Author’s response to reviews

Title: Penicillin resistance and serotype distribution of Streptococcus pneumoniae in Ghanaian children less than six years

Authors:

Nicholas TKD Dayie (nicholasdayie@yahoo.com)
Reuben E Arhin (rearhin@gmail.com)
Mercy J Newman (newmerci@yahoo.co.uk)
Anders Dalsgaard (adal@sund.ku.dk)
Magne Bisgaard (mbi@sund.ku.dk)
Niels Frimodt-Møller (nfm@ssi.dk)
Hans-Christian Slotved (hcs@ssi.dk)

Version: 3 Date: 23 August 2013

Author’s response to reviews: see over

Thank you very much for considering the manuscript for publication in BMC Infectious Diseases. We appreciate the reviewers’ thoughtful comments and we are pleased to have the opportunity to address these in our revised manuscript. Our responses to the reviewers’ comments are below:

Editor's comment:

The manuscript needs further revisions in line with the comments from both reviewers.

**Answer:** We have addressed the reviewers’ comments, see below.

Reviewer number: 2

**Reviewer's report**

**Title:** Penicillin resistance and serotype distribution of Streptococcus pneumoniae in Ghanaian children less than six years  
**Version:** 2  
**Date:** 1 August 2013  
**Reviewer:** Susan Morpeth

**Reviewer's report:**

Thanks for sending the revised manuscript and cover letter.

My further comments are:

Abstract and Results

1. Some of the percentages given have a decimal place and others do not. I suggest rounding them all off to the same number of decimal places for consistency, and would personally use no decimal places.  
   (Discretionary revision)  
   **Answer:** We have rounded off, using no decimal as suggested.

Methods, Results & Discussion

2. The authors have explained in their cover letter that the population includes urban and slum-dwelling children, but this has not been well explained in the methods of the manuscript. Some mention of the generalizability of the study population to that of all children under the age of 6
years in Ghana needs to be added, as readers will not be familiar with the socio-economic population structure or rural/urban divide of Ghana. The discussion could be expanded to further discuss the generalizability of the results to the general Ghanaian population of <6 year-olds, referring back to the methods.

**Answer:** We have expanded the method and discussion section including the answers from our previous response, as suggested by the reviewer.

3. In addition, the fact that the study population contains mostly 2-6 year old children should be added to the methods, or pointed out clearly early in the text of the results, so that the reader is clear in their mind about the study population as they go on to read the results and discussion. The fact that very few children under the age of 2 years are included is too important to only mention in the discussion. The discussion of the carriage prevalence found, could also refer to the limitation of the lack of <2 year-olds in the study population; the carriage prevalence would have been higher if the younger age group was better represented.

**(Major revisions)**

**Answer:** We specified and added a sentence in the results and discussion section on the limitation of the study with regard to the low representation of children from the age group less than two years.

**Discussion**

3. I agree with the other reviewer that the increase in penicillin resistance is not entirely clear, with differing results due to different study populations and methods, and would suggest toning this down in the discussion. For instance I would call it a possible increase.

**(Discretionary revision)**

**Answer:** We have rephrased the sentence in the discussion.
Reviewer number: 1

**Reviewer's report**
**Title:** Penicillin resistance and serotype distribution of Streptococcus pneumoniae in Ghanaian children less than six years  
**Version:** 2  
**Date:** 19 July 2013  
**Reviewer:** Kim Hare  
**Reviewer's report:**  
Only minor essential and discretionary revisions, including some language corrections, are required. These are listed in a file to be attached.

**Comments on revised manuscript**
Thank you to the authors for their extensive revision. I do still have a few suggestions, and apologise if I missed these previously.  
**Answer:** Thank you very much, for taking the time to go through the manuscript a second time.

**Abstract**
The abstract reads much better now. I would only suggest one small correction, to change 45.1% to 45% in the results (for consistency).  
**Answer:** We have removed the decimal from all calculated percentages all through the manuscript.

**Background**
First paragraph, last sentence: remove ‘the’ preceding PCV (as there are several PCVs).  
Third paragraph, second sentence: suggest changing ‘to inform on the vaccine policy and treatment strategy’ to ‘to inform vaccine policy and treatment strategies’.  
**Answer:** Has been changed as suggested.

**Methods**
**Characterization of S. pneumoniae**
Suggest deleting ‘test’ after ‘Quellung reaction’.  
**Answer:** Has been changed as suggested.

I am then confused by the description for screening multiple serotypes. Is the ‘latex agglutination using serotype specific antisera (SSI Diagnostica, Denmark)’ mentioned first (line 5) the same as the ‘pneumotest latex agglutination kit (SSI-Diagnostica, Denmark)’? There should not be a ‘-’ after SSI.  
**Answer:** It is pneumotest latex agglutination kit (SSI-Diagnostica, Denmark) followed by Quellung reaction, that has been used, we have rephrased the sentence.

