Author's response to reviews

Title: Screening for oral potentially malignant disorders among areca (betel) nut chewers in Guam and Saipan

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Author's response to reviews: see over
October 9, 2014

Dear Dr. Morawska:

I hereby submit the revisions to MS 1969757046134849 entitled “Screening for oral potentially malignant disorders among areca (betel) nut chewers in Guam and Saipan” by Yvette C. Paulino, Eric L. Hurwitz, Saman Warnakulasuriya, Robert R. Gatewood, Kenneth D. Pierson, Lynnette F. Tenorio, Rachel Novotny, Neal A. Palafox, Lynne R. Wilkens, and Grazyna Badowski for consideration in BMC Oral Health. We have addressed all the reviewers’ concerns. Please see our detailed response attached to this cover letter.

We still believe that this manuscript is appropriate for publication in BMC Oral Health because it describes the epidemiology of oral health in a population at risk for poor oral health outcomes. Our manuscript offers an innovative approach to simplifying the modeling of the complexity of betel nut chewing exposure. This technique may be useful in other betel-nut disease association studies with considerable exposure variability. Furthermore, our manuscript provides one of the first estimates of oral potentially malignant disorders, oral cancer, and HPV infection in betel nut chewers in the Pacific where these topics, which carry significant public health relevance, have been understudied.

This manuscript has not been published and is not under consideration for publication elsewhere. We have no competing interest to disclose.

Thank you for your consideration!

Sincerely,

Yvette C. Paulino, PhD
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Response to Reviewers’ Comments
Note: The highlighted responses correspond to the changes in the manuscript.

Reviewer's report
Reviewer: Zohaib Khan

1. In the "Methods" section perhaps it will be more appropriate if the number of participants from Guam was described in the "Results" section rather than the methods and only the strategies used to recruit participants were included in the "Methods". We moved the recruited numbers to the results section (see p12-line 2-3).

2. Under the "Results" section, subheading "Oral Screening": Since the analysis is based on "Number of participants having lesions" and not the "Number of type of lesions" perhaps it would be appropriate to substitute the number of type of lesions with the number of individual having different types of lesions e.g. 8 % (n=6), where n = number pf participants, had both white and red lesions. As this may cause confusion among the reader.

The numbers given here are actually subject numbers. We revised the text to reflect that subject numbers are given (and not lesion numbers). The statement above clarified that some subjects had more than one lesion, and therefore the numbers do not total to 46.

3. Under the "Discussion" section, in the second paragraph, it has been stated that, "the prevalence of Oral Pre Malignant Disorders may have been underestimated especially after considering previous reports", given the general objective of this study was to pilot test methods to study the condition, It would be apt, if a plausible explanation is given for this difference.

Having given consideration to our previous statement, and comparing with more extensive regional studies we modified the text to say as follows. A substantial reference was added [26] see p 15 “The prevalence of oral potentially malignant disorders recorded in this study is consistent with the published prevalence data of OPMD (leukoplakia and OSF) from several countries in the region [26].”

4. The authors build up a case for this study by citing higher prevalence of oral cancer in Micronesia as compared to the U.S population, however in the "Discussion" section, findings with regards to screening etc are mainly compared to other regions rather than the U.S. Comparison with the findings from a few U.S studies will be more appropriate.

We added the following citing US data and a new reference (p 15). “US data from NHANES 111 Survey report [27] a much lower prevalence figure of oral leukoplakia, 0.66 ± 0.14% for males, 0.21 ± 0.05% in females and 0.42 ± 0.08% in both genders. The higher prevalence of OPMD in Micronesia is due to oral submucous fibrosis commonly found in this population and contrasting lifestyle habits in Micronesia compared with the US population.”

5. Since it is stated that the general objective of the study was to pilot test methods, the "Conclusions" section should include the authors conclusion/s about the effectiveness/appropriateness etc of the methods described in the study with regards to the study of oral pre-malignant disorders in the region.

