World Health Organization

Weekly epidemiological record

No. 32, 2026, 101, 166 **http://www.who.int/wer** **14 August 2026**

Contents

Position paper on typhoid vaccines, 2026

Introduction

In accordance with its mandate to provide normative guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers[1] on vaccines and combinations of vaccines against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale vaccination programmes.

The position papers are intended for use by national public health officials and managers of immunization programmes. They may also be of interest to vaccine advisory groups, international funding agencies, health professionals, researchers, the scientific media, vaccine manufacturers and the general public.

Recommendations on the use of typhoid vaccines were issued by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization[2] at its meeting on 10 March 2026 and endorsed by WHO thereafter. Evidence presented at this meeting, as well as SAGE's conflict of interest assessment, can be accessed at textit<https://www.who.int/news-room/events/detail/2026/03/09/default-calendar/strategic-advisory-group-of-experts-on-immunization-march-2026>.

Following the meeting, the vaccine position paper is developed by the WHO SAGE Secretariat with input from WHO staff at both headquarters and regional levels. The vaccine position paper summarizes essential background information on diseases and vaccines and concludes with the current WHO position on the use of typhoid vaccines worldwide. The position paper is reviewed by a large group of external subject-matter experts and end-users before finalization. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) and the Evidence-to-recommendation tables are published alongside the position paper. The methods followed by SAGE[3] and the processes[4] for preparation of vaccine position papers are described on the WHO website.

In recent years, there have been important developments in the field of typhoid fever, including updated estimates of disease incidence and burden, new evidence on the effectiveness and population impact of typhoid conjugate vaccines (TCVs) following their introduction in several countries, and data on the duration of protection conferred by a single dose, including how duration of protection varies by age at vaccination and the epidemiological setting. There are also additional immunogenicity data following booster doses of TCV, and there is additional evidence on the emergence and spread of antimicrobial-resistant *Salmonella* Typhi. This document replaces the 2018 WHO position paper on typhoid vaccines[5] and, given the new available evidence, focuses primarily on TCVs.

Background

Epidemiology

Typhoid fever is an invasive bacterial infection caused by *Salmonella enterica* serovar Typhi (*Salmonella* Typhi). Humans are the only known reservoir of infection, and transmission occurs through ingestion of food or water contaminated with faeces from infected individuals, including symptomatic cases, asymptomatic persons, convalescent shedders and chronic carriers.[6,7]

[1] WHO Vaccine Position Papers (www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers (http://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers)).
[2] Strategic Advisory Group of Experts (SAGE) on Immunization (https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization).
[3] Guidance for the development of evidence-based vaccine-related recommendations. Geneva: World Health Organization; 2017 (www.who.int/publications/m/item/guidance-for-the-development-of-evidence-based-vaccine-related-recommendations).
[4] Supplement to WHO Vaccine Position Papers. Geneva: World Health Organization; 2020 (www.who.int/publications/m/item/who-position-paper-process).
[5] See No. 13, 2018, pp. 153–172. (https://www.who.int/publications/i/item/typhoid-vaccines-who-position-paper-march-2018).
[6] Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive Salmonella infections. Clin Microbiol Rev. 2015;28(4):901–37. https://doi.org/10.1128/CMR.00002-15.
[7] Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. N Engl J Med. 2002;347(22):1770–82. doi:10.1056/NEJMra020201.

