southern India) whereas the corresponding figure of Bihar (located in eastern part of India) was 48% as per the National Family Health Survey [21]. Similarly, Infant Mortality Rate which is considered to be one of the key indicators of human development and health system performance substantial variations evident from highest at 63.5 infant deaths per 1000 live births in Uttar Pradesh to 5.6 in Kerala[21]. A recent study showed that dual use of both smokeless tobacco and smoking were ranging from 16.5% in Arunachal Pradesh to 1% in states like Andhra Pradesh, Tamil Nadu and Goa[15].”

Comment: Page 10, line 34, “Of the 74037 sample”: Would 74037 respondents be more appropriate?
Response: We have revised as “Of the 74037 respondents” in the revised doc.

Comment: Page 10, line 37: Does” illiterate” mean the same as “no formal education2 (as in the Suppl Table 1)? Please use one term exclusively.
Response: Yes, it’s “no formal education”. We have used this terminology throughout the revised paper.

Comment: Page 10, line 49: Men used gutka the most. Please include if this was statisitcally tested or postulated otherwise (e.g. loooking at whether 95% CIs overlapped).
Response: We have added results of statistical significance testing in the revised Table 1.

Comment: Page 11, line 9, Regional and socioeconomic disparity in areca nut, Include the term “use” in the section heading. The section includes also age, marital status which are not regional nor socioeconomic factors. Should the heading be “Demographic and regional differences” etc.? Also, the next section is “Determinants of areca nut use” but I think this section also considers determinants of areca nut use.
Response: We have now divided the sections as follows: Regional disparity in areca nut consumption and Demographic and socioeconomic differences in areca nut consumption

Comment: Page 11, line 47: The reader might wonder why is the result for widowed/separated/divorced presented but not for other groups?
Response: We decided to highlight results with a higher percentage of consumption; comprehensive results can be consulted in tables.

Comment: Page 12, line 11–12, “Regression results suggest that the likelihood of areca nut use in both forms were positively associated with increase in age”. With the current study design, would this be the other way around? So that increase in age results in the higher likelihood of areca nut use?
Response: We have adjusted the sentence to better reflect that the results are from a cross-sectional studyh.

Comment: Page 12, lines 23: ‘”dual use was declining with increase...”. Could it be stated more accurately that the probability of areca nut use declined etc.?
Response: We have revised as “However, the probability of areca nut consumption with tobacco and in dual-form was declining with increase in the education level of respondents.”

Comment: Table 4: Please providide explanation of the conducted statistical test and p-values.
Response: We have performed Chi-squared test for each demographic and socioeconomic groups, separately for all four forms of areca nut. Since, we found statistical significant less than <0.001 for all, we had originally reported this in the footnote of the table.
However, to avoid any confusion we have now inserted the p-values in the revised table.

Comment: Table 5: It might be good idea to switch the position of the columns “p-value” and “95% CI”. Also add what is the reference category in the analysis.
Response: We have switched the positions of the columns and indicated the reference category as suggested.

Comment: Suppl Table 1: Please, write out “SLT”
Response: Done as suggested.

Comment: Suppl Table 2: Would it be better to move the column “Areca Nut of Any Type” to the far right? If that is a more comprehensive class than “Gutka, Areca Nut-Tobacco Lime Mixture, or Mawa”. I am sorry if I have understood something incorrectly.
Response: We have revised the table as suggested.

Comment: Suppl Table 3 & 4: These tables have the same title but different contents. It should be stated in the title that Suppl table 3 desribes urban/rural differences while Suppl table 4 describes gender differences.
Response: Revised as per the suggestion.

Discussion

Comment: Overall, I would like to have read more implications/possible explanation regarding the proposed results (“Why is this so?”). Currently, the discussion is rather descriptive. Also, more discussion on the interplay between tobacco control and areca nut use control would be welcomed.
Response: Thank you for the observation: We have modified the manuscript and added further information in the discussion section.

Comment: Page 12, lines 37, “making areca nut a much bigger public health challenge”. Bigger public health challenge than what? Also, is the areca nut in itself or its use the problem?
Response: Thank you for your observation. we have revised the sentence to read as below:
"making areca nut a bigger public health challenge, compared to smokeless tobacco (199 million users), in dealing with substance abuse and addiction in the country. Given the adverse health impacts of areca nut - a known carcinogen - its high prevelance in itself presents a huge public health challenge for the country.

Comment: Page 12, line 40: “Moreover, nearly 10% consumed areca nut with tobacco”. It must be stated that of the areca nut users, 10% consumed it with tobacco (rather than 10% of the population used it with tobacco as it currently leads to interpret).
Response: No, 10% consumed areca nut with tobacco to the overall population of the study and not that of the areca nut user.