We added to the conclusion (p18): “The screening model used by us in this pilot study to recruit participants in Saipan was effective and appropriate but required modification for Guam as the prevalence of betel quid chewers was much lower and needed additional methods of recruitment.”
Minor Essential Revisions

1. The email address of (SW) needs correction. This is now corrected s.warne@kcl.ac.uk

2. In the "Abstract" under the result sub-section (Page 3, Line 21) "for" shall be added between "chewing" and "more years". Word “for” added

3. In the "Background Section" of the main text, most of the text pertains to previous evidence from Guam and very little for Saipan. Also there is a difference between the age demographic between the participants of that cited study in the Saipan region (School going) versus the participants (> 18) of the current study, may be some more evidence regarding use of Betel nut and/or OPMDs (if available) from the Saipan or CNMI may be included. The study reported from CNMI was conducted in Saipan. This was added to reflect on the data from Saipan p7-line 1 “In the Commonwealth of the Northern Mariana Islands (CNMI), in Saipan, a high prevalence (63.4%) of regular betel nut use was documented in a cross-sectional survey of high school students [13]”

4. In the "Methods" section, once again given this was a pilot study of methods, perhaps it would be appropriate to include the percentage of potential participants who were asked to participate but refused to take part in the survey. This would be advantageous to future researchers who might want to deploy the methods used in this study. We have now inserted compliance rate in the results section: p 12 line 3 (we think this belongs to results and not methods) “Among the people approached through our house-to-house recruitment almost 100% complied, only 1 person refused to volunteer in the study. Difficulties in identifying chewers in Guam are presented in the methods section, this mainly being inaccessibility to their front doors. There were a few refusals among community gatherings, but it was difficult to quantify the number of refusals in that setting.”

5. Sticking to the "Methods" section under the subheading recruitment (Page 8, Line 11,12,13), the sentence can be rephrased to something like "All eligible candidates within a household were invited with an upper limit of three participants/household; in cases where there were more than three a die was used to randomly select the three participants.”

Thank you, sentence revised to: “All eligible candidates within a household were invited with an upper limit of three participants/household; in cases where there were more than three a die was used to randomly select the three participants.”

6. Referring to "Point 1" under the "Major Revisions" section of this review, again given the objectives of the study it would be beneficial to the reader to have the exact number of participants recruited through "advertisements" and "community meetings" in Guam. The remaining 54 participants (39% of the total Guam sample) were recruited through advertisements (n=22) and community gatherings (n=32) from the rest of the island.
7. Under the "Methods" section in the subsection "Questionnaire" (Page 9, Line 13), the spelling of questionnaire shall be corrected. Corrected to questionnaire

**Discretionary Revisions**

1. Under "Methods" and "Results", if any effort was made to record the reasons and the recorded reasons, for dropping out of the participants after initial screening, shall be stated. If not available, can the authors state possible explanations for the drop out in the discussion section?

   We added in p13:
   
   We have no data to explain reasons for non-compliance by 19 subjects who did not attend the specialist. In the discussion we added: p16 lines 3-5
   
   “We did not contact our patients who did not show up to find out reasons for non-compliance. Previous studies have reported ill health, economic reasons and work disturbance as main reasons for non-compliance following a screen detection [33]”

2. In the "Discussion section" (page 15, Para 1, Line 4), the sentence sounds like, IARC concluded something from this study, may be it can be rephrased e.g. however IARC has previously concluded. Changed to:

   IARC has “previously” concluded

**Reviewer's report**

Reviewer: Sree Vidy Krishna Krishna Rao

Major comments: The overall purpose of the paper is reasonable - to conduct a screening of oral potentially malignant disorders in betel nut chewers, measure the betel nut, chewing practices of those chewers, and assess the prevalence of oral human papillomavirus (HPV) infection in a subset of betel nut chewers. The participant selection in this study was by convenience sampling. Moreover, the study is limited to comparing demographic and chewing characteristics of Class I and II chewers. Further, the paper's contribution to the field is small. The authors could conduct further analysis according to the study design to contribute more to the field.

We do not feel any further analysis is possible on this pilot study; We have generated maximum amount of possible data and analysed by appropriate statistical methods, as confirmed by referee 2.

Minor comments:

In Table 1 and 2 authors mention p values “0.00”. This could be written as <0.001.

We have changed to p<0.001.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests.