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There are more than 11 million cases of enteric fever every year, mainly affecting children and young adults in regions of the world where there is inadequate access to clean water and sanitation infrastructure is poor. The spread of highly resistant strains of Salmonella Typhi has caused recent public health concern. New typhoid conjugate vaccines (TCVs) developed over the past decade are immunogenic but there were only limited efficacy data from a prototype TCV 20 from years ago to support widespread introduction. We used a human challenge model of typhoid infection to demonstrate efficacy of the new vaccine and simultaneously showed efficacy in the model of a licensed plain polysaccharide vaccine, which had previously been found to be efficacious in field studies. Results from the challenge model showed that the new TCV was at least as potent as the licensed vaccine and that it induced memory B cell production (unlike the licensed product), supporting global policy recommendations in 2017. Data are now emerging from analysis of challenge model samples on potential correlates of protection, which will inform introduction in different regions and the ongoing development of vaccines by other manufacturers. These data also supported release of funding for field studies to evaluate implementation approaches, which have now confirmed efficacy in an interim analysis.

For paratyphoid vaccines, there are no licensed products and disease burden is currently very much lower than it is for typhoid. For this reason, field efficacy studies may not be feasible. Thus, establishing efficacy data for licensure of a novel paratyphoid vaccine, and identifying potential correlates of protection, might best be undertaken through the use of a human challenge model, supported by field data on immunogenicity. Possible routes to licensure will be discussed.

A bivalent vaccine, developed with the use of a human challenge model, providing protection against typhoid and paratyphoid could have a considerable impact on the burden of enteric fever among some of the world’s most vulnerable children and help in the fight against antimicrobial resistance.