

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The association of allergic diseases with children's life satisfaction: population-based study in Finland
<b>AUTHORS</b>	Haanpää, Leena; af Ursin, Piia; Nermes, Merja; Kaljonen, Anne; Isolauri, Erika

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Mark Ferro University of Waterloo, Canada
<b>REVIEW RETURNED</b>	19-Sep-2017

<b>GENERAL COMMENTS</b>	<p>This study examine the association between allergic disease and life satisfaction among school-aged children. The research question is interesting, but there are a number of weaknesses that limit enthusiasm for the manuscript.</p> <p>Strengths/Limitations</p> <ul style="list-style-type: none"><li>- While it is true that the study did not assess symptoms of allergic disease, I think the more important point is that diagnoses of allergic diseases were self-reported and not verified with medical records.</li><li>- I do not think that relying on child self-reports of their life satisfaction is a limitation of the study. Given the content area, parents and especially medical experts, should not be viewed as “gold standard” informants.</li></ul> <p>Introduction</p> <ul style="list-style-type: none"><li>- The first sentence of the introduction needs to be appropriately referenced.</li><li>- The second paragraph of the introduction highlights the burden associated with allergic disease, particularly those burdens that are not physical in nature. However, this section is sparsely referenced. A couple of relevant papers include:<ul style="list-style-type: none"><li>o Ferro &amp; Boyle. Self-concept among children and adolescents with a chronic illness: a meta-analytic review. <i>Health Psychology</i>, 2013, 32(8), 839-848.</li><li>o Ferro MA, Van Lieshout RJ, Ohayon H, Scott J. Emotional and behavioral problems in adolescents</li></ul></li></ul>
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and young adults with food allergy. *Allergy*, 2016, 71(4), 532-540.

- It would seem that a brief overview of findings related to quality of life in children with allergic disease is also warranted in the introduction. For example:
  - o Cui W, Zack MM, Zahran HS. Health-related quality of life and asthma among United States adolescents. *J Pediatr* 2015;166:358-64.
- After stating the objectives, the authors note that previous research has used parental reports of child well-being (which ignore the child's perspective), suggesting that a strength of the current study is the use of child self-reports. However, this seems to contradict the authors' point in the strengths/limitations section.

#### Methods

- Details of the original Children Worlds survey is needed, particularly the original objectives of that study.
- The item adapted from Diener should be provided in the description of the SLSS.
- The rating scales, total scores, direction of scores, and alpha reliabilities of the SLSS and BMSLSS should be provided separately.
- The number of items per domain on the BMSLSS should be provided.
- Evidence of the validity of the ISAAC questionnaire to identify childhood diagnoses is needed. Importantly, was there no opportunity for the authors to verify diagnoses with children's medical records?
- There is the potential for considerable error in child reports of parental employment status (assuming the yes/no response refers to whether both parents are working full- or part-time) and whether a child had a pet at the time of their birth.
- It is unclear what was meant when the authors stated that means, SD, medians, and ranks were used instead of original values.
- It is unclear as to what are the five asthma variables.
- There is no mention of missing data, the extent to which the data were missing at random, and why multiple imputation was not used. Analyses that examine variables associated with missing outcome data are needed.

#### Results

- Given the highly skewed distribution of the outcome variables, it may be useful for the authors to conduct ordinal regression models. This might help improve the clinical relevance of the results.
- The number of allergic diseases should be included as a variable in the models.
- Based on how allergic disease was measured in the study, how do the authors know that children with asthma were on appropriate medication. This seems highly speculative.
- It would be helpful for the authors to run models that identify which aspects/domains of the BMSLSS are most affected by allergic disease.

#### Discussion

- The authors note that treating asthma promotes physical activity and that physical activity is associated with life

