Author's response to reviews

Title: Absent otoacoustic emissions predict otitis media in young Aboriginal children: a birth cohort study in Aboriginal and non-Aboriginal children in an arid zone of Western Australia

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Author's response to reviews: see over
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To the Editor
BMC-series journals

Re MS: 1664895199174690
Absent otoacoustic emissions predict otitis media in young Aboriginal children: a birth cohort study in Aboriginal and non-Aboriginal children in an arid zone of Western Australia
Deborah Lehmann, Sharon Weeks, Peter Jacoby, Dimity Elsbury, Janine Finucane, Annette Stokes, Ruth Monck and Harvey Coates

Thank you for sending the further comments and criticisms of reviewers. We have addressed these below and revised the manuscript which is attached.

Below I have addressed point-by-point the comments from reviewer 2.

We look forward to hearing from you soon.

Yours sincerely,

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Response to reviewers with regard to revised manuscript
MS: 1664895199174690: Absent otoacoustic emissions predict otitis media in young Aboriginal children: a birth cohort study in Aboriginal and non-Aboriginal children in an arid zone of Western Australia

Thank you for the latest reviewers’ comments.

We are pleased reviewer 1 has no additional comments and has recommended publication. We are also delighted that reviewer 2 now notes ‘some value in published form’.

It is unclear what specific issues reviewer 2 would like us to address. We therefore go through his comments paragraph by paragraph.

I am still unimpressed by the lack of clear conceptualisation and expression of the argument. This is fundamentally a routine service audit but with some new instrumentation tacked on rather than thoroughly designed new research. It is not to be criticised for that as in the present funding environment this is the only way that many people can push knowledge forward. However, criteria do then have to be set in terms of novelty, sample size, tightness of argument and general quality.

The rationale behind the paper has been laid out in the introduction, namely:

1. The enormous burden of disease (paragraphs 1 and 2), and particularly in Aboriginal children whose illness begins very early in life (paragraph 3). We point out a lack of data on Aboriginal children living in an urban setting and no population-based data for non-Aboriginal children for 30 years. Our description of the burden of OM in such a population, namely Aboriginal and non-Aboriginal children living in an urban setting in an arid zone, is therefore novel (Introduction, last paragraph).

2. We have extended paragraph 3 of the introduction to emphasise the lifelong disadvantage of Aboriginal people, the enormous burden of OM and its consequences and hence the urgency of identifying ways of detecting those children as young as possible who are at high risk of OM in a setting where there is currently no routine screening of children between birth and primary school entry. We clearly need novel approaches that will identify such children at the primary health care level.

3. In paragraph 5 we report that previous studies suggest measurement of OAEs might be one way of identifying high-risk children in early infancy but in those studies OAEs were only measured during the neonatal period. There is a need to determine whether measurement of OAE in the postneonatal period might offer a relatively easy and cheap screening tool to identify children at high risk of OM. This is particularly important in Aboriginal children who develop disease very early in infancy. This is a novel approach.
As indicated in paragraph 6 of the introduction and under ‘Strengths and limitations of the study’ in the discussion section, this paper forms part of a wider study investigating causal pathways in Aboriginal and non-Aboriginal children – the study is in fact unique in Australia and, to our knowledge, worldwide. We agree that the study was not established to investigate specifically the benefits of a particular screening method but we established a screening process that was appropriate for the setting. Limitations of the study, including sample size, have been addressed in the discussion section.

I sympathise with the dilemma that there are two stories in here, somewhat conflicting in terms of message and audience: the population need and the technological possibility

The ‘stories’ are linked i.e. there is a very high burden of disease from a young age in Aboriginal children and hence we want to identify a high risk group in need of prompt attention and monitoring. We sought to publish in BMC Pediatrics to draw the attention of as many paediatricians as possible to the high prevalence of disease and a novel way of identifying high-risk children early in life.

For very young children it is already known that only high-frequency variants of conventional tympanometry give reliable results, so standard tympanometry here can be seen only as a follow up marker. I am not saying that the authors mislead, only that the these truths that the reader needs are fudged to bolster the apparent adequacy of the work rather than being starkly stated at the start to educate the non-specialist reader. [author: the preceding sentence is unclear] The article does not refer to these high-frequency variants as the appropriate comparator for judging whether or not the additional early prediction of OM histories from OAE is specifically strong. The authors cannot be blamed for not having that other instrumentation to hand, but in terms of conclusiveness it would be better to represent the present findings as somewhat preliminary. The recommendations for further research logically therefore should divide into two phases: (a) replication of the present result and direct comparison with high-frequency tympanometry as the comparator, including an analysis of metric problems: whether, given that the fundamental physical reason for the “problem” response is the same, the advantage of OAE may be due to a more continuously graded or wide-range response; (b) later health economic evaluation of a whole programme of early intervention based on the more predictive of the two types of instrumentation.

