Reviewer's report

Title: Recurrent wheezing is associated with intestinal protozoan infections in Warao Amerindian children in Venezuela: a cross-sectional survey

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Reviewer: Maiza Campos Ponce

Reviewer's report:

Comments on:
Recurrent wheezing is associated with intestinal protozoan infections in Warao Amerindian children in Venezuela: a cross-sectional survey

This is a potentially interesting article reporting on atopic diseases, asthma and infections in a very special population.

Major Compulsory Revisions

Objective:
1. In the abstract and introduction the research question is formulated as "We performed a cross-sectional survey to study the association of helminth and protozoan infections with atopic eczema and recurrent wheezing in Warao Amerindian children aged 0 to 2 years."

However in the methods section it seems as if there was a different approach: "To determine which characteristics were associated with atopic eczema and recurrent wheezing, multivariate logistic regression models were built. Only variables with a p-value <0.20 in univariate analyses were considered as candidates for the multivariate model ....."

This latter approach gives the impression that a prediction model was built. However if the authors meant to build a prediction model then I the method section should be expanded to show how the prediction model was built (i.e. was a forward or a backward approach used? What is the AUC etc).

On the other hand: If the authors meant to study the association between helminth and protozan infections and atopic asthma and recurrent wheezing a different statistical analysis should have been performed.

Please clarify as this is a fundamental issue. Also please change the objective in either the objective or methods section accordingly as well as the whole paper. For example in the abstract the conclusion and objective do not match:

"Objective: a cross-sectional survey to investigate the association between helminth and protozoan infections and recurrent wheezing and atopic eczema in Warao Amerindian children in Venezuela."
While the conclusion is:
“High prevalence rates of atopic eczema and recurrent wheezing in Warao Amerindian children under 2 years of age were related to stunting and intestinal protozoan infections respectively.” (stunting was not part of the research question under investigation according to the stated objective)

Introduction:
2. “Atopic disorders comprise a range of allergic diseases including asthma, anaphylaxis, allergic rhinitis and atopic eczema.”
   Asthma is not necessarily an allergic disease (please read: Moncayo et al., 2010 Risk factors for atopic and non-atopic asthma in a rural area of Ecuador) this could have implications for this research.

3. I would be grateful if the authors could explain why this sentence is relevant to this article:
   The hygiene hypothesis is consistent with the extremely high prevalence of asthma in Tristan da Cunha [12, 13] and the Western Carolinas [14, 15], two isolated, highly inbred island communities with a low incidence of respiratory and other viral infections.

Methods section:
4. Data collection:
   “Warao Amerindian children aged between 0 and 2 years from 11 villages that are geographically spread throughout the Orinoco Delta were included in a cross-sectional survey.”
   So this is not a random sample, please comment on the effects this may have on the conclusions being drawn in the limitations section.

5. “A physical examination including anthropometric measurements of the child and inspection of the skin was performed and documented on a standardized data collection sheet.”
   Please elaborate on how anthropometric measurements were taken.

Statistical analysis:
6. “Only variables with a p-value <0.20 in univariate analyses were considered as candidates for the multivariate model.”
   The way the model is explained it appears to me that many predictors/determinants are used to build a model: in this case the term multivariable should be used. The term multivariate regression refers to cases where there is more than one outcome. Please explain (I would recommend to read Multifarious terminology: multivariable or multivariate? cunivariable or univariate?)
7. I would also appreciate if the authors can explain why: “Age and sex were retained in the final multivariate model, irrespective of their p-values in univariate analysis.”

Results:

8. In table 1 the characteristics of the study are shown. It gives the impression not many variables were measured. However in the methods section the authors mention that they performed a (modified) ISAAC questionnaire, this questionnaire includes far more questions than displayed in table 1. Important to show: How many children had eczema, wheezing etc, also why do the authors not show the prevalences of helminths and protozoa in this table. In addition to the named variables, all important variables (eg potential confounders/effect modifiers or predictors) should be shown in this table.

On the other hand if this really is the only data that was collected, I think the data are not enough to do these analyses. The commonly known confounders/effect modifiers or determinants are not measured)

9. Table 2 should be changed according to which objective is being answered (see my earlier comment of the objective statement being different in methods and introduction).

Also in my opinion it is a very confusing table. The authors are trying to put too much information in 1 table. It would be better to make 2 different tables 1 for wheezing and 1 for eczema and then also include the OR (CI) and p value for the univariate analysis.

10. “Children with recurrent wheezing suffered more often from atopic eczema than children without recurrent wheezing, but this was not statistically significant (32% vs. 16%, p=0.055).”

This sentence does not make sense to me. Either children suffer more from eczema (and then is is statistically significant, or they do not suffer more from eczema, because its not statistically significant!

Alternatively in this case the authors could argue that its borderline significant!

Discussion:

11. There is not clear limitations section. I would like to urge the authors to include a limitations section discussing amongst others:

1. The way the study population was chosen and what kind of effects that may have on the interpretation of the results

2. The limitations of the a questionnaire (recall bias etc) and the ISAAC questionnaire in particular (e.g definition for wheezing)

- Minor Essential Revisions

12. Abstract: the objective is written in the methods section. According to the
journals guidelines it should be in the introduction section.

13. Discussion: Please check the layout of the 4th paragraph, its not in line with the others paragraphs.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

'I declare that I have no competing interests'