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## Typhoid Fever and Vaccination in India: Clarifications

There is no fixed cut-off figure of disease burden that dictates a national vaccination policy for an infectious disease. This decision has to be based on calculations taking into account burden of disease (number, complications, morbidity/mortality), epidemiology with respect to host and organism, transmission pattern, efficacy and effectiveness of the intervention (vaccine), safety profile, absolute cost of vaccine and vaccination program, cost-effectiveness, expected short and long term outcome, and the likely impact of the absence of a policy on the same. Although the investigators of the paper(1) claimed that the burden of typhoid is large enough to warrant vaccination in India, their data do not support this assertion.

The importance of a specific definition of typhoid (based on blood culture) is that (i) this is what has been used to calculate disease burden in various studies; (ii) calculation of vaccine efficacy from various trials is based on this definition; (iii) the ratio of blood-culture negative to blood-culture positive ‘typhoid cases’ is not known; and (iv) if a more sensitive but less specific definition/test of typhoid is used, many non-typhoid cases would be included(2) in whom the vaccine(s) would be expected to be efficacious, but will not be. Thereby overall effectiveness would decrease, and not increase.

Neither the detection of culture proven typhoid cases nor the ‘large’ number of suspected typhoid cases in young children can be taken as evidence that “*the incidence is going up even in children around two years of age.*”

Cochrane reviews are meant to aid decision-making processes, and not dictate the decision to be taken. However, it should be noted that the review on typhoid vaccines(3) did not identify trials comparing different typhoid vaccines against each other; in fact most trials compared one of the typhoid vaccines with a placebo/control vaccine. Therefore interpreting this information to suggest that a particular typhoid vaccine is superior, indeed amounts to assumption by extrapolation.

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## Licensing of New Vaccines

Several issues raised by the authors are beyond the scope of discussion as my original article did not cover those topics. Following are some of my thoughts relevant to remarks by Drs Kalra and Vashishtha.

To me the first and foremost important authority is the local regulatory authority in any country as far as a ‘stamp’ of authenticity is concerned. However other bodies like ICMR/IAP etc recommending use of any vaccine will make it more acceptable for the