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Title: Typhoid Vi-conjugate vaccine for outbreak control in Zimbabwe

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Joe Bilcke and colleagues investigated the cost-effectiveness of alternative delivery strategies for typhoid Vi-conjugate vaccine (TCV) in each of the 54 countries eligible for financial support from Gavi, the Vaccine Alliance. In settings with high *Salmonella enterica* serovar Typhi incidence, an approach of routine vaccination of infants plus a catch-up campaign to the age of 15 years seems cost-effective and would reduce the number of cases in Zimbabwe by 68% over the next 10 years. [1]

Recently Zimbabwe conducted a one-off mass TCV vaccination campaign funded by Gavi targeting children 6 months to 15 years of age in communities affected by an on-going typhoid outbreak.[2] This has been the first use of TCV and the first typhoid outbreak response vaccination campaign in Africa. The present and past outbreaks of cholera and typhoid are a terrible consequence of Zimbabwe's failure to invest in and manage both its basic water and sanitation infrastructure and its health care system.[3] In addition, dilapidated infrastructure, lack of diagnostics and drugs, brain drain, prohibitive user fees in health facilities and strikes by medical personnel have contributed to most recent outbreak of typhoid..

FIEBRE (Febrile Illness Evaluation in a Broad Range of Endemicities, https://www.lshtm.ac.uk/research/centres-projects-groups/fiebre), a multi-country study investigating the causes of fever in sub-Saharan Africa and southeast Asia has been enrolling adults and children presenting with fever at health facilities in Harare since June 2018. As part of the study, multiple diagnostic investigations are performed including; automated blood cultures, bacterial identification and drug susceptibility testing. *S.* Typhi has been isolated from 23/133 and 38/183 blood culture in children and adults respectively. Of the 61 *S*. Typhi isolates 54(88·5%) were multi-drug and 4 in 5 (80·3%) displayed diminished fluoroquinolone susceptibility. In the first three months after the vaccination campaign we observed a sharp decrease in one of the worst affected communitiesin the proportion of confirmed and suspected typhoid cases among children, but not adults. In this community, 23 (21·1%) of 109 blood cultures from children were positive for S Typhi before vaccination compared with zero

of 24 after vaccination. By contrast, 18 (15·4%) of 117 blood cultures from adults were positive for S Typhi before vaccination compared with 20 (30·3%) of 66 after vaccination.

While the TCV vaccination campaign seems highly effective in reducing the typhoid incidence among children, a more comprehensive approach such as vaccination of adults and WASH (Water, sanitation and hygiene) interventions will be needed to halt this and future typhoid outbreaks once established.

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Author contributions:

IDO, NF and KK contributed to the idea, concept and design of the manuscript. IDO and KK analyzed and interpreted the data. All authors contributed to drafting the manuscript, revised and approved the final draft for publication.

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