Author's response to reviews

Title: Using Breath Carbon Monoxide to Validate Self-Reported Tobacco Smoking in Remote Australian Indigenous Communities.

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Author's response to reviews: see over

Dear Editor,

USING BREATH CARBON MONOXIDE TO VALIDATE SELF-REPORTED TOBACCO SMOKING IN REMOTE INDIGENOUS AUSTRALIAN COMMUNITIES

Thank you for the opportunity to revise and resubmit this paper. We look forward to your final decision about the suitability of this paper for publication in your journal.

The reviewers' comments are addressed in the following. (Please note: Reviewer David Hendrick is referred to as DH and Martin A Javors as MJ).

Response to reviewers' general comments:

We are encouraged by MJ's comment about our effort to identify a BCO cut-off that accurately identifies non-smokers from smokers. We agree with DH that a study relating to expired CO and smoking is hardly novel. However, in this special population in remote Australia, where smoking rates are extraordinarily high, it is of considerable importance in the current context to have accurate measures of smoking status. Both government and community-controlled health services are investing considerable resources to reduce smoking rates, as indicated in the first paragraph of our introduction, and it is important to have reliable evidence describing people's smoking status in these communities to evaluate any effects of these programs. It is hoped that publication of this paper will contribute to improving the available methods for compiling reliable evidence.

Responses to reviewers' major comments:

Major: DH#1 and MJ#2:
Both reviewers suggested that it would be appropriate to combine the data for males and females to take full advantage of the power in the study and to 'obtain a more valid cutoff' (MJ). We took up this suggestion. To present results for the entire sample for which both BCO and tobacco smoking information were available necessitated i) re-analysis of the data along with ii) substantial revision of the results section and iii) revisions of descriptions of how the study was conducted overall. The principal changes to the manuscript occur in the Abstract (Methods and Results sections) where differences between males and females reported in the original version were removed. In the first paragraph of the Results section in the main body of the manuscript under the subheading 'Community Survey: self-reported tobacco smoking and BCO levels', data describing differences between male and female tobacco users were removed. Similarly, discussion of differences between males and females were also removed from the first paragraph under the subheading 'Sensitivity and Specificity' in the Results section. Tables 1a and 1b were merged into Table 1 and Table 2a and 2b were merged into Table 2, and Figures 1a and 1b were merged into Figure 1. Figures 2a and 2b were deleted (see below). Figure 3 was accordingly renamed as Figure 2.

Major: DH#2 and MJ#2:
Both reviewers suggested that the definition of smoking status was not optimal (MJ#2) and that the few 'intermediate' smokers (DH#2) who reported they had not smoked during the 24 hour period before the BCO test should be removed (DH#2 and MJ#2). In the re-analysis, 11 self-reported tobacco smokers were omitted on this basis. This necessitated changes to Table 1, Table 2, Figure 1 and Figure 2. In the Abstract, the Methods now describe the approach to analyzing data for 249 self-reported tobacco smokers and 60 people who reported they did not smoke tobacco. In the Abstract, the results summarise the greater sensitivity and specificity found when the data were re-analysed, as predicted by both reviewers DH and MJ. In the Methods section under the subheading 'Community Survey: Self-reported tobacco smoking and BCO' the revised inclusion criteria were modified to now read as follows:

"Data were included in the analysis if: (i) self-reported smokers reported smoking tobacco within the preceding 24 hours (ii) self reported non-smokers reported never smoking tobacco or not smoking tobacco for ≥6 months[43]. Given the short half-life of BCO, data from self-reported occasional tobacco smokers who reported last smoking tobacco greater than 24 hours previously were not included in the analysis."

In the Results section, all results are now reported for 249 self-reported tobacco smokers and 60 self-reported non-smokers of tobacco. Similar changes were made to the Methods section of the abstract in order to reflect these changes in the text in the main body of the manuscript.

Major: DH#3 and MJ#2:
DH#3 stressed that the potential importance of smoking cannabis is of some interest. MJ#2 stressed that the authors must decide whether to include cannabis smokers in the smoker group or to exclude them from the analysis. We decided to retain the cannabis users in the analyses in order to highlight its importance consistent with DH#3's suggestion. The importance of the self-reported cannabis users in terms of their impact on validating tobacco smoking was highlighted through the following changes and additions to the text.

Abstract-Results: The following was added

"With data for two self-reported non-smokers who also reported that they smoked cannabis removed from the analysis, specificity increased to 96.6%."

Abstract-Conclusion: The following was added

"In further studies of tobacco smoking in these populations, cannabis use should be considered where self-reported non-smokers show high BCO."

Results-Sensitivity and Specificity: The second paragraph was modified to now read:

"Of the four self-reported non-smokers with BCO ≥7 p.p.m., three were males, two of whom stated they did not smoke tobacco but smoked cannabis (BCO 8 p.p.m. and 33 p.p.m.) (Figure 1). The third male (BCO 14 p.p.m.) provided no comment but local research workers later suggested that he smoked cannabis (Figure 1). One self-reported female non-smoker with BCO ≥7 p.p.m. (BCO 9 p.p.m., Figure 1) provided no further detail at interview and local research workers were not present at interview to assist to clarify the discrepancy."

