

Summary of the WHO Position Paper on Typhoid vaccines: WHO position paper – March 2018

This position paper published in March 2018 replaces the WHO position paper on typhoid vaccines published in 2008.¹ It re-emphasises the importance of vaccination to control typhoid fever and presents the WHO recommendations on the use of a new generation of typhoid conjugate vaccine.

Background

Typhoid fever is an acute generalized infection, caused by an enteric bacterium, *Salmonella enterica* serovar Typhi, generally termed *Salmonella* Typhi (*S. Typhi*). Global estimates of typhoid fever burden range between 11 and 21 million cases and approximately 128 000 to 161 000 deaths annually.^{2,3} Children are disproportionately affected by typhoid fever, with peak incidence known to occur in individuals aged 5 to <15 years of age.

If the circulating *S. Typhi* strains are susceptible, acute typhoid fever and carriage of *S. Typhi* can be effectively treated with antibiotics. The emergence of antimicrobial resistant strains⁴ of *S. Typhi* and subsequent trends over the past few decades and recent outbreak of ceftriaxone-resistant typhoid in Pakistan⁵ demonstrate the importance of understanding local resistance patterns to enable the selection of appropriate antibiotics.

Currently three types of typhoid vaccines are licensed for use: i) typhoid conjugate vaccine (TCV); ii) unconjugated Vi polysaccharide (ViPS) vaccine; and iii) live attenuated Ty21a vaccine. The second and third types have been recommended by WHO since 2008 for endemic and epidemic settings.

WHO Position

WHO recommends programmatic use of typhoid vaccines for the control of typhoid fever. All typhoid vaccination programmes should be implemented in the context of other efforts to control the disease. TCV⁶ is preferred at all ages in view of its improved immunological properties, use in younger children and longer duration of protection. TCV should be prioritized in countries with high burden of disease or antimicrobial resistance. Countries may also consider the routine use of ViPS vaccine in those ≥ 2 years, and Ty21a vaccine for those > 6 years.

WHO recommends a 0.5 mL single dose of TCV in children from 6 months and in adults up to 45 years in endemic regions. WHO also encourages routine programmatic administration of TCV at the same time as other vaccines, at 9 months or in the second year of life.⁷ When ViPS is used, a single dose of the vaccine should be administered intramuscularly or subcutaneously from 2 years. For Ty21a, a 3-dose oral immunization schedule, administering the vaccine every second day, is recommended above 6 years. Catch-up vaccination with TCV up to 15 years of age is recommended when feasible and

¹ See No. 6, 2008, pp. 49–59.

² See No. 48, 2017, pp.729-747.

³ WHO. Background paper to SAGE on Typhoid Policy Recommendations. 2017. Available at http://www.who.int/immunization/sage/meetings/2017/october/1_Typhoid_SAGE_background_paper_Final_v3B.pdf?ua=1, accessed December 2017.

⁴ Resistance to the traditional first-line antibiotics ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole

⁵ Yousafzai MT et al. Outbreak investigation of ceftriaxone resistant *S. Typhi* in Hyderabad, Pakistan. 10th International Conference on Typhoid and other Invasive Salmonellosis. April 4-6,2017. Kampala, Uganda.

⁶ Only one of the two licensed products was assessed in the review.

⁷ WHO. Evidence to Recommendation Table: Typhoid Vaccines. Available at http://www.who.int/immunization/sage/meetings/2017/october/6_SAGE_Typhoid_E2R_Final.pdf?ua=1, accessed December 2017.

supported by epidemiologic data. Catch-up vaccination of multiple age cohorts is likely to accelerate impact.

WHO recommends vaccination in response to confirmed outbreaks of typhoid fever and in humanitarian emergencies depending on the risk assessment in the particular setting.

The potential need for revaccination with TCV is currently unclear. When ViPS or Ty21a vaccine is used, revaccination is recommended every 3 years for ViPS, and every 3 to 7 years in most endemic settings for Ty21a or every 1 to 7 years for travellers from non-endemic to endemic areas, depending on national policies.

Vaccination of special populations, contraindications and precautions

TCV and ViPS vaccines are contraindicated for individuals with known hypersensitivity to any component of the vaccine. Ty21a should not be administered to persons taking antibiotics. Certain antimalarials exhibit activity against Ty21a. Ty21a may be taken with chloroquine but should not be taken until 8 to 24 hours after administration of mefloquine.

Typhoid vaccination should be considered for professional food handlers in typhoid endemic areas, travellers from non-endemic going to endemic areas and clinical microbiology laboratory staff with a recognized risk of occupational exposure. Data are currently lacking on typhoid vaccine use in pregnant women, however there are no theoretical safety concerns for ViPS and TCV. Use of the live attenuated Ty21a vaccine during pregnancy should be avoided.

Immunocompromised persons, including those with HIV infection, should receive TCV or ViPS vaccine. Ty21a vaccine can be administered to HIV-infected, immunologically stable individuals with a CD4 percent >25% for children aged <5 years or CD4 count ≥ 200 cells/mm³ if aged ≥ 5 years.

Administration of typhoid vaccines

TCV is administered by intramuscular injection and ViPS is administered by intramuscular or subcutaneous route. Both vaccines should be injected into the anterolateral aspect of the thigh for infants or into the deltoid muscle for older children and adults.

Monitoring and research priorities

WHO recommends: i) post-licensure monitoring of effectiveness and safety of TCV especially in special population groups; ii) use of Brighton Collaboration case definitions; and iii) analysis of non-specific effects of vaccination. WHO also recommends that endemic countries strengthen the surveillance of typhoid fever in all age groups, and monitor antimicrobial resistant strains before and after introduction of vaccines.⁸

Research priority should focus on vaccination policy and programmes, particularly in the following areas: identifying at risk populations; risk of transmission and strategies to identify and treat carriers; correlate(s) of protection for typhoid vaccines; co-administration with other vaccines; safety and immunogenicity in special populations; duration of protection for a single dose of TCV and need for revaccination; whether the tetanus toxoid carrier protein of the Vi-TT conjugate vaccine provides protection equivalent to a booster dose of tetanus vaccine; and the impact of different TCV strategies including target age ranges for routine and catch-up vaccination as well as the impact of vaccination for outbreak control.

⁸ WHO. Surveillance standards for typhoid and other invasive *Salmonellosis*. In: WHO Vaccine Preventable Diseases Surveillance Standards. (In press)