Chronic carriers may represent an ongoing reservoir of infection and contribute to the persistence of typhoid fever transmission through ongoing shedding of *Salmonella* Typhi into the environment.[8] The Global Burden of Disease Study estimates that typhoid fever caused approximately 6.2 million cases (95% Uncertainty Interval [UI]: 4.8–8.0 million), 72 000 deaths (95% UI: 38 000–120 000), and 5.4 million disability-adjusted life years (DALYs) (95% UI: 2.8–8.8 million) globally in 2023.[9] The DALY burden is concentrated in South Asia and sub-Saharan Africa, although substantial heterogeneity exists both between and within countries.[10,11,12] The WHO Food Diseases Epidemiology Reference Group (FERG) estimated that typhoid fever accounted for approximately 7.2 (95% UI 5.6–9.3) million typhoid illnesses, 94 700 (95% UI 46 900–161 000) deaths and 7.5 (3.8–12.9) million DALYs globally in 2021, of which expert elicitation estimated that the percentage that was foodborne was 38.1% (95% UI 15.5–63.4).[13] A 2019 systematic review and meta-analysis of the incidence of blood culture-confirmed typhoid fever based on studies published through to January 2018 reported pooled incidence estimates of approximately 154 illnesses per 100 000 person-years in population-based studies and 142 cases per 100 000 person-years in hybrid studies in typhoid-endemic countries using sentinel surveillance data adjusted for under-ascertainment.[10] In population-based analyses, incidence was higher in typhoid-endemic settings in Asia (268 per 100 000 person-years) than in Africa (112 per 100 000 person-years). An update of the 2019 systematic review incorporating additional datasets published through to 2024 confirms substantial geographical heterogeneity, with pooled estimates from newer studies of approximately 206 illnesses per 100 000 person-years from population-based studies and 133 illnesses per 100 000 person-years from hybrid surveillance studies, with marked geographical heterogeneity and the highest incidence observed in southern Asia.[11] Estimates varied widely across settings and study designs, reflecting differences in disease ascertainment and adjustment approaches. The type and quality of case ascertainment may account for some of the heterogeneity between different regions.

Typhoid fever affects a broad age range of people but the highest incidence overall is usually observed in children and adolescents in high- and very-high-incidence settings. Meta-analyses of global pooled age-occurrence data indicate that 1.3% (95% Credible Interval [CrI]: 1.0–1.6) of typhoid fever illnesses occur before 6 months of age, 1.9% (1.5–2.4) before 9 months, 3.6% (3.0–4.3) before 15 months, 18.7% (15.7–21.9) before 5 years and 55.5% (50.8–59.5) before 15 years.[14] Approximately 36.8% of illnesses occur between 5 and 15 years of age.[14] Geographical variation in age distribution has been observed, with differences in the peak age of disease occurrence between settings and even between surveillance sites within the same country.[12,14]

Pathogen

Salmonella Typhi is a Gram-negative, facultative anaerobic bacterium of the family *Enterobacteriaceae* within the order *Enterobacterales,* and the causative agent of typhoid fever. It is taxonomically classified as *Salmonella enterica* subspecies *enterica* serovar Typhi.[15]

Salmonella Typhi is characterized by surface antigens that are used for serological classification, including the somatic O antigen, the flagellar H antigen, and the capsular Vi polysaccharide. The Vi antigen contributes to the virulence of *Salmonella* Typhi and has been linked to resistance to complement-mediated bacterial lysis and reduced activation of the alternative complement pathway.[16]

Other *Salmonella enterica* serovars – including *Salmonella* Paratyphi A, *Salmonella* Paratyphi B and, less commonly, *Salmonella* Paratyphi C – cause paratyphoid fever, which is a clinically similar disease. Typhoid and paratyphoid fever are collectively referred to as enteric fever. The Vi polysaccharide antigen is expressed by the *Salmonella enterica* serovars Typhi and Paratyphi C and has also been reported in some strains of *Salmonella enterica* serovar Dublin and *Citrobacter freundii,* although it is rare; the Vi locus is absent in serovars Paratyphi A and B.

[8] Gunn JS, Marshall JM, Baker S, Dongol S, Charles RC, Ryan ET. Salmonella chronic carriage: epidemiology, diagnosis, and gallbladder persistence. Trends Microbiol. 2014;22:648–55. doi:10.1016/j.tim.2014.06.007.

[9] GBD 2023 Causes of Death Collaborators. Global burden of 292 causes of death in 204 countries and territories and 660 subnational locations, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023. Lancet. 2025;406:1811–72. doi:10.1016/S0140-6736(25)01917-8.