Comment: Page 12, line 44–47, regulation of areca nut products. This would be important background information for the readers already in the Introdution: what is the current state of legislation considering areca nut and its use.
Response:
As suggested, we have added this background information in the introduction:
"controlling SLT[10]. The regulatory framework for areca nut control has also remained limited to prescribing health warnings on areca nut products by the Food Safety and Standard Authority of India (FSSAI). Further, use of tobacco and nicotine as an ingredient in any food item is also prohibited under FSSA regulations, thereby restricting mixing of tobacco in areca nut products and vice-versa[1].

Comment: Page 13, lines 6–8, “As far as other SES determinants..:”. Age, gender, marital status, and religion are not determinants of socioeconomic position/SES. Please see for example Galobardes et al. 2006 https://dx.doi.org/10.1136/jech.2004.023531
Response: We have rephrased the whole sentence from “As far as other SES determinants are concerned, the findings confirmed age, gender, marital status, education, occupation, social group and religion are significantly associated with areca nut use” The sentence now reads “As far as other determinants are concerned, the findings confirmed that age, gender, marital status, education, occupation, social group and religion are significantly associated with areca nut use”.
Comment: Page 13, line 25, “..and elsewhere[11]”. Where actually? This could be stated.
Response: Thailand and Taiwan have been added.

Comment: Page 13, lines 27–29: “in 11 states, areca nut use was higher among women as compared to men”. I find it rather inconvenient to present altogether new results in the
Response: We have removed this sentence from the revised manuscript.

Discussion section.

Comment: Page 13, lines 34–36, “were highly addicted and less aware about the cessation methods.” It is unclear for me in which results does this refer to? Was dependence measured?
Response: No this hasn’t been covered in the study; we have dropped this sentence from the revised manuscript.

Comment: Page 14, line 41: “often start at younger age”. Why is this a limitation? When examining determinants of areca nut use – not areca nut use initiation – I don’t view this as a limitation.
Response: We think that the restricted age range is a limitation regarding a comprehensive overview of Areca nut consumption and its determinants. Knowledge about prevalence of use and its determinants at ages younger than 15 years may also have important policy implications.

Comment: Page 15, line 15: “... in the country”. In which country? Would urgent policy interventions be applicable to one country only?
Response: We have added ‘India’ as suggested.

Reviewer: 3

Comments to the Author:

Comment: The research work titled "Areca nut use among the adult population in India: a nationally representative cross-sectional study" is the need of the hour as the use of smokeless tobacco, particularly those with areca nut is being increasingly used by the young Indians. About 2 decades back it was estimated that about 600 million use globally, areca nut in some form. Since then, this reference by Gupta PC was used as the standard reference for across most of the areca nut literature. In 2015, Thavarajah R et al., estimated the Pan Masala and Gutka users across India using NFHS data. The overall areca nut consumption in India as well as number of people projected to regularly chew areca nut was not reported. This present work attempts to address the same. Areca containing products poses severe public health challenge and its aftermath, a terrible socio-economic-health burden. Such a burden warrants policy alterations to combat the areca use epidemic. For this to happen, the epidemiology of areca nut consumption across India needs to be studied. This study moves in that direction. As outlined in the reference 1, the areca nut use across India has not been documented and this GATS 2016-2017 data might be one of the best available way to have a robust estimate. This robustness needs to be stressed and the value of this exercise cannot be ignored. Authors have clearly justified the need of the study and answered partly to a direction suggested by the Thavarajah R, Ranganathan K, Joshua E, Rao UK. Areca nut use disorder: A dynamic model map. Indian J Dent Res 2019;30:612-21. In this regard, this article could add valuable insights to existing body of literature.
Response: Thank you for your kind words.

Comment: As such the introduction part has no major issues barring minor language and typographical corrections. The methodology part is clear, reproducible - However, as it is a secondary data analysis, the readers should be warned of the limitations of study design, extra-polation and limitations of India specific GATS survey - Perhaps the limitation paragraph in discussion could be expanded.
Response: In the revised manuscript we have addressed your observations including language editing, and expansion of study limitations in the discussion.

