Author's response to reviews

Title: Contextual and Individual Assessment of Dental pain period prevalence in adolescents: a multilevel approach

Authors:

Marco A Peres (mperes@ccs.ufsc.br)  
Karen G Peres (karengp@ccs.ufsc.br)  
Antonio C Frias (acfrias@usp.br)  
José Leopoldo F Antunes (leopoldo@usp.br)

Version: 2 Date: 10 June 2010

Author's response to reviews: see over
Natalie Pafitis MSc
The BioMed Central Editorial Team
BMC Oral Health

Dear Natalie,

On behalf of all authors, I am submitting the revised version of the manuscript of Contextual and Individual Assessment of Dental pain period prevalence in adolescents: a multilevel approach to your appreciation and to editorial analysis of the BMC Oral Health, as to the possibility of its publication.

The text has been revised according to indications of reviewers. We thank comments and suggestions, which we truly believe contributed to improve the text. We have prepared a response to the reviewers, addressing each of their comments. Each of the modification is in bold words in the new version of the manuscript.

The manuscript has not been published before, and is not being considered for publication elsewhere. We agree to assign exclusive copyright to the BMC Oral Health if and when the manuscript is accepted for publication.

Yours sincerely,

Marco Aurélio Peres
REVIEWER 1
Reviewer: Anne Nordrehaug Astrom
Reviewer's report:
Review: Contextual and individual assessment of dental pain period prevalence in adolescents: A multilevel approach. This large scale cross sectional survey from Sao Paulo in Brazil describes determinants of period dental pain in adolescents aged 12 and 15 years of age. Independent variables were analyzed according to their assumed level of proximity to the outcome variable in hierarchical multivariable Poisson regression analyses. Moreover, an area based measure of Human development (HDI) was assessed and analyzed together with the individual level variables in multilevel regression analyses using STATA. The article is justified by referring to the absence of multilevel analyses in the dental literature. Overall I think this is an interesting article with potential to be published in BMC Oral health. However, I have some comments and questions that should be considered by the authors in a major revision of the current manuscript.
Authors: We would like to thank the reviewer for her comments about our work.

1) The English writing should be improved considerably
   Authors: The new version of the manuscript has been reviewed by a professional English native speaker.

2) The journal guidelines for how to prepare the manuscript should be adhered to (see for instance – figures/figure legends, the references, etc
   Authors: It was done.

3) Method section could be improved – particularly the sampling procedure could be described in more detail. How many students were eligible for study? What were the reasons for non response? Drop outs were compensated by adding individuals to the calculated sample sizes. On page 6 it says that the original sample size was enlarged by adding 1.565 15 yr olds. On page 5, 1565
15 yr olds were the total number of school children examined in the survey – this appears confusing - please clarify

Authors: We provided additional explanations about these aspects in the second version of the manuscript.

In page 5: “All students aged 12 (179,674) and 15 years (184,537) in the city were eligible to participate in the study.”

In page 6: “The refusals and drop-outs were not replaced”.

In page 9: “The main reason for refuses and drop-outs were the lack of written consents and school absenteeism when the study was carried out”.

4) Results: I miss a sample profile for this study

Authors: We have drawn a new table (Table 1) describing the study sample profile.

5) Table 1: shows the unadjusted associations between dental pain period prevalence (at the individual level) and individual level socio-economic characteristics and dental status in addition to an area based measure of human development. What was the N in the analyses using HDI as independent variable?

Authors: We added information about the number of participants in both the HDI categories.

6) Table 2 shows results from multilevel Poison regression using both aggregate and individual level variables as correlates of period dental pain in the same model. I am not experienced with this type of analyses – however it seems strange the PR for HDI was the same in table 1 and table 2 – that is both in unadjusted analyses and after having adjusted for several individual characteristics. To me that appears to imply that none of the effect at area level are mediated or taken account of by individual correlates. The authors should justify this whilst describing the results.

Authors: Model 1 was performed including all individual-level characteristics adjusted by contextual variable (HDI). The most proximal variables (dental status) were adjusted intermediate variables, such as
socioeconomic status and demographic variables, and then by contextual variable (HDI). We used a hierarchical approach as proposed by seminal paper wrote by Victora and colleagues (Victora CG, Huttly SR, Fuchs SC, Olinto AMT. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. International Journal of Epidemiology 1997; 26(1):224-227). According to this strategy, the most distal determinants are not adjusted by intermediate and proximal determinants, while the latter are adjusted by the determinants placed in the above-mentioned levels. As this kind of modeling may cause misunderstanding, we ran a new model, named model 2 where HDI (contextual variable) was adjusted by individual-level variables, and sure, gave a different value of prevalence ratio. In addition, we added more explanation about statistical modeling in the methods section.