[10] Marchello CS, Hong CY, Crump JA. Global typhoid fever incidence: a systematic review and meta-analysis. Clin Infect Dis. 2019;68(Suppl 2):S105–16. https://doi.org/10.1093/cid/ciy1094.

[11] Murthy S, Hagedoorn NN, Faigan S, Rathan MD, Sharples KJ, Marchello CS et al. Global typhoid fever incidence: an updated systematic review with meta-analysis. Lancet Infect Dis. 2025;25(12):1347–62. https://doi.org/10.1016/S1473-3099(25)00359-7.

[12] Garrett DO, Longley AT, Aiemjoy K, Yousafzai MT, Hemlock C, Yu AT et al. Incidence of typhoid and paratyphoid fever in Bangladesh, Nepal, and Pakistan: results of the Surveillance for Enteric Fever in Asia Project. Lancet Glob Health. 2022;10(7):e978–88. https://doi.org/10.1016/S2214-109X(22)00119-X.

[13] Majowicz SE, Scallan WE, Pires SM, Minatoi Y, Founou L, Devleesschauwer B et al. WHO estimates of the global, regional, and national burden of eight foodborne non-diarrhoeal enteric disease hazards, 2000–21: an updated data synthesis. Lancet Glob Health. 2026; published online 16 June. https://doi.org/10.1016/j.langlo.2026.103981.

[14] Batool R, Gamble C, Murthy S, Aung T, Akinlabi OS, Baker S et al. Age distribution of typhoid fever, paratyphoid fever, and non-typhoidal Salmonella invasive disease: a secondary analysis of global epidemiologic data [version 1]. VeriXiv. 2026;3:213. doi:10.12688/verixiv.3426.1.

[15] List of Prokaryotic names with Standing in Nomenclature (LPSN). *Salmonella enterica* subsp. *enterica* serovar Typhi. https://lpsn.dsmz.de.

[16] Wilson RP, Winter SE, Spees AM, Winter MG, Nishimori JH, Sanchez JF et al. The Vi capsular polysaccharide prevents complement receptor 3-mediated clearance of Salmonella enterica serotype Typhi. Infect Immun. 2011;79(2):830–7. doi:10.1128/iai.00961-10.

Other preventive interventions

Access to safe water and food, adequate sanitation, health education, appropriate hygiene among food-handlers, and typhoid vaccination are all effective strategies for the prevention and control of typhoid fever. Improvements to water supplies, including disinfection by chlorination, have contributed to large reductions in typhoid fever incidence and to sustained control in settings with well-developed water and sanitation (WASH) infrastructure.[17]

Disease

Following ingestion, *Salmonella* Typhi invades the intestinal epithelium and disseminates via the bloodstream to the reticuloendothelial system where it replicates intracellularly within macrophages.[6,7]

After an incubation period, typically of 7–14 days (range 3–60 days), patients develop a systemic febrile illness of variable severity.[7] Common clinical features include persistent fever, abdominal discomfort, malaise and headache, with gastrointestinal symptoms such as diarrhoea or constipation varying across age groups.[6,7]

Severe complications may occur – including intestinal haemorrhage, intestinal perforation and encephalopathy – particularly in untreated or prolonged disease.[6,7] An updated global systematic review and meta-analysis of typhoid fever complications and mortality, including reports published from 1980 through to 2025, found an overall pooled case fatality ratio of 2.1% (95% CI: 1.7–2.7) among non-surgical typhoid fever reports.[18]

The pooled case fatality ratio was 2.7% (95% CI: 1.8–4.0) among children aged ≤15 years and 1.8% (95% CI: 1.3–2.4) in mixed-age (children and adults) populations. Insufficient adult-only estimates precluded direct comparison of children with adults.[18] A separate systematic review of typhoid intestinal perforation reported that intestinal perforation occurs in approximately 1–2% of typhoid fever illnesses, although estimates vary substantially by setting, and is associated with high mortality.[19] Case fatality varies by setting and is influenced by timely diagnosis, access to effective antimicrobial therapy, and access to appropriate clinical and surgical care.