Comment: In results section- the proportion of any areca nut use in India can be projected as a choropleth map to show the high geographical variation for ease of understanding to ordinary reader and perhaps which could be used liberally by policy makers in future.
Response: We have prepared a map showing the pattern of any form of areca nut use across states in India, separately for men and women. Please refer to Figure no. 1

Comment: The authors may consider highlighting the following facts in discussion - The calibration of different forms of Areca nut across a socio-economic-religio-culturally diverse country such as India in GATS was not performed as that was not the primary intention of GATS. The nomenclature of various areca nut products in geographically diverse location intrinsically could be a source of concern and there by cloud the results - For example, Khaini, ("HANS") a smokeless tobacco product, has probably no or very little of areca nut shaving but been considered as areca nut product by several investigators. This diversity in areca nut- tobacco products could have bio-psycho-social ramifications when translated/accounted for policy based decisions. The issue of health effects difference between traditional chewing practice and newer ones, (as per the study of ICAR-CPCRI, Arecanut Research and Development Foundation, Directorate of Arecanut and Spices Development in the Indian Journal of Arecanut, Spices and Medicinal Plants (Vol 22-I) by C T Jose, S Keshava Bhat, K P Chandran, S Jayashekara and Ananda Gowda) has to be considered.

Response: We have added this fact that “different forms of Areca nut across different socio-economic-religio-culturally diverse country like India have not been covered in the survey” in the limitation section of the study.

Comment: Authors need to include the fact that a substantial part of this data has been covered in the publication - Arora M, Shrivastava S, Mishra VK, Mathur MR. Use of Betel Quid in India from 2009 to 2017: An Epidemiological Analysis of the Global Adult Tobacco Survey (GATS). Subst Use Misuse. 2020;55(9):1465-1471. doi: 10.1080/10826084.2020.1726393. As this particular work was carried in a chronoenvironment, the peculiar habit dynamics have been captured. Authors of the present work failed to consider and include in discussion this work. In the present study and that of Arora M study, it was observed that Areca /Betel Quid use was higher in certain parts of the country. This variation has got huge policy level ramifications, as betel quid has a great socio-religious and cultural sanction.
Response: Thank you for your suggestion. We did not include this study as it only captured betel quid use among different population groups, while, our study focuses on all different forms of areca nut use in India which have been covered the first time in GATS 2 (2016-17). Any comparison between a subset of products used with the full range of Areca nut products would be prone to bias.

Comment: Areca nut Cessation programs in such parts of India would bank on social determinants and level of awareness to formulate their microlevel policies. Also, past UP/Lucknow based population level screening has revealed that a substantial part of the pan masala chewing population suffers with oral precancerous states. Considering all this facts, the conclusions of the study has huge public health ramifications. There is no second thought that the projected numbers of Areca nut chewers or the role of determinants – However, these are robust estimates. These data would help to refining an exhaustive but pertinent Areca nut usage screening survey. Probably such a survey would yield the much needed accurate answers for the research questions.
Response: We agree with your comments and observations and this is what we intended to highlight in this study.

Comment: The reports of use of pan masala and gutka in males/females/urban-slums has been previously reported using a nationally representative sample - this work and its conclusion has also not been considered in discussion. Though they do not represent the entire areca nut using population at that point of time, those data have captured most of the reported trend, at least a decade ago. These articles could greatly contribute to the discussion as findings of social determinants could be compared.
Response: We did not include this study as it only captured pan masala and gutka use among different population groups, while, our study focuses on all different forms of areca nut use in India which have been covered the first time in GATS 2 (2016-17). Any comparison between a subset of products used with the full range of Areca nut products would be prone to bias.

Comment: The RRR of various Areca nut product, as compared to north India, for other parts have increased RRR. The reason behind this phenomenon, as compared to NFHS data, would be interesting to compare and explore the reasons for the difference.
Response: Thank you for your suggestion. However, comparison with NFHS would be altogether a different study and may not be feasible to do it in the context of present study.

VERSION 2 – REVIEW

REVIEWER	Ruokolainen, Otto National Institute for Health and Welfare, Helsinki
REVIEW RETURNED	18-Mar-2021