Results-Alternative Cut-off Level: The following was added to paragraph#1:

"With the data for the two male cannabis users who said they did not smoke tobacco excluded from analysis, with a BCO cut-off of ≥ 5 p.p.m., specificity increased substantially to 96.6% (data not shown).

Results-Alternative Cut-off Level: The following was added to paragraph#2:

"With the data for the two male self-reported cannabis smokers excluded from the ROC analysis, the area under the curve at a BCO cut-off of ≥5 p.p.m. increased marginally to AUC=0.989."

and

"With data for the two male cannabis smokers excluded, using a cut-off level of ≥5 p.p.m. would have estimated tobacco smoking prevalence of 81%, the proportion of self-reported smokers in the sample of 400 people interviewed in the study overall."

These analyses necessitated a re-emphasis in our conclusions to stress the importance of cannabis use in validating self-reported smoking in these communities. So the following was added to the Discussion section under the subheading: Optimal BCO cut-off levels: (last paragraph in this section):

> "With better information in future studies about those who smoke cannabis and not tobacco in these communities, the proportion of self-reported non-smokers of tobacco verified could be as high as 96.6%."

Although cannabis smoking is an important consideration for this study of tobacco smoking, there is good evidence that in these communities those who smoke cannabis and not tobacco are very few, with almost all cannabis users blending their cannabis with tobacco. To stress this, the following was added to the third paragraph in the Discussion section under the subheading 'Discrepancies between self-report and BCO level can be accounted for':

> "It is possible that exposure to second hand-smoke contributed to the small number of false positives in this study however cannabis use in this population is likely to be an important factor. Studies of cannabis use in similar communities in the same region indicate that most cannabis users (94%) blend cannabis with tobacco and smoke the mixture in hand-made 'bucket bongs' with tobacco smokers around 19 times more likely than non-smokers to also smoke cannabis [45]."

Our study focused on tobacco smoking with appropriate ethics approvals in place for this jurisdiction. To study the use of both cannabis and tobacco in the same disadvantaged and disempowered population where relationships with government authorities, particularly police, have been historically problematic, would require a very cautious approach in a community survey. To emphasize these challenges of assessing cannabis smoking alongside tobacco smoking the following was also added to the third paragraph in the Discussion section under the subheading 'Discrepancies between self-report and BCO level can be accounted for':

> "The present study did not systematically collect data about cannabis use at interview. A study investigating both tobacco and cannabis smoking requires a different approach including suitable protocols designed to minimise the ethico-legal risks of studying illegal behaviours in these disadvantaged and disempowered populations in Australia [45]."

Finally, to address both DH#3 and MJ#2 concerns regarding the importance of cannabis in the study, and to make a clear distinction between tobacco smoking and cannabis smoking, at most places in the text where 'smoking' is mentioned, the word 'tobacco' was inserted before 'smoking' to add appropriate emphasis but mindful that the term may appear repetitive.

Major: DH#2:
This reviewer suggests that it would have been more useful to fix the specificity (say 95%) and then determine the cut-off threshold and sensitivity. We addressed this suggestion by including in the text our view that "a test should ideally have high sensitivity and high specificity" near the end of the first paragraph in the Methods section under the subheading 'Data analysis and approvals'.

Major: MJ#1
This reviewer believed it was a major concern that 'the purpose of using the breathalyzer in this unique population' should be stated more clearly and that how engaging the population using the

instrument could assist to reduce harmful smoking should be explained more thoroughly. DH (minor comment#2) also asked why the use of the hand-held BCO analyzer as a health promotion was a conclusion in the Abstract. In considering these questions, we realised that this topic was not addressed with any evidence in the original version of our mansucript and so most references to this aspect of the hand-held BCO analyzer were removed from the Abstract and from the text in the revised version. Another paper will address this topic more thoroughly and more appropriately. However, a shortened comment on its utility for recruiting study participants and for engaging community people in the study was moved from the last paragraph in the Discussion to the end of the third paragraph in the Methods section under the subheading 'Community Survey: Self-reported tobacco smoking and BCO'. The last two sentences of the paragraph now read.

> "In trials of survey procedures, the acceptability of using a portable BCO analyser with this population proved to be high. During the study, it was the experience of DM, JR and AC that using the BCO analyser attracted participants into the study. The immediate return of BCO results provided an opportunity for participants to actively engage and have direct benefit from participating."

Response to reviewers' minor comments:

Minor comment: DH#1
We take the point that the BCO test was to validate reported tobacco smoking rather than tobacco smoking. To reflect this and emphasise it consistently, the words 'self-reported' were inserted before 'tobacco smoking' in appropriate places throughout the text e.g., starting with the title which now reads:

> **USING BREATH CARBON MONOXIDE TO VALIDATE SELF-REPORTED TOBACCO SMOKING IN REMOTE AUSTRALIAN INDIGENOUS COMMUNITIES**

Minor comment: DH#2:
We have already addressed the issue of the rationale for highlighting the usefulness of the hand-held BCO analyzer in response to MJ#1's major concern above.