Approximately 2–5% of infected individuals become chronic carriers of *Salmonella* Typhi, and this is more common among older adults and those with underlying gallbladder disease.[20] Chronic carriers may shed bacteria intermittently for prolonged periods and contribute to ongoing transmission.

Diagnosis

The clinical presentation of typhoid fever is non-specific and overlaps with other causes of febrile illness in endemic settings, making clinical diagnosis unreliable.[6,7]

Laboratory confirmation typically relies on isolation of *Salmonella* Typhi by blood culture. However, the sensitivity of a single blood culture is limited at approximately 55–60% and is influenced by the volume of blood obtained and prior antimicrobial exposure.[21] In addition, blood culture is not available in many endemic settings. Bone marrow culture is more sensitive than blood culture but is rarely performed in routine clinical practice.[7]

In many endemic settings, diagnosis relies on serological assays, most commonly the Widal agglutination test, which detects antibodies to *Salmonella* O and H antigens. However, these assays have poor and highly variable diagnostic accuracy due to cross-reactivity with other pathogens, persistence of antibodies following prior infection or exposure and lack of standardized thresholds. Newer rapid diagnostic tests, including Typhidot® (Reszon Diagnostics International Sdn. Bhd., Shah Alam, Malaysia) and TUBEX® (IDL Diagnostics AB, Bromma, Sweden), have been developed and also show variable diagnostic accuracy. A Cochrane review reported average sensitivity of approximately 78–84% and specificity of 77–87% across commonly used assays, with substantial heterogeneity between studies.[22] These tests are not sufficiently accurate to replace appropriately collected blood culture as a practical reference standard.

[17] Phillips MT, Owers KA, Grenfell BT, Pitzer VE. Changes in historical typhoid transmission across 16 U.S. cities, 1889–1931: quantifying the impact of investments in water and sewer infrastructures. PLoS Negl. Trop. Dis. 2020;14:e0008048 (2020). https://doi.org/10.1371/journal.pntd.0008048.

[18] Murthy S, Hagedoorn NN, Faigan S, Rathan MD, Marchello CS, Crump JA. Complications and mortality of typhoid fever: an updated global systematic review and meta-analysis. Lancet Infect Dis. 2026;26:270–83. https://doi.org/10.1016/S1473-3099(25)00551-1.

[19] Hagedoorn NN, Birkhold M, Murthy S, Rathan MD, Faigan S, Marchello CS et al. Post-operative complications and mortality of typhoid intestinal perforation: a systematic review and meta-analysis. 14th International Conference on Typhoid and Other Invasive Salmonelloses, Phnom Penh, Cambodia, 24–26 March 2026.

[20] Gonzalez-Escobedo G, Marshall JM, Gunn JS. Chronic and acute infection of the gall bladder by *Salmonella* Typhi: understanding the carrier state. Nat Rev Microbiol. 2011;9:9–14. doi:10.1038/nrmicro2490.

[21] Antillon M, Saad NJ, Baker S, Pollard AJ, Pitzer VE. The relationship between blood sample volume and diagnostic sensitivity of blood culture for typhoid and paratyphoid fever: a systematic review and meta-analysis. J Infect Dis. 2018;218(suppl_4):S255–67. https://doi.org/10.1093/infdis/jiy471.

[22] Wijedoru L, Mallett S, Parry CM. Rapid diagnostic tests for typhoid and paratyphoid (enteric) fever. Cochrane Database Syst Rev 2017; 5. https://doi.org/10.1002/14651858.CD008892.pub2.

Treatment and trends in antimicrobial resistance

Antimicrobial resistance (AMR) in *Salmonella* Typhi shows substantial geographical and temporal heterogeneity. Recent systematic reviews of phenotypic data and genomic analyses indicate that multidrug-resistant (MDR) *Salmonella* Typhi – defined as resistance to ampicillin, chloramphenicol and trimethoprim–sulfamethoxazole – is highly prevalent in parts of sub-Saharan Africa where resistance determinants are often chromosomally integrated.[23,24] In contrast, MDR is still present, but prevalence has declined in many parts of South Asia, coinciding with reduced use of first-line antimicrobials and the emergence of resistance to newer agents.

