Author's response to reviews

Title: Determinants of poor adherence to secondary antibiotic prophylaxis for rheumatic fever recurrence on Lifou, New Caledonia: a retrospective cohort study

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Version: 2 Date: 6 November 2012

Author's response to reviews: see over
Dear editor of BMC Public Health,

We are pleased to resubmit our manuscript “Determinants of adherence to secondary prophylaxis of acute rheumatic fever recurrence on the island of Lifou (New Caledonia): a retrospective cohort study”

All contributing authors have read and approved the submission of this revised manuscript. This manuscript has not been and will not be submitted for publication elsewhere.

In revising the manuscript we have taken into account both comments. Our responses are presented in red inserted underneath each comment and modifications were made in the manuscript.

We hope that the editorial board will accept our modifications and will consider this new version.

Sincerely yours,

Eric D’Ortenzio on behalf of the authors

Noumea, New Caledonia, October 28th, 2012,
Editor comments and responses:

Reviewer 1

Major compulsory revisions:

1) There are major issues in this paper with English language. I don’t believe that this issue should influence the editorial decision, but if accepted for publication the manuscript will have to be edited heavily with this in mind.

The paper has been reviewed and corrected by an English speaking person.

2) The conclusions of the study are a series of recommendations for improving adherence. I am not sure that all of the recommendations follow on from the results of the actual study – for example recommendation 1 is to establish an active recall system while the data in this study do not necessarily support that, and recommendation 2 is to raise the awareness of ARF despite the fact that it appeared that the knowledge of treatment objectives for secondary prophylaxis was very high in both groups. While it is not completely unreasonable to propose some recommendations, it would also be appropriate to propose further research to better answer the question as to what makes some patients adhere to their injection and others not so. This might include: expanding the sample size, or embarking upon a qualitative study to define new hypotheses to be tested, or developing an intervention that could be tested in a randomized fashion.

Recommendations and conclusions were reconsidered as proposed by the reviewer. See the conclusion section.

Minor essential revisions

1) The authors state that the questionnaire was “standardized”. How was this done? Did the questionnaire go through a pilot phase? Did the authors use any published data to decide upon the choice of variables in the questionnaire?

The questionnaire was conceived by the investigators based on their experience with a previous study on risk factors of RHD in New Caledonia. We also chose our variables based on previous adherence studies already published and the WHO recommendations (World Health Organization: Adherence to long-term therapies. Evidence for action. Geneva, Switzerland: World Health Organization 2003). The questionnaire went through a pilot phase for 10 persons.

2) The first 2 sentences of the Discussion should be in the results section. It seemed to me that adherence was not normally distributed and that the data would be better expressed as median and IQR. Indeed a presentation of adherence in the whole sample in a graphical representation would be helpful to get a better idea of the spread of adherence.

The first 2 sentences of the discussion were replaced in the results section

We added the interquartile range for the description of adherence. The median was already given. We also added a graphical representation of adherence regarding the good or poor adherence and regarding the age (< and ≥16 years).

3) The Discussion is too long

The discussion was shortened.

4) There is very limited discussion of the limitations of the study – this needs to
be expanded.
The section talking about the limitations of the study was expanded.

Discretionary revisions:

1) It would be helpful to include the prevalence figure calculated above to indicate the high burden of disease in this community— that is, an all ages prevalence of RHD of 9 per 1000 s VERY high.
We added the prevalence figure calculated for people with an history of ARF or RHD and receiving antibiotic prophylaxis in Lifou.

2) Did the authors consider comparing those with very good adherence to those with very poor adherence?
We did not compare patients with very good adherence and patients with very poor adherence because of the low number of patients included (n=70) in our study. Twelve patients with a very poor adherence (<50%) were included. A sub-group analysis in these groups was not possible because of a lack of power.

Reviewer 2

Major compulsory revisions:

1. The manuscript provides only aggregate information about the interviews. Were questions open or closed, were multiple choices provided?
We specified in the method section that the questions were close-ended and with binary choice.

2. How were the interviews conducted with (young) children? Did all children answers questions themselves or was the interviewer informed by parents or caregivers?
We interviewed both the child and one of his parents at least when the child was in age to understand but < 16 years old. For very young children, one of the parents at least was interviewed. We added a sentence in the methods section.

3. The authors mention in the introduction that the prophylaxis should be applied every 3-4 weeks. Yet, the definition for adherence is one injection every 3 weeks. The authors should explain why they made this choice. Perhaps 3.5 weeks would have been better? Or conduct sensitivity analysis with a 4 week threshold?
One injection every 3 weeks is the frequency recommended by the health agency in charge of the ARF program in New Caledonia. That’s why we made this choice. In the ARF Australian guideline, the recommendation is every 3-4 weeks, depending on the history of ARF or RHD. We added a sentence in the methods section.

4. I miss a table with baseline characteristics. The text in the result section provides some background, but a table would be more informative, by not only presenting mean and SD but also range for e.g. age.
We added a baseline characteristics table (Table 1).

5. Given the sample of (young) children and adults I would have expected subgroup analysis of children vs. adults (e.g. <16 years old, since this was also a factor in the univariate analysis). It can be expected that adherence to medication among children is different than
among adults. The authors do reflect on some age related factors (missing school) for non-adherence in the discussion as well.

We added a histogram with the rate of adherence according to age (< or ≥ 16). A sub-group analysis in these groups was not possible because of a lack of power.

6. Too much emphasis is placed on the results of the univariate analysis in both text and Table 1. The purpose of the univariate analysis is to identify variables for inclusion in the multivariate analysis. The p-value is of importance (based on the threshold of p=0.25 of the authors), but presentation of the findings should merely be aimed at transparency. By emphasizing the results and including the odds ratios in Table 1, an important effect of these variables is implied.

We simplified our table of univariate analysis and we removed the column with the odds ratios.

7. The legend in table 2 lists the variables that were included in the multivariate analysis. Based on the p-values in Table 1, I miss parental occupation. I also do not understand the difference between the two listings of parental occupation in Table 1.

We didn’t include the parental occupation in the multivariable analysis because this variable only concerned the children. In the table 1, there were the parental occupation and the paternal occupation. We agree that the reader can be confused.

Regarding for this comment and your comment n°6, we deleted maternal, paternal and parental occupation in Table 1.

Minor essential revisions:

8. The title does not include rheumatic heart disease

The secondary prophylaxis main objective is to prevent GAS sore throat to prevent ARF recurrence, so we think the message will be more efficient if we talk about secondary prophylaxis to prevent ARF recurrence.

9. The abstract includes abbreviations ARF and RHD without clarification.

We clarified abbreviations in the abstract.

10. How can adherence be higher than 100% (line 121)?

The adherence rate can be higher than 100% in the case of a patient with more injections than recommended. In our study, one patient had 18 injections in 2011 instead of the 17 injections recommended.

11. Global adherence to treatment of chronic disease (line 121)

We added treatment of in the text.

12. Provide initials of the interviewer (line 173)

We added the initials of the interviewer: BG=Brunelle Gasse in the text.

13. Individuals in the household with adherence (line 254)

We added “in the household” in the text.

14. Reference is missing (line 176)

We added the reference in the text.
15. What is concret dwelling? (Table 1)
In fact, there was a mistake. It was not “concret” but “concrete”. We changed it the table.

16 Reference #4 and #6: WHO is not correctly referred to as author
We corrected these references in the text.