Minor comment: DH#3.
To eliminate possible confusion to references about disparities in smoking rates in subsections of the Australian population where rates of change in smoking rates differ, we deleted the first sentence in the first paragraph of the Introduction in the original version. That is, the following sentence was deleted:

> "Despite Australia being a world leader in tobacco control, significant disparities in smoking rates exist between Indigenous and non-Indigenous Australians."

Minor comment: DH#4:
To clarify that the smoking rates are not 'simply 59% to 92%' and that there is some variability in smoking rates in remote Indigenous communities in the Northern Territory, the last sentence in the introduction was modified to now read:

> "For example, much higher rates of between 59% to 83% [3-8] have been documented in some remote communities of the Northern Territory (NT) with up to 92% of people reporting a history of tobacco use in one community [3]."

Minor comment: DH#5:

This comment was addressed in the modifications to Figure 2 and Figure 3 in the original version. The titles in Figure 2 were altered to read 'self-reported non smoker' and self-reported smoker' in line with this comment and also to address Minor Comment DH#1.

Minor comment: DH#6.
We acknowledge this error in table 1(b) in the original manuscript and which is now corrected in Table 1 in the revised version.

Minor compulsory: MJ#3:
This reviewer recommended that we comment on the effect of second-hand smoke on the number of false positives in the study, which we believe is very small in these populations, especially in light of the importance of cannabis smoking in these communities and the clear evidence for cannabis use among the false positives. To address this, in the Discussion section, subheading 'Discrepancies between self-report and BCO can be accounted for' the following was inserted into the third paragraph:

> "It is possible that exposure to second hand-smoke contributed to the small number of false positives in this study however cannabis use in this population is likely to be an important factor. Studies of cannabis use in similar communities in the same region indicate that most cannabis users (94%) blend cannabis with tobacco and smoke the mixture in hand-made 'bucket bongs' with tobacco smokers around 19 times more likely than non-smokers to also smoke cannabis [45]."

Minor compulsory: MJ#4.
We recognize that the calibration of the BCO analyzers used in the study is an important feature of accurate BCO measurement. To answer this reviewer's request, the following was inserted in the last paragraph in the Methods section under subheading 'Community Survey: Self-reported tobacco smoking and BCO':

> "The BCO analysers used in the study were calibrated by the manufacturer in May 2008 before the survey commenced and recalibrated by DM, according to manufacturers specifications, in November 2008."

Minor compulsory: MJ#5.
This reviewer suggested that the differences between males and females could be explained in terms of the numbers of cigarettes smoked and requested more information about the number of cigarettes smoked if possible. Data for smoking levels were not available for this analysis. Differences between males and females are no longer highlighted in the revised paper (see DH#1 and MJ#2 above) which reduces the need to address this query.

Minor compulsory: MJ#6.
We agree that there was considerable confusion about how data for the study participants were included in the analyses in our original manuscript. We recognize that this was confused in the original version by our clumsy attempts to describe a complex picture of tobacco use, styles of use, smoking rates in males and females in the sample, smoking rates in the subset of the sample analysed and the proportion of BCO tests achieved overall. We have attempted to simplify our description of how the 249 self-reported smokers and self-reported non-smokers who provided a BCO test met the selection criteria. In the revised manuscript this is set out in the first paragraph in the Results section under the subheading 'Community Survey: Self-reported tobacco smoking and BCO levels'. It now reads as follows:

> "Among the 400 people interviewed, 300 (75%) reported they smoked tobacco and 100 (25%) reported they did not. Four of the 400 interviewed explicitly refused a BCO test and 19 were in such poor health that a BCO test would have been unnecessarily intrusive. BCO was not tested in a further 57 people

interviewed primarily because they had no time to take the BCO test (n=40) or because a BCO analyser was not available at the time of interview (n=17). The remaining 320 people who provided both a BCO test and information about their tobacco use included 260 who self-reported they smoked tobacco and 60 people self-reported they did not smoke tobacco. Eleven of the 260 were occasional tobacco smokers and reported they had not smoked within the preceding 24 hours. In accordance with inclusion criteria, these 11 occasional smokers were not included in the analysis. Therefore BCO tests for 249 self-reported smokers and 60 self-reported non-smokers were analysed. The proportions of self-reported smokers (81%=249/309) and non-smokers (19%=60/309) in this subsample were similar to proportions of self-reported smokers (75%) and non-smokers (25%) in the sample overall ($|z|=1.90$, $P=0.057$)."

Other minor changes not requested by reviewers, but included in the revised version of our paper include the following:

1. Reference on the title page to the relative contributions to the paper of DJM and ARC were deleted since it was felt that this did not adequately reflect the other authors' contributions to the paper.
2. In the Reference list, the journal titles for references number 14, 15, 20, 22, 32, 34, 36, 41, 43 and 44 were abbreviated according to the standard PubMed abbreviations.