7) Finally individual level multiple variable logistic regression were conducted stratified by the area level measure of HDI. This is another feature that should be justified – to conduct analyses with individual level variables stratified by a variable measured at another level? Some interactions are indicated – between social context and age and type of school on dental pain. These interactions of effect modifications have not been tested statistically which should be recognized when writing and interpreting results.

Authors: We used the most traditional and understandable approach to assess interaction or effect modify. When interaction is present, we should report separate exposure effects for each stratum, instead of presenting just the p values of the interaction terms.
REVIEWER 2

Reviewer's report

Reviewer: WAEL SABBAB

Reviewer's report:
Contextual and individual assessment of dental pain period prevalence in adolescents; a multilevel approach.

This is an interesting and well written paper that addresses the contextual and individuals determinants of dental pain among Brazilian adolescents. However, I have some concerns about the paper and the methods.

Authors: We would like to thank the reviewer for his comments about our work.

Introduction:

• The authors should expand in their justification for using multilevel analysis to examine the contextual determinants of dental pain. The authors reported few studies which used multilevel analysis in relation to certain dental condition. Did the use of multilevel analysis in these dental studies explain more of the variation in oral health on top of that explained by the individual's determinants?

Authors: The aim of this study was to show if there is an association between Human Development Index (contextual variable) after adjustment for well-known individual characteristics associated with dental pain. We performed a multilevel Poisson regression modeling and added, in the second version of the manuscript, the values of -2-loglikelihood for each step allowing the assessment of goodness of fit of the model.

• The objective of the study should state explicitly the contextual determinants that will be examined in the multilevel model.

Authors: We agree with the reviewer. We introduced this information in the second version of the manuscript.

Methods:

• It would have been useful to conduct the analysis in two steps, first at the
individual level including all explanatory variables, second conduct the multilevel analysis including the level 2 variable (Human development index). This will inform us of the variation in dental pain explained by including level 2 on top of that explained by the individual’s determinants.

Authors: As we mentioned in our answer to review 1, Dr. Anne Nordrehaug Astrom, Model 1 was performed including all individual-level characteristics adjusted by contextual variable (HDI). The most proximal variables (dental status) were adjusted intermediate variables, such as socioeconomic status and demographic variables, and then by contextual variable (HDI). We used a hierarchical approach as proposed by the seminal paper wrote by Victora and colleagues (Victora CG, Huttly SR, Fuchs SC, Olinto AMT. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. International Journal of Epidemiology 1997; 26(1):224-227). This is one of the most cited paper in Epidemiological literature (310 times web of sciences 21th May 2010) and has been influencing many researchers. According to Victora et al.’s strategy, the most distal determinants are not adjusted by intermediate and proximal determinants, while these latter are adjusted by the determinants placed in the above-mentioned levels. As this kind of modeling may cause misunderstanding, we ran a new model, named model 2 where HDI (contextual variable) was adjusted by individual-level variables and gave a different value of prevalence ratio. In addition, we added more explanation about statistical modeling in the methods section. Our statistical modeling is correct from a technical point of view; there are many options to perform multivariable regression models.

• The number of geographical areas included in level 2 analysis was not stated in the method or the results.

Authors: You are correct. We added this information in the second version of the manuscript.
• The authors should explicitly indicate all the variables included in each regression model.

**In the methods section, there is a detailed explanation about modeling procedures as follows:**

“At the individual level, demographic characteristics were selected as the first block, thus allowing the assessment of all remaining covariates to be adjusted for the distribution of participants by sex, age and ethnic group. Income, education and type of school comprised the second block, thus allowing proximal covariates on the third block (dental status) to be adjusted for differences of socioeconomic status in the sample (Figure 1). All associations were adjusted for covariates positioned in the same and in upper levels of the hierarchical model. Finally, multivariable Poisson regression models were performed stratified by two levels of the Human Development Index – low and high.”

**Results:**

• Table 1 reports the prevalence of dental pain by individual’s characteristics and human development index. However, the table reports prevalence ratio, it is not clear whether these prevalence ratios reflect the results for unadjusted (binary) analysis or adjusted analysis. If these prevalence ratios were obtained from adjusted models, what were these models adjusted for?

*Authors: We added information about crude and adjusted analysis in the new version of the manuscript.*

• In the same table (1), for the variables (skin colour, income, father education and mother education), the authors stated a single p value for each of these variables. What these p values reflect? Traditionally in a categorical variable a p value should be reported for each category of the variable.
Authors: We respectfully do not agree with the reviewer’s point of view. The p values must be reported for the variable and not for its category. For instance, the criteria to keep or remove a variable of a multivariable model are not the p value of a category, but the p value for a variable (Hosmer and Lemeshow, 1989; Kirkwood and Sterne, 2003).