We have included a paragraph (paragraph 4) in the introduction on tympanometry and have pointed out that high-frequency tympanometry screening equipment has only recently become available. In the methods section (‘Tympanometry’ section) we indicated that the conventional tympanometer has previously been reported to have good specificity in young children, acknowledging that 226Hz is not generally recommended. In our discussion we have commented on the benefits and limitations of OAE measurement in comparison with high-frequency tympanometry which has only recently become available as a screening tool. We have now recommended that
screening of young infants either by OAE testing or high-frequency tympanometry be done (see Recommendations for surveillance, paragraph 2). We previously indicated that future research is planned to evaluate the performance of OAE as a predictor of subsequent disease (Discussion, Recommendations for future research 3.). We thank reviewer 2 for suggesting that we compare OAE testing with high-frequency tympanometry and have included such a comparison in a study due to start in 2009 (see Discussion, Recommendations for future research 4.).

The present manuscript refers to the advantages of early detection and we must consider this further but ultimately the thing needing real-world evaluation is not so much the fine issues of accuracy of the screen technique which (a) ought largely to have addressed, but the net health gain, in relation to its cost, from identifying and intervening.

This statement is unclear but we did indicate the intention to undertake an economic evaluation of our proposed future research program (Discussion section, recommendations for surveillance, paragraph 3). Furthermore the evaluation of the ear health program in the Goldfields in Western Australia will determine the ‘health gain’ of early screening. We have also included economic evaluation when comparing OAE testing with high-frequency tympanometry (see Discussion, Recommendations for future research 4.).

Vaccines are mentioned but so far with these vaccinations the evidence points more to a policy of universal vaccination, and not of screening to find an at-risk sub-population, because the individuals with the early histories do not produce a good immune response anyway to some of these vaccines.

This statement is unclear but there are in fact preliminary data to suggest that young children can elicit adequate immune responses to pneumococcal conjugate vaccine. The lead author is conducting a trial of pneumococcal conjugate vaccine in neonates and early infancy in Papua New Guinea; preliminary data suggest a good response to vaccination in this high-risk population that also suffers high rates of OM. As vaccination is not the major focus of the present manuscript we are not including any further comment on vaccination programs.

In relation to this information need the study s less conclusive than made out. Table 4 does not contain an interaction test for the cross-over in magnitude of hazard ratio with age as between Aboriginal and non-Aboriginal groups to justify the discussion of sub-groups as legitimate. In other words it is not clear that the disaggregation by age or by ethnic group or both is really justified. The CIs rather suggest that it may not be and that a fair description of all the data might be a hazard ratio of about 1.5 for all sub-groups. It could be stated that the first 3 months is not a sensible time to do this screen anyway, but that merely makes those into background data and the above general comment still applies. Alternatively only one figure is of real application interest the 2.64 for the older Aboriginal children and the discussion should move to (a) how the conflict with
one of the previous two studies is to be best resolved, and if this estimate is to be taken as good enough for projecting whether it is high enough to base a screen on.

With respect to the statement ‘In relation to this information need the study s less conclusive than made out’ we have amended sentence 3 of the conclusions.

Data were not disaggregated by age as the reviewer states but OAE test results at ages 0-<1m and 1-2m were examined separately as potential predictors of subsequent diagnosed ear disease. It is not clear what interaction test the reviewer is recommending. The OAE hazard ratio for subsequent OM was significantly greater than 1 amongst Aboriginal children aged 1-2m and it is this result which forms the basis of the recommendations in the paper. We would have been unable to identify and describe this effect if data from Aboriginal and non-Aboriginal children had been aggregated. Given the different epidemiology and socioeconomic characteristics of Aboriginal and non-Aboriginal children it is important to examine the populations separately. By doing so we have been able to identify an intervention that is appropriate for Aboriginal children but not for non-Aboriginal children. Hence we can limit the proposed screening with OAE to a small high risk group.

With regard to…the discussion should move to (a) how the conflict with one of the previous two studies is to be best resolved, and if this estimate is to be taken as good enough for projecting whether it is high enough to base a screen on.: In the discussion, under the heading ‘OAE as predictor’ we have discussed reasons for the disparity between our findings and the study in indigenous children in North America. However, we are actually in agreement with Hunter et al that absent OAEs were not predictive of subsequent disease during the neonatal period. In this paragraph we also recommend further studies in other indigenous populations.

Throughout: Indigenous is not a particular name so should not receive a capital letter.
It is standard practice in Australia to capitalize Indigenous when talking about Indigenous Australians. We have made lower case for ‘indigenous populations’

P5 It is OK to impute when one ear data is missing as this is inevitable in a field study. However some indication should be given of the prevalence of missings and the reasons for them: also whether; they are even-handed or biased (falling in a particular group).

In table 3 we have included information on the proportion of evaluations for which diagnosis was based on successful examination of one ear only.

Additional changes by authors:
1. We have edited paragraph 2 of the methods section to clarify the age at which different methods were used to assess ear health.
2. In the discussion, under ‘Recommendations for surveillance’, paragraph 3 has been edited in line with proposed changes to the screening program being undertaken in the Goldfields.