

## Authors' reply

We thank Drs Suresh and Aneja for their interest in our observations about a misleading press release related to the Bangladesh Hib study. We cannot however, agree with their arguments and we will explain why.

Hib disease is rare in Asia as compared to the West and Africa. Studies from India and other Asian countries have all underlined this point<sup>1-6</sup>. An editorial in the *Bulletin of the WHO* had highlighted this, way back in 1999<sup>7</sup>. This is why data from Argentina and Ghana have little relevance for India. However, it is not as if the disease is non-existent here. Drs Suresh and Aneja write that they have seen 5 deaths from Hib meningitis. Unfortunately they do not provide a figure which can be used as a denominator to determine the disease burden in the community and as such it cannot help their argument. If the 'population attributable risk' is low and the numbers needed to vaccinate (NNT) is large, disease control with universal vaccination may not be a cost-effective proposition.

The correspondents make four rather unique assertions in their letter:

1. They point out that the Bangladesh study had shown benefit with two doses and this shows that even partially immunized children are protected. They say we ignored this.

Admittedly we did ignore it, but for good reason. Ninety three per cent of the population under study received the full 3 doses of vaccine. There was no benefit in the population receiving 3 doses, when either radiologically confirmed pneumonia or meningitis was compared with

matched community controls and these were the primary end point for analysis. Data dredging and post-hoc analysis found statistical significance in vaccine effectiveness against pneumonia after two doses of vaccine. Ordinarily these results of post-hoc analysis should be explicitly labeled to avoid misleading readers and unadjusted *P* values must be interpreted in light of the fact that these are a small and selected subset of a potentially large group of *P* values<sup>8</sup>. Post-hoc analysis greatly inflates the total number of statistical tests and necessitates the use of multiple testing procedures to compensate. In the absence of such analysis we ignored the finding. This avoids the bizarre suggestion that partially immunized children are better protected than those fully immunized.

2. The correspondents contend that we misrepresent the 'concept of statistics significance' by insisting that results that are not statistically significant are not valid. This is not true. Results are just as valid regardless of statistical significance. In statistics, a result is called statistically significant if it is unlikely to have occurred by chance. That is the standard interpretation for all scientific data. We will not labour that point. It is not very meaningful to discuss point estimates without providing data on the confidence limits.
3. The correspondents assert that in the Indonesian study, the increase in incidence of radiological pneumonia [89 per 100,000 child years (95% CI -71 to 248)] was *compensated* by a reduction in incidence of clinical pneumonia [1467 per 100000 child years (95% CI -60 to 2994)]. We cannot agree. We insist that neither the increase in radiological pneumonia nor the decrease in clinical pneumonia is statistically significant.
 

The Press Release did not bring up the issue of meningitis in the Indonesia study, and as such we did not refer to it. The correspondents suggest that Hib vaccine may be helpful to prevent meningitis. Again this is not borne out by the figures. The vaccine preventable incidence of microbiologically confirmed Hib per 10<sup>5</sup> child-years was 20 (95% CI -0.43 to 40) and of meningitis admissions it was 36 (95% CI -85 to 157)<sup>9</sup>. This suggests that there was no real benefit for the vaccinated compared to placebo recipients.
4. Finally the correspondents assert that Hib is used by some parents of well-to-do families for their children and so the Government of India must provide it free for the poor. Such assertions appear

to be in line with the view pushed by manufacturers of the vaccine and others with vested interests. We fail to understand this reasoning.

The discussion above shows Hib disease is rare in Asia and further that Hib vaccine - for all its cost - is no better than placebo. The poor need equity in a large number of areas but definitely, they are not hankering after the useless vaccines the rich may be taking. To foist this programme on them in the name of equity is a cruel means of siphoning off the limited funds available for the poor, and in its place providing them a service they do not need and which does them no good. When the evidence is so clear, it is the duty of all to protect them and the country from such misuse of resources.

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