See the example below, extracted from an article published in the BMC Oral Health (Kuhnen et al., 2009).

Table 2 – Toothache and independent variables. Poisson regression analysis (Prevalence ratio – PR and confidence intervals- 95% CI).

<table>
<thead>
<tr>
<th>Levels</th>
<th>Variables</th>
<th>Model 1* PR (95% CI)</th>
<th>Model 2* PR (95% CI)</th>
<th>Model 3* PR (95% CI)</th>
<th>Model 4* PR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sex</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>1.6 (1.3;2.0)</td>
<td>1.6 (1.3;2.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age group-years</td>
<td>p=0.004</td>
<td>p=0.001</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>20 – 29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 – 39</td>
<td>0.9 (0.7;1.1)</td>
<td>0.9 (0.7;1.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40 – 49</td>
<td>0.6 (0.4;0.8)</td>
<td>0.5 (0.4;0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50 – 59</td>
<td>0.6 (0.4;0.9)</td>
<td>0.5 (0.3;0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skin colour</td>
<td>p=0.001</td>
<td>p=0.003</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lighter-skinned blacks</td>
<td>1.3 (0.9;1.7)</td>
<td>1.2 (0.9;1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dark skinned blacks</td>
<td>1.5 (1.2;2.0)</td>
<td>1.5 (1.1;1.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yellow</td>
<td>1.5 (0.9;2.6)</td>
<td>1.4 (0.7;2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amerindian</td>
<td>1.4 (0.7;3.1)</td>
<td>1.6 (0.7;3.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Per capita income-BMWa</td>
<td>p&lt;0.001</td>
<td>p&lt;0.002</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1,59 – 19,74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0,89 – 1,58</td>
<td>1.5 (1.0;2.2)</td>
<td>1.3 (0.9;1.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0,60 – 0,88</td>
<td>1.6 (1.0;2.2)</td>
<td>1.2 (0.9;1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0,02 - 0,50</td>
<td>2.4 (1.7;3.4)</td>
<td>1.7 (1.2;2.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Educational attainment-years</td>
<td>p&lt;0.001</td>
<td>p=0.083</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>≥12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 – 11</td>
<td>1.4 (1.1;2.0)</td>
<td>1.2 (0.9;1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 – 8</td>
<td>1.5 (1.7;2.0)</td>
<td>1.4 (0.9;2.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 4</td>
<td>1.8 (1.2;2.7)</td>
<td>1.6 (0.9;2.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAGE score</td>
<td>p=0.156</td>
<td>p=0.004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------</td>
<td>---------</td>
<td>---------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1</td>
<td>1.0 (0.9;1.1)</td>
<td>1.4 (1.1;1.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Smoking status**

<table>
<thead>
<tr>
<th>Smoking status</th>
<th>p&lt;0.001</th>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoked</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ex-smoked</td>
<td>1.2 (1.0;1.6)</td>
<td>1.3 (1.0;1.6)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.7 (1.4;2.1)</td>
<td>1.5 (1.2;1.9)</td>
</tr>
</tbody>
</table>

**Consumption of cigarettes- Package year**

<table>
<thead>
<tr>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smoker</td>
</tr>
<tr>
<td>&lt;10</td>
</tr>
<tr>
<td>≥10</td>
</tr>
</tbody>
</table>

**Type of dental service in the last attendance**

<table>
<thead>
<tr>
<th>p=0.049</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private</td>
</tr>
<tr>
<td>SUS – public</td>
</tr>
<tr>
<td>Others</td>
</tr>
</tbody>
</table>

**Use of dental service in the last year**

<table>
<thead>
<tr>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

* Brazilian Minimum Wage (worth of US$ 200,00).

*Model 1 – crude unadjusted analysis

*Model 2 – variables in the block 1 adjusted for variables in the same level

*Model 3 – variables in the block 2 adjusted for variables in the same level and the levels above.

*Model 4 – variables in the block 3 adjusted for variables in the same level and the levels above.

**excluded due lost the statistical significance

All analysis were adjusted for the clustered sampling design and by the number of teeth.

p value = Wald test.

• In Table 2 the authors claimed that the regression model was adjusted for
human development index. However, the prevalence ratio for Human development Index in Table 2 was similar to that reported in Table 1. This is a mystery? How can a variable have exactly the same association with the dependent variable in two different regression models?