GENERAL COMMENTS	Review for 'Areca nut use among the adult population in India: a nationally representative cross-sectional study' (bmjopen-2020-043987.R1) by Sing et al. submitted to BMJ Open. I thank the authors for their exhaustive response to the reviewer comments. The authors have incorporated comments and suggestions by the reviewers into the manuscript and thus the manuscript has, in my opinion, markedly improved. I have only few further comments. Running head • Would "Areca nut consumption" be more accurate/appropriate than "Areca nut addiction"? Abstract • Participants: • Results: "About 23.9% (95%CI 23.1-24.8) of the adult population consume areca nut, i.e. approximately 223.79 million people in India, 9.7% (95%CI 9.1-10.4)...". Is the "9.7% (95%CI 9.1-10.4)" some erratum? I find it hard to comprehend its meaning in this sentence. • Conclusion: The conclusion concentrates on areca nut use without tobacco while the results section concentrates more on areca nut use with tobacco. In the results it is stated that areca nut with tobacco is the dominant pattern of use while the opposite is stated in the conclusions. I am sorry if I misunderstood this. • Strengths and Limitations: Last bullet: "The survey is cross-sectional..." Is it proposed that the study design is a limitation? In my opinion cross-sectional design is well justified in this context and maybe should not be viewed as a limitation? However, not being able to look into trends of areca nut use could be seen as a limitation (or the scope for future studies). Thus, the authors may want to consider if the last bullet would be (for example): "The survey cannot provide insights into trends of Areca nut consumption over time." Methods and materials • Study Design and Participants: Thank you for including the response rates on the manuscript. However, if household response rate was 96.7% and person-level response rate 96.0%, how is the overall response rate 92.9%? Shouldn't it be higher than this? Discussion • Page 14, lines 34–35: "We found protective effect of secondary and above level education in the case of areca nut consumption with tobacco and in both forms." Did I understand this correctly, should the sentence read as follows? "We found protective effect of secondary and above level education in the case of areca nut consumption with and without tobacco."

REVIEWER	Thavarajah, Rooban Marundeeshwara Oral Pathology , Oral Pathology
REVIEW RETURNED	15-Mar-2021

GENERAL COMMENTS	All the corrections suggested were considered and due explanations provided.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Dr. Otto Ruokolainen, National Institute for Health and Welfare, Helsinki

Comments to the Author:

Review for 'Areca nut use among the adult population in India: a nationally representative cross-sectional study' (bmjopen-2020-043987.R1) by Sing et al. submitted to BMJ Open.

I thank the authors for their exhaustive response to the reviewer comments. The authors have incorporated comments and suggestions by the reviewers into the manuscript and thus the manuscript has, in my opinion, markedly improved.

I have only few further comments.

Running head

Comment: Would "Areca nut consumption" be more accurate/appropriate than "Areca nut addiction"?

Response: Thank you. Yes, we agree with your suggestion and changed the running head accordingly.

Abstract

Comment: Results: "About 23.9% (95%CI 23.1-24.8) of the adult population consume areca nut, i.e. approximately 223.79 million people in India, 9.7% (95%CI 9.1-10.4)...". Is the "9.7% (95%CI 9.1-10.4)" some erratum? I find it hard to comprehend its meaning in this sentence.

Response: Thank you for pointing this out. We have removed 9.7% from the revised version.

Comment: Conclusion: The conclusion concentrates on areca nut use without tobacco while the results section concentrates more on areca nut use with tobacco. In the results it is stated that areca nut with tobacco is the dominant pattern of use while the opposite is stated in the conclusions. I am sorry if I misunderstood this.

Response: Thank you. We have added with tobacco and revised the sentence as

"The on-going tobacco control efforts would not address the majority of areca nut users until greater attention to areca nut consumption with and without tobacco is reflected in health policies in India".

Comment: Strengths and Limitations: Last bullet: “The survey is cross-sectional...” Is it proposed that the study design is a limitation? In my opinion cross-sectional design is well justified in this context and maybe should not be viewed as a limitation? However, not being able to look into trends of areca nut use could be seen as a limitation (or the scope for future studies). Thus, the authors may want to consider if the last bullet would be (for example): “The survey cannot provide insights into trends of Areca nut consumption over time.”

Response: Thank you. We have modified this as suggested in the revised manuscript. “The survey cannot provide insights into trends of Areca nut consumption over time”.

Methods and materials

Comment: Study Design and Participants: Thank you for including the on the manuscript. However, if household response rate was 96.7% and person-level response rate 96.0%, how is the overall response rate 92.9%? Shouldn’t it be higher than this?

Response: Thank you for highlighting this. We have corrected the whole sentence in the revised manuscript as:

“The person level response rate was 96.0 percent (95.6% in urban areas and 96.3% in rural areas). The overall response rate, calculated as the product of response rates at the household and person level, was 92.9 percent”. Please refer to the page no. 6, 3rd paragraph.

Discussion

Comment: Page 14, lines 34–35: “We found protective effect of secondary and above level education in the case of areca nut consumption with tobacco and in both forms.” Did I understand this correctly, should the sentence read as follows? “We found protective effect of secondary and above level education in the case of areca nut consumption with and without tobacco.”

Response: Yes, absolutely correct. We have revised the sentence as suggested in the revised manuscript. Please refer to the page no. 14, 3rd paragraph.