Letters

Incidence of pneumonia is not reduced by pneumococcal conjugate vaccine

Madhi et al.[1] write that the pneumococcal conjugate vaccine (PCV) is an effective instrument for pneumonia prevention in children. This is not strictly true. WHO data[2] suggest that there are 450 million cases of pneumonia each year and that it causes 3.9 million deaths. In the sub-Saharan region of Africa, 1 022 000 die and 702 000 die in south Asia.[1] The pneumonia referred to is "clinical pneumonia" – a diagnostic syndrome within the Integrated Management of Childhood Illness – WHO and United Nations Children's Fund (UNICEF) system for triage and clinical management in developing countries.[3] The Cochrane database[4] states that PCV does not reduce the incidence of clinical pneumonia, although it has been shown to reduce vaccine-serotype bacteraemic pneumonia and radiological pneumonia. The benefit of reducing bacteraemic pneumonia and radiological pneumonia is so minimal that it has no effect on "clinical pneumonia". Poor nations will need to assess its cost utility carefully.

A study from the Gambia showed that mortality was 16% lower in a PCV immunized group compared to placebo recipients (25.2/1000 children years versus 30.1/1000 children years).[5] Data are also provided on adverse effects and deaths within 1 week of receiving any dose of the vaccine or placebo. The mortality benefit was seen in the first week after injection, well before vaccine efficacy could have been established. There were 12 deaths in the vaccine group and 15 among controls (23.8/1000 children years versus 29.8/1000 children years). This suggests that factors other than vaccine efficacy are responsible for the difference in mortality between the groups compared.

There is also another issue that we hope to raise here. The paper states that the vaccine programme would exceed the WHO threshold in 69 eligible countries. The authors assert that these findings are conservative in the sense that they did not assume any herd protection and did not assume protection beyond the age of 2.5 years. Beutels[6] has cautioned against this trend of noting the "positive" uncertainties (herd immunity, protection beyond 2.5 years) without reporting the "negative" ones (serotype replacement,[7] increased incidence of asthma),[8] which could dampen enthusiasm for the intervention. ■

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Pneumococcal conjugate vaccine is efficacious and effective in reducing the burden of pneumonia

While Chowdhary & Puliyel[1] are correct that there has been a non-significant reduction in clinically diagnosed pneumonia in the vaccine-efficacy trials conducted to date, their assertion that pneumococcal conjugate vaccine (PCV) does not reduce severe pneumonia or reduce mortality in the Gambia is fundamentally flawed. Updated estimates indicate that there are 155.8 million clinical episodes of pneumonia globally, which contribute to approximately 1.9 million deaths, 70% of which occur in Africa and south-east Asia.[2] The major drawback in evaluating the efficacy of PCV against "clinical pneumonia" is the lack of specificity of this clinical outcome measure that was designed for case management of pneumonia. The choice of clinical pneumonia as an endpoint is therefore biased in favour of high sensitivity, at the expense of specificity, in contrast to the more specific endpoints usually used in vaccines efficacy trials. Indeed, a large proportion of the cases that meet the case definitions for clinical pneumonia have a low positive predictive value and are, therefore, not pneumonia.[3] In the case management strategy, one accepts a level of over-treatment because of the important mortality reduction benefits. Nevertheless, that pneumococci contribute to significant pneumonia-related mortality is evident in the success of the WHO case-management strategy of pneumonia, which is premised upon early antibiotic therapy especially targeting *S. pneumoniae* and

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