	<p>satisfaction. Thus, it is possible that physical activity mediates the association between asthma (or potentially other allergic disease) and life satisfaction. If this is the case, the inclusion of physical activity in the models could explain the lack of association between allergic disease and life satisfaction. While the data are cross-sectional, the authors could explore this possibility.</p> <ul style="list-style-type: none"> <li>- The authors did not discuss the age-related effects observed in their model.</li> <li>- None of the statements in the concluding paragraph relates directly to the results from the study and should be completely rewritten.</li> </ul> <p>Table 1</p> <ul style="list-style-type: none"> <li>- The yes/no responses for ethnicity, parental employment do not make intuitive sense.</li> <li>- Some p-values contain &lt; symbol when not appropriate to do so.</li> <li>- It is not clear why tests are being made across covariates. Tests of variables between those with and without allergic disease is much more relevant and helpful in identifying potential confounders.</li> </ul> <p>Table 2</p> <ul style="list-style-type: none"> <li>- I am not convinced that the variables included in the model represent true confounders. The inclusion of such variables should be strongly based in theory and previous empirical evidence. The authors are encouraged to review the literature on the use of directed acyclical graphs to identify relevant confounders.</li> <li>- T-values are not needed.</li> <li>- Please provide standard errors or 95% confidence intervals.</li> </ul>
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<b>REVIEWER</b>	Srđan Banac Department of Paediatrics Clinical Hospital Center Rijeka Croatia
<b>REVIEW RETURNED</b>	02-Nov-2017

<b>GENERAL COMMENTS</b>	<p>Manuscript entitled „Active allergic disease diminishes life satisfaction in childhood: population-based study" is an original article. Authors have presented their investigation and original results related to impact of allergic diseases on the subjective well-being and life satisfaction of school children in Finland. In short, there were 1947 subjects (mean age 11 y; age range 10-12 y; girls 51%) who completed the adapted versions of Student Life Satisfaction Scale and Brief MultiDimensional Student Life Satisfaction Scale (response rate 68%). The subgroup of subjects (n=965) who reported to have at least one of three allergic conditions (asthma; seasonal allergic rhinitis; eczema) were detected using questions from ISAAC Phase One core questionnaire. A significant difference in subjects own perception of life satisfaction emerged only between non-allergic subjects and subjects with eczema. Subjects not having eczema, having working parents and having a physically active life style were found to have significantly better life-satisfaction. Authors concluded that active allergic disease reduces the child's own perception of well-being. Authors have presented their original results which in my opinion</p>
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	<p>are correctly presented and are of a considerable scientific interest. Two informative tables were used. The discussion is properly written containing enough criticism. Relevant references are cited. I believe that the manuscript and the results of the study are worth to be published.</p> <p>However, there are some minor issues and comments that in my opinion need to be considered by the authors:</p> <ul style="list-style-type: none"> <li>• It is not clear why authors reported that 40.3% of subjects had been detected to have doctor-diagnosed seasonal allergic rhinitis while in the both tables perennial rhinitis is listed?</li> <li>• A significant difference in life satisfaction between non-allergic and allergic subjects had been found only in the case of subjects with eczema. Thus, the title could be more informative (eg. "Eczema diminishes life satisfaction in...")?</li> <li>• There is an minor oversight in the table 1. Mean value of SLSS in subjects with asthma probably should be 89.3 (not 899.3)?</li> </ul>
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### VERSION 1 – AUTHOR RESPONSE

#### Editorial Requirements:

- Please revise your title to state the research question, study design, and setting (location). This is the preferred format for the journal.

Thank you for this information. The title has been changed to the preferred format.

- Please work to improve the quality of English throughout the manuscript, either with the help of a native speaking colleague or with the assistance of a professional copyediting agency.

The original versio was checked by a native editor, and also this revised version has been sent to a professional copyediting agency.

#### Reviewer #1 comments

##### A) Introduction

1. The first sentence of the introduction needs to be appropriately referenced.

1. Thank you for bringing this to our attention, the references in question has been added. See Page 4, line 10.

2. The second paragraph of the introduction highlights the burden associated with allergic disease, particularly those burdens that are not physical in nature. However, this section is sparsely referenced. A couple of relevant papers include: o Ferro & Boyle. Self-concept among children and adolescents with a chronic illness: a meta-analytic review. Health Psychology, 2013, 32(8), 839-848. o Ferro MA, Van Lieshout RJ, Ohayon H, Scott J. Emotional and behavioral problems in adolescents and young adults with food allergy. Allergy, 2016, 71(4), 532-540.

3. It would seem that a brief overview of findings related to quality of life in children with allergic disease is also warranted in the introduction. For example: o Cui W, Zack MM, Zahran HS. Health-related quality of life and asthma among United States adolescents. J Pediatr 2015;166:358-64.

2. & 3. Thank you for noticing these points. We have extended paragraphs in introduction section and included additional as well as proposed references. See page 4 beginning from line 34.

