Reviewer's report

Title: High rate of pneumococcal bacteremia in a prospective cohort of older children and adults in an area of high HIV prevalence in rural western Kenya

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Reviewer: Zitta B Harboe

Reviewer's report:

This is a very interesting study that attempts to measure the burden of PB in terms of morbidity in older children and adults in an area in rural Africa. Interesting data on serotype distribution and case fatality after PB are also presented. The study is based on data collected in a unique surveillance setting, and pneumococcal serotyping and MIC determinations are performed following current standards. The analysis is well presented and discussed properly.

Some comments:

1. Under “Surveillance methods”, second line: “Three other Ministry of Health outpatient health facilities are in or near the surveillance area.” It is not clear from the text if patients attending these facilities are included in the study. Are there any "private" clinics in the area that may lead to referral bias of cases? (selection of patients who attended the referral centre?). There is no statement on the access of patients to HAART. A brief comment on this is important because HAART is known to have an effect in the incidence of IPD in HIV patients and this study reported a very high prevalence of HIV in the population.

2. In the limitations, other possible sources of bias and confounding should be discussed. Importantly, socioeconomic conditions, like crowding, alcoholism related conditions, smoking, and other life style variables affect the susceptibility and mortality related to the disease. Some general discussion on this topic in the context of Lwak would be of value. Were also the “first two patients” seen in the clinic selected by the nurses because they were more clinically compromised than the other patients waiting? This may also be a source of bias. I think that one of the main limitations of the study is that the investigators could not adjust the incidence estimates for the HIV-status of patients. In this setting, this may strongly affect the results presented and leading to an overestimation of the crude and adjusted rates in the assumed non-HIV population. This is mentioned in the limitations but should be discussed further.

Some Minor Essential Revisions:

1. In the Results, first paragraph: “Of these, 1,301 (8%) had blood cultures done”. In the abstracts it is stated that 1,342 blood cultures among persons > 5 years were taken”, this information is missing in the results.

2. Page 13, in the first sentence in the paragraph referring to MIC results, the word “isolates” is missing.
3. The median age of the 51 patients, IQR would be nice to see.

4. Persons > 5 years old or persons #5 years old? – lack of consistency

5. The name and manufacturer of the vaccines should be mentioned.

6. Statens Serum Instituts – remove the last s.

7. The titles of the tables should be more accurate, since data are presented for patients included in the study and not only for PB patients. Also the number of decimals should be the same for all the proportions (%) presented in the tables.

8. Table 1 and 2: in “Pneumococcus recovered (% cultures)”, consider instead "Pneumococcus recovered (% of positive cultures)"

9. Consider in Table 3, to do the ranking of serotypes according to their prevalence. Also, “PCV7 vaccine specific” it should say: "PCV7 serotypes", also for the other two vaccines.

10. Table 4: It would be of interest to see the 95% CI of the estimates of crude and adjusted incidence and also for the HIV rates.

- Discretionary Revisions

1. Abstract: in the results, clarify how many blood cultures have positive findings (for any bacterial species) among the 1,342 blood cultures taken from 1,301 patients. Maybe the authors can describe already here that the pneumococcus was the most common bacterial spp. obtained from blood cultures.

2. Community interviewers visited enrolled households every two weeks to inquire about illnesses. It is not clear from the text how many households were actually enrolled, and how these households were chosen. A brief comment on this would be important because it has to do with the validity of the data collected and possible sources of bias.

3. Regarding recurrent cases: "(One patient had bacteremia with serotype 6B pneumococcus in February and August 2007.)". Is this the only patient with a recurrent IPD? It is interesting because 1/51 cases corresponds to approx. 2% of recurrent cases, which is similar to the rate reported from populations with low prevalence of HIV, and much lower than what could be expected in a population with the HIV prevalence that is described in the methods section. This should be discussed in the discussion section.

4. In page 13, the authors should underline that the results regarding serotype distribution and coverage of the vaccines in HIV-infected individuals must be interpreted with caution, because of the relatively small number of patients with known HIV status in the study. Also, a reference to published data on HIV from the surveillance population obtained from the home-based HIV testing initiative would be appropriate.

5. In the abstract it is stated that “Nineteen (61%) of 31 patients with HIV results were HIV-positive", also in the tables. It seems that these 31 patients were tested
after inclusion? Maybe the authors can state more clearly which HIV data you are using for doing the extrapolation and which for doing the estimations on serotype coverage of conjugate vaccines.

6. You report a 7.7% 30-day case fatality which is actually quite low compared with other studies from industrialized countries reporting mortality from PB in adults - even in studies that do not include pneumococcal meningitis patients. The authors could discuss the reasons behind this finding.

7. Data on antibiotic resistance are presented in the results and abstract but are not discussed. It appears from the text that data on antibiotic consumption before culturing were also retrieved, however not presented. The low res to beta lactams and macrolides in contrast to high trim-sulfa should be discussed.

Level of interest: An article of importance in its field

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