Outbreak response vaccination (ORV) against typhoid outbreaks.

Typhoid fever is caused by the bacterium *Salmonella* *enterica* *serovar* Typhi, transmitted through water and food contaminated with human feces (1). It remains a significant global public health concern, particularly in low- and middle-income countries (LMICs), where access to clean water and sanitation facilities is limited. Studies estimate that globally over 10,000,000 typhoid cases occur every year (2–5) with around 1% of those cases being potentially fatal.

In addition to improving water, sanitation, and hygiene, vaccines provide a nearer-term solution to typhoid fever, specifically with emergence of drug-resistant *S*. Typhi. Typhoid conjugate vaccines (TCVs) are suitable for children from six months and adults up to 45 years of age (6). They have been proven to be effective in randomized controlled trials (7–9) and during outbreaks by drug-resistant *S*. Typhi (10,11). As of February 2024, three TCVs—

Typbar-TCV (Bharat Biotech), TYPHIBEV (Biological E), and SKYTyphoid (SK Bioscience)—

have been prequalified by WHO and are therefore eligible for public procurement by UN organizations. Multiple LMICs including Pakistan, Nepal, Zimbabwe, Liberia, ana Samoa, with Gavi’s support, have introduced typhoid conjugate vaccines in their routine immunization programs along with catch-up campaigns (12).

While WHO recommends the use of TCVs during confirmed outbreaks of typhoid fever, data on their value in outbreak response is limited (6). Historically, typhoid outbreaks in LMICs, reported from 1989 to 2018, have been large and prolonged (13). This highlights ORVs can be particularly beneficial in these settings and necessitates the exploration of effective ORV strategies. Also, the presence of drug-resistant *S*. Typhi, wihch can lead to more severe and longer-lasting outbreaks, underscores the critical need for effective ORV strategies.

Effective ORV strategies will likely vary by setting and exploring various options can be facilitated by more detailed epidemiologic information. Few time series data are available for existing typhoid outbreaks. The striking difference between 45,215 cases from 25 countries reported during outbreak from 1989 to 2018 (13) and the estimated over 10,000,000 cases per year may imply that potentially many outbreaks are not detected.

Modeling can be useful in exploring the potential impact across various strategies, such as targeting high-risk populations and differing age groups. More contextualized strategies can be developed with added information. Modeling can also be used to examine longer-term and broader benefits on healthcare systems and communities and the impact on preventing future outbreaks, rather than focusing solely on the averted number of cases and deaths from the outbreak. The timing of vaccination will be critical in determining the impact of ORVs and therefore potential benefits of maintaining a stockpile may be explored.

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