Reviewer’s report

Title: Effect of heptavalent pneumococcal conjugate vaccination on invasive pneumococcal disease in preterm born infants

Version: 1 Date: 9 October 2009

Reviewer: Eugene Millar

Reviewer’s report:

Major compulsory revisions are required.

The manuscript presents the very relevant issue of invasive pneumococcal disease (IPD) and its prevention among pre-term infants. Pre-term birth is a known risk factor for a number of infectious diseases, thus the evaluation and identification of effective prevention strategies in this sub-group is warranted.

[1] The limitations of this paper are quite clear. The author’s reference to ongoing surveillance activities ‘in all German pediatric hospitals’ is not substantiated with requisite information. How many hospitals and approximately how many providers are included? What is the approximate size of the population served?

[2] They mention that the pediatricians surveyed were contacted by postcards, but there is no mention of the total number of providers surveyed or the response rate among this population. This is critical to the interpretation of the case numbers and the incidence rates that stem from those numbers.

[3] The method of estimation of the pre-term born infant population (seven percent of all births) is very crude. I am not convinced this is an appropriate or reliable measure of the population at-risk of the primary endpoint of IPD. When comparing a ‘reduction’ in annual number of cases from 14 (2000) to 8 (2007), it is not difficult to imagine how an uncertain denominator would distort the results and interpretation even more.

[4] Given the bounds of uncertainty around the rate estimates (26.1 per 100 000 in 2000 versus 16.7 per 100 000 in 2007), one cannot argue that rates of IPD among pre-term born infants have decreased. Furthermore, if the suggested decline is to be attributed to 7-valent pneumococcal conjugate vaccine at all, some indication of serotype distribution among the 14 cases in 2000 would have been helpful. There is no suggestion of how serotype information was obtained nor whether a systematic method of serotype identification is already in place.

[5] Lastly, in a manuscript which struggles to argue for declining rates of IPD among this select risk group, the absence of trend data (or, at the very least, the absence of an explanation for the non-use of data) is the greatest deficiency. One would assume that surveillance activities, while imperfect by nature, are ongoing. The inclusion of data from 2001-2006 would have been very useful in interpreting these trends.
I am in full agreement with the authors that IPD is a serious and preventable disease among pre-term born infants and that the routine use of PCV7 will contribute significantly to prevention efforts. Evidence for the role of PCV7 in reducing disease among vaccinated as well as unvaccinated populations continues to mount. However, those conclusions are drawn from other population-based studies, not the one presented here.

Major revisions and/or supplements to the existing data are required before I would consider this for publication.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.