Authors: As explained earlier, we followed the modeling strategy proposed by Victora et al (1997). This is not a mystery, but a modeling based not just in statistics, but in theory. In this way, the most distal variables are not adjusted for those placed in the lower hierarchical levels and then the PR for the most distal variable is the crude PR (0.67 (0.56–0.81). We ran a model 2 adjusted contextual variable for individual characteristics and informed the PR 0.74 (0.64–0.85).

- In Table 2, again it is not clear how the regression model was conducted. Were all the variables in Table 2 included in one regression model, or did the authors include one individual variable at the time and adjusted only for Human Development Index?

Authors: We added new explanation in the table.

- The authors should report how much of the variation in dental pain was explained by including level 2.

Authors: We included the $-\log_{10}\text{likelihood}$ values for each step of statistic modeling allowing the readers to identify goodness of fit for each separate step.

- In Table 3 the authors stratified the sample according to Human Development Index and conducted two different models of regression. The associations between most of the explanatory variables and dental pain lost significance in these two models. The authors claimed that this happened because the relationship between individual’s characteristics and dental pain was confounded by human development index. Did the authors consider that the lack of association resulted from using smaller number of individuals in the stratified regression models than that used in the original model reported in Table 2? If the contextual variable (Human development index) confounded the
relationship between individual characteristics and dental pain, then this relationship should have disappeared in Table 2 since it was adjusted for level 2.

Authors: Good point. We are talking about the effect modification and confounding. The most traditional way to assess confounding and interaction is stratification. Effect modification is detected by varying the selected effect measure for the factor under study across levels of another factor (Last 2001). We believe that our sample is big enough to perform stratified analysis.

Discussion:

• Page 11, 2nd paragraph, the authors stated “As the outcome was relatively common statistical analysis used Poisson regression instead of multivariable logistic regression” this statement should have been made in the method section not in the discussion.

Authors: Thank you for suggestion, but we are discussing our methodological options. In the methods section, the outcome prevalence – a result – had not been presented yet.

• Later in the same paragraph the authors stated that they stratified the analysis to assess effect modification and interaction. I do not recall reporting any interaction in the results.

Authors: We adopted stratification as a way to show effect modification, instead of showing complicated cross-level interaction terms.

• Page 12, 2nd paragraph, the authors stated that the use and availability of dental care should be associated with contextual environment. What is the reference for this statement? Even if this statement was valid in certain countries, is it applicable to the study population and geographical area. In fact one of the major limitations of the paper is the lack of adjustment for the use and availability of dental services.
Authors: We strongly agree with the review. The lack of information about dental care ate geographical area is a clear limitation of our work. We stressed this aspect in the new version of the manuscript.
REVIEWER 3
Reviewer's report
Reviewer: Marc W Heft
Reviewer's report:
The authors report on multilevel analyses of epidemiological data of adolescents aged 12 and 15 yrs residing in San Paulo, Brazil addressing factors contributing to the prevalence of dental pain. The study is well-designed and the analytic approach geared to address the research question.
The manuscript requires substantive editorial revision prior to publication.

Authors: The new version of the manuscript has been reviewed by a professional English native speaker.

I have identified several specific points that require clarification:
Page 2, last paragraph: What is meant by “socio development level”?
Authors: We replaced socio development level with Human Development Index.

Page 3, paragraph 1: Clarify “period prevalence” and “point prevalence”. Either eliminate or improve the “No author given, 2009” reference.
Authors: We added definitions as follows: “Period prevalence refers to the number of person known to have had the pain at any time during a specified period, usually six months in dental pain studies. Point prevalence refers to the number of persons with pain at a specified point in time (Last, 2001).”

Page 3, last paragraph: What is meant by “through a limited biological point of view”?
Authors: We rewrote as “adopting a point of view limited to biological aspects”

Page 4, second paragraph: “unsounded teeth”?
Authors: We corrected as “unsound teeth”.

Page 4, second paragraph: “unsounded teeth”?
Page 6, last paragraph: Please clarify the “human development index” and how does it differ from the other sociodemographic data collected by the authors?

Authors: We informed that “The human development index (HDI) is a composite measurement summarizing information on income, educational, level and longevity for each geographic area.”
REVIEWER 4

Reviewer's report

Reviewer: Alexandrina Lizica A Dumitrescu

Reviewer's report:

Minor Essential Revisions are:

a. On page 4: there are several studies in the dental literature focused on periodontal disease:


Authors: We thank the reviewer for her attention. We refer to the scarcity of study using multilevel modeling in dental public health literature.

Authors: We thank to the reviewer for her attention. We refer to the scarcity of study using multilevel modeling in dental public health literature.

b. Please correct on page 6: CI95% with CI 95% and Sao Paulo, 27 with Sao Paulo, 2002.

Authors: It was corrected.