I would suggest a separate paragraph for penicillin resistance (as in the original manuscript). I would suggest the heading **Ethical approval** (or just **Ethics**) rather than **Ethical issues**.  
**Answer:** Has been changed as suggested.
Results
First paragraph: I’m assuming the confidence interval is 95%? i.e., ‘(32.3%, 95% CI 29.2 – 35.5)’.
Third paragraph Antimicrobial resistance: There is an extra ‘.’ after ‘Etest strips’.
Fourth paragraph Vaccine coverage: Delete ‘of’ on 3rd line, i.e. ‘covers 55%’.
Answer: Has been changed as suggested.

Discussion
First paragraph, last sentence: suggest replacing ‘identify problems’ with ‘answer questions’.
Answer: Has been changed as suggested.

Second paragraph, first sentence: delete ‘for’ after ‘provides’.
Second paragraph, second sentence: suggest replacing ‘The’ with ‘Carriage’ to make it clear that you are talking about carriage prevalence, since the first sentence referred to carriage and serotype distribution. I would also just say the prevalence was 31-34% rather than ‘around 30% (31%-34%)’.
Second paragraph, third sentence: suggest replacing ‘which used’ with ‘of’, i.e. ‘the previous study of children ≤13 years’.
Answer: Has been changed as suggested.

Third paragraph, last sentence: the comma should be after ‘resistance’, before ‘and’.
Answer: Has been changed as suggested.

The fourth and fifth paragraphs still need some work to reduce repetition (especially as the fifth paragraph is new).
Fourth paragraph, first sentence: delete ‘of the serotypes identified’ at the end of the sentence (this is repetition).
Answer: Has been changed as suggested.

I would suggest starting the fourth paragraph with the sentence ‘Prior to our study, limited data were available on serotype distribution among *S. pneumoniae* in Ghana [18,19].’
Answer: Has been changed as suggested.

Did the authors of ref [19] state that their work was done pre-2003?
Answer: Yes, the data was collected between 1998 – 2003.

Ref [18] was published in 2010 so the work was likely done before then. I don’t think these dates are necessary. This could then be followed by the sentence ‘Thus, in contrast to what is recommended [7, 8] recent surveillance data on prevalent serotypes was not available in Ghana when the PCV-13 was introduced in May 2012.’ The findings from this study could then follow on.
Answer: Has been changed as suggested.

Fifth (new) paragraph, first sentence: replace ‘mean’ with ‘means’, and ‘was’ with ‘were’. Second sentence: replace ‘in that’ with ‘as’, and ‘has’ with ‘have’.
Answer: Has been changed as suggested.

Should that be very high vaccine coverage in this age group?
Answer: Has been changed.

Third sentence: delete the second stating of ‘nurseries and kindergartens, i.e. ‘However the reason for choosing nurseries and kindergartens is that they are characterized by overcrowding and constitute an optimal environment for horizontal spread of pneumococci [31].’
Answer: Has been changed as suggested.

I would suggest deleting the rest of paragraph five. I’m not convinced that nurseries and kindergartens are where ‘PCV is expected to have the highest impact on the serotype distribution’. (The preceding words ‘the effect of’ are obsolete.) In many countries children are vaccinated at 2, 4, 6 months of age, and there is a big impact on serotype distribution in the <11 month olds. However I note that the authors say: ‘PCV-13 is currently used nationwide in Ghana to vaccinate children ≤ 5 years’. At what age does vaccination start?
Answer: The sentence has been changed. The vaccination age is six, 10 and 14 weeks and has been added in the discussion.

The last two sentences in paragraph five are, I think, unnecessary.
Answer: We feel that mentioning these sentences are important for presenting some of the topics, we find important for this study. We would therefore like to maintain the sentences.

Conclusions
There is still some repetition here which can be reduced. I suggest deleting ‘The serotypes reported in’ from the second sentence, leaving it as ‘The current study shows…’
I would also change and shorten the last sentence to reduce repetition of ‘future vaccine formulations’ and also define that it pertains to Ghana, i.e. ‘Our study provides the most recent baseline data for pneumococcal serotypes and penicillin resistance in Ghanaian children.’
Answer: Has been changed as suggested.

Table 2
On the last line I would suggest ‘Other’ in the Serotype column. The last column says ‘Non-vaccine serotypes’.
Answer: Has been changed as suggested.

Table 3
Delete ‘pneumococci’ from the end of the title.
Answer: Has been changed as suggested.

Figure
The figure looks good. In the legend I would delete ‘remaining’ and add ‘to serotype 33F’ in the last sentence: ‘Except for serotype 6A the serotypes in the PPV-23 are listed consecutively from serotype 4 to serotype 33F.’
Answer: Has been changed as suggested.