4. After stating the objectives, the authors note that previous research has used parental reports of child well-being (which ignore the child's perspective), suggesting that a strength of the current study is the use of child self-reports. However, this seems to contradict the authors' point in the strengths/limitations section.

4. Thank you this suggestion: we consider asking children as a strength, since knowledge of children's perceived quality of life has rarely been asked directly from children and the objective information was not the purpose of the present study. We have revised limitation excluding the contradictory claim (page 10, line 21).

##### B) Methods

1. Details of the original Children Worlds survey is needed, particularly the original objectives of that study.

1. Thank you for this comment. We have added the text of the objectives of the study on page 5 line 21 accordingly.

2. The item adapted from Diener should be provided in the description of the SLSS.

2. This comment has been reacted by adding the item of the description of the scale in page 5, line 47.

3. The rating scales, total scores, direction of scores, and alpha reliabilities of the SLSS and BMSLSS should be provided separately.

3. The rating scales and total scores as well as direction of scores were included in the original version in page 6, lines 19-21. Alpha coefficients have been added in page 5, line 6, line 5 (SLSS) and page 6, line 25 (BMSLSS).

4. The number of items per domain on the BMSLSS should be provided.

4. This information has been added on page 6, line 14.

5. Evidence of the validity of the ISAAC questionnaire to identify childhood diagnoses is needed. Importantly, was there no opportunity for the authors to verify diagnoses with children's medical records?

5. In Finland, the ISAAC core questions on asthma have been validated against anti-asthmatic medication reimbursement data of the Finnish Social Insurance Institution and found to be highly valid. Although there are no specific validation data about ISAAC questions on eczema in Finnish language, it has been shown that, in general, ISAAC-questionnaire-derived symptom prevalences are sufficiently precise on population level (see page 6, line 43 onwards).

6. There is the potential for considerable error in child reports of parental employment status (assuming the yes/no response refers to whether both parents are working full- or part-time) and whether a child had a pet at the time of their birth.

6. This point has been discussed in study limitations.

7. It is unclear what was meant when the authors stated that means, SD, medians, and ranks were used instead of original values. - It is unclear as to what are the five asthma variables.

7. Thank you for bringing this to our attention. We have described more precisely these two items (page 7, line 12 onwards). The sentence in the paragraph Statistics was rewritten more clearly: "Continuous non-normally distributed outcome variables SLSS and BMSLSS were characterized using means, standard deviations, medians and mean ranks. Ranks, counted over the total data, were used in analyses because of the extremely left skewed distributions of the outcome variables SLSS and BMSLSS."

The five asthma variables; A pet when born, A pet now, Asthma, Eczema, Perennial rhinitis were opened up in the text, on page 7, line 34.

8. There is no mention of missing data, the extent to which the data were missing at random, and why multiple imputation was not used. Analyses that examine variables associated with missing outcome data are needed.

8. Thank you for bringing this to our attention. The survey was carried out at school, so only the pupils who were absent from school that specific day missed the survey, and we don't have any data from them to use in drop out analysis. On the other hand, multiple imputation was not needed, because the presumption of missing completely at random is probable in this study. See page 7, line 41 for the clarification of the handling of missing values. We have described the centralized data handling process.

### C) Results

1. Given the highly skewed distribution of the outcome variables, it may be useful for the authors to conduct ordinal regression models. This might help improve the clinical relevance of the results.

1. We used linear regression modelling, but the original values were transformed to ranks to improve the clinical relevance of the results.

2. The number of allergic diseases should be included as a variable in the models.

2. Thank you for bringing this to our attention. We have now tested the effects of the suggested variable in the model. However, no effects were found and we made the decision of not including it the model.

3. Based on how allergic disease was measured in the study, how do the authors know that children with asthma were on appropriate medication. This seems highly speculative.

3. Thank you for your comment. The children with asthma diagnosis used inhaled  $\beta$ 2-agonists, inhaled steroids or both. However, we don't know if the medication was appropriate in each case. Therefore we have modified the sentence "It is of note that all subjects with asthma diagnosis were on inhaled asthma medication" in the Results section.

4. It would be helpful for the authors to run models that identify which aspects/domains of the BMSLSS are most affected by allergic disease.

