Reviewer's report

Title: Otitis media in children vaccinated with either 7-valent or 10-valent pneumococcal conjugate vaccines: a cross sectional comparison

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Reviewer: Arto Palmu

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MS ID: 1158376878122939
Title: Otitis media in children vaccinated with either 7-valent or 10-valent pneumococcal conjugate vaccines: a cross sectional comparison

Reviewer comments

This manuscript describes sustained high morbidity due to otitis media during two different consecutive PCV vaccination programmes in a high-risk population of Australian indigenous children.

The topic is interesting and important and merits publication. However, there are several points that should be considered to increase the quality of the report.

Major Compulsory Revisions

1) In the current form I would not accept the main finding of differences between the vaccination programmes (see below). The current main finding would be the sustained high morbidity despite vaccination programmes.

2) Title: This is not cross-sectional comparison, but a comparison of two different consecutive PCV vaccination programmes with data collected in cross sectional design.

3) Mainly the text is clear and well-written, but the whole manuscript is not at the level of extreme carefulness needed for manuscript submission as there are several typos and poorly phrased sentences, see below for some examples.

4) Risk differences are mainly reported in statistical analysis. First, in cross-sectional design the concept of risk is not fully valid due to lack of follow-up time. Therefore, prevalence is suggested instead. Second, only risk (=prevalence) differences are reported. Prevalence ratios would also be interesting, even though differences would be regarded as the primary analyses.

5) There are a multitude of variables collected and reported in the study which might (partly) explain the differences in addition to or instead of the two different vaccination programmes:
   a. age distribution of participants
   b. vaccination schedules (3 PCV + PPV23 vs. 3+1 PCV) and number of doses actually received
   c. impact of the PPV23
d. season of data collection (not reported)
e. gestational age, birth weight
f. other health problems, respiratory symptoms
g. prior antibiotic use
h. number of children in household

Therefore, multivariate analysis would be recommended or a justification for univariate analyses only. A statistician’s review would be highly recommended.

6) If the primary aim is to compare the different vaccines as the exposure, then restriction of data analysis to children with equal number of vaccine doses without any additional vaccines would be clearer for the reader. Is this possible? Now the table 1a gives a very complicated mix of the exposure in the two groups.

7) The main findings of the study presented in table 2a are the different designations for the OM outcomes; i.e. more AOMwoP in the first group and more OME in the second. However, this is highly dependent on the subjective otoscopic assessment. Therefore, more emphasis on the description of this assessment is needed in the methods. The value of the assessment would be higher if there had been elements of objective assessment, blinding etc. Furthermore, AOMwoP is defined as bulging but no symptoms are required contrary to the most common definitions for AOM. Lastly, in case the definitions were defined a priori and not post hoc would be important to report.

Minor Essential Revisions

Abstract methods: data collection years to be mentioned in the methods. specify comparison.

Abstract results: “Similar results”? to what? please specify.

Introduction
row 82: are there any pre-introduction data for OM morbidity to give as baseline?

Methods:
“since 2001” ? specify data collection years. Specify data collection seasons.
“overarching” not clear.
“voroscope” not clear.
data collection for “antibiotics” oral/topical or both?

Handling with missing data: “unsure, the data were coded as missing”. However, page 6, row 145: “We categorised ‘not sure’ as absent.”

“The study was funded by…” Please state if equal contributions.

Results:
row 206 “We included 957 children”. However, row 185 states “Only the first visit per child is included in this analysis unless visits were separated by a period of at least 120 days.” Were there recurrent visits by some children?
row 214: RD does not make sense for age difference!
row 233: “Comparisons restricted to 3 dose recipients (443 in the PCV7 group and 370 in the PHiD CV10 group) were almost identical for OME, AOMwoP, AOMwiP and CSOM”. This is not clear. Identical to the differences shown above or identical between the outcomes? Please clarify.

Discussion
row 273: add “during PCV era” as the main finding.
row 309: reason to be suggested for the low compliance.
row 322:”It is not known whether compliance outside a clinical trial setting is achieved in this population.” this “compliance” is not self-explaining.
row 344: “Differences in other risk factors fail to explain these findings.” I would disagree with this in the absence of any multivariate analysis.
RCTs described in the abstract could be introduced in the end of discussion in more detail.

Table 1 a: PPV23 doses not mentioned?
Table 2a: the columns do not add up to the total number of participants due to the inclusion of the combination outcomes in the same table. Re-organize so that numbers add up.
Table 3: “Skin normal” and “Any skin problem” do not add up to “successful skin examination”
“denominator range” not clear.
Table 4: ”No. children consented”. Children of this age do not consent.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

My institution has received major research funding from the vaccine manufacturer of PHiD-CV10 (GlaxoSmithKline) that co-funded this study.