4. As proposed, we checked the domain-specific associations with bivariate correlation analysis. The following sentence was added in page 8, line 19. An additional correlation analysis showed that all the domains of BMSLSS were statistically significantly associated with eczema. The most affected domain was body image ( $r=-.10$ ,  $p<.001$ ).

#### D) Discussion

1. The authors note that treating asthma promotes physical activity and that physical activity is associated with life satisfaction. Thus, it is possible that physical activity mediates the association between asthma (or potentially other allergic disease) and life satisfaction. If this is the case, the inclusion of physical activity in the models could explain the lack of association between allergic disease and life satisfaction. While the data are cross-sectional, the authors could explore this possibility.

1. Indeed, this is an important observation. We cross-analysed all the pairwise interactions between the background variables (Grade, Parental employment, Sports) and the five Asthma variables to outcome variables (SLSS, BMSLSS), but none of them were even near statistical significance. We continued analysing now, by your request, the effect of physical activity and asthma/allergic variables to categorical life satisfaction SLSS (low, middle, high) by ordinary logistic regression analysis, but the results were as before, no interactions were found. On the other hand, the small frequency (78 / 1884) of the pupils exercising less than once a week makes it difficult to observe any interactions.

2. The authors did not discuss the age-related effects observed in their model.

2. We have added discussion of the effect of age. See page 9, line 30.

3. None of the statements in the concluding paragraph relates directly to the results from the study and should be completely rewritten.

3. The conclusions are repeated in the final part of the discussion. We also wished to make a recommendation to medical care of these children, to promote the assessment of the life satisfaction also from the children's perspective. (Page 10, line 39)

#### E) Table 1

1. The yes/no responses for ethnicity, parental employment do not make intuitive sense.

1. These responses have been revised to make better sense and to be more understandable. We ended up choosing this model in order to keep it simple as we already have two different outcomes to explain with several explanatory factors.

2. Some p-values contain < symbol when not appropriate to do so.

2. Also these mistakes have been corrected.

3. It is not clear why tests are being made across covariates. Tests of variables between those with and without allergic disease is much more relevant and helpful in identifying potential confounders.

3. This is an important note. We have discussed about this option in our research team.

However, since we already have two outcome variables (SLSS; BMSLSS) we decided not to split the data into two samples.

#### F) Table 2

1. I am not convinced that the variables included in the model represent true confounders. The inclusion of such variables should be strongly based in theory and previous empirical evidence. The authors are encouraged to review the literature on the use of directed acyclical graphs to identify relevant confounders.

1. This is also an important notion. We have now discussed the justifications for our confounders throughout the paper more precisely. See page 9, line 32 onwards on ethnic background and parental employment status.

2. T-values are not needed.

2. T-values were deleted.

3. Please provide standard errors or 95% confidence intervals.

3. Standard errors were provided in Table 2.

Reviewer #2 comments

A) Results/tables

1. It is not clear why authors reported that 40.3% of subjects had been detected to have doctor-diagnosed seasonal allergic rhinitis while in the both tables perennial rhinitis is listed?

1. Thank you for bringing this mistake into our attention. Perennial should be seasonal.

2. A significant difference in life satisfaction between non-allergic and allergic subjects had been found only in the case of subjects with eczema. Thus, the title could be more informative (eg. "Eczema diminishes life satisfaction in...")?

2. The title has been changed based on the recommendation of the editor.

3. There is a minor oversight in the table 1. Mean value of SLSS in subjects with asthma probably should be 89.3 (not 899.3)?<

3. Mean value has been corrected.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Srđan Banac Paediatric Clinic - Department for Pulmonology, Allergology and Immunology Clinical Hospital Centre Rijeka, Croatia
<b>REVIEW RETURNED</b>	27-Dec-2017
<b>GENERAL COMMENTS</b>	The manuscript has been corrected according to the comments and suggestions given by the reviewer. I believe the manuscript can be accepted for publication now.

#### VERSION 2 – AUTHOR RESPONSE

Dear Mr. Bedi,

Referring to the latest email (16.1.) regarding our manuscript ID bmjopen-2017-019281.R1 entitled "The association of allergic diseases with children's life satisfaction: population-based study in Finland" I'm attaching the final revised version of our article for publication in the BMJ Open.

We have now completed the final changes you requested. The changes made are described according to the decision letter in the submission page in the BMJ Open home pages.

Sincerely,

Leena Haanpää