Reduced susceptibility to fluoroquinolones is widespread globally, although high-level resistance is largely concentrated in South Asia.[24] Extensively drug-resistant (XDR) *Salmonella* Typhi, defined as MDR plus resistance to fluoroquinolones and third-generation cephalosporins, was first reported in Pakistan and remains largely restricted to this setting.

Recent reports of the independent emergence of resistance to azithromycin, third-generation cephalosporins, and carbapenems in South Asia are of particular concern, as resistance to all major antimicrobial classes used to treat typhoid fever has now been reported in that region.[24,25,26,27,28]

Timely and effective antimicrobial therapy is essential to avert poor typhoid fever outcomes, including complications and deaths. Treatment recommendations vary by setting because AMR patterns differ geographically and change over time. Empiric treatment should therefore be guided by local patterns of AMR. WHO's "Access, Watch, Reserve" (AWaRe) guidance is that, in settings with a low risk of fluoroquinolone resistance, ciprofloxacin is listed as a treatment option for mild and severe disease. Where fluoroquinolone resistance is common, azithromycin is listed for mild disease and ceftriaxone for severe disease or when oral treatment is not possible. Empiric fluoroquinolone use should therefore be avoided in settings where fluoroquinolone non-susceptibility is common, and treatment should be guided by local antimicrobial susceptibility data and revised once culture and susceptibility results are available.[29]

Infection-acquired immunity

Evidence from controlled human infection studies suggests that prior infection reduces, but does not eliminate, the risk of subsequent typhoid fever.[30] Individuals rechallenged with the same *Salmonella enterica* serovar after previous infection remained susceptible, indicating that infection-acquired immunity is incomplete. Protection was not observed against symptomatic infection with a different serovar, suggesting that immunity is serovar-specific. Among those who developed disease following re-exposure, clinical manifestations were comparable between previously exposed and naïve individuals, indicating no clear attenuation of disease severity.

Although both humoral and cellular immune responses are induced by infection, measured antibody responses, including those directed against Vi, lipopolysaccharide and flagellar antigens, have not been shown consistently to distinguish protected from susceptible individuals, and do not appear to correlate with protection.

Vaccines

Three types of typhoid vaccines are currently licensed for use globally: the live attenuated Ty21a vaccine, unconjugated Vi polysaccharide (ViPS) vaccines, and TCVs. TCVs were first recommended by WHO in 2018 and most new evidence since the 2018 position paper relates to their use. This position paper therefore focuses primarily on TCVs, while summarizing key characteristics of ViPS and Ty21a vaccines.

[23] Murthy S, Hagedoorn NN, Faigan S, Rathan MD, Marchello CS, Crump JA. An updated global systematic review on *Salmonella* Typhi antimicrobial resistance. Abstract 7917. 74th American Society of Tropical Medicine and Hygiene annual meeting, Toronto, Canada. 9–13 November 2025.

[24] Carey ME, Dyson ZA, Ingle DJ, Amir A, Aworth MK, Chattaway MA et al. Global diversity and antimicrobial resistance of typhoid fever pathogens: insights from a meta-analysis of 13,000 *Salmonella* Typhi genomes. eLife. 2023;12:e85867. https://doi.org/10.7554/eLife.85867.

[25] Hooda Y, Tanmoy AM, Nath SD, Jul AB, Amin A, Rahman H et al., Outbreak of Ceftriaxone-resistant Salmonella enterica > Serovar Typhi, Bangladesh, 2024. Emerg Infect Dis J. 2025;31(7):1460–65. https://doi.org/10.3201/eid3107.241987.

[26] Nizamuddin S, Khan EA, Chattaway MA, Godbole G. Case of Carbapenem-resistant Salmonella Typhi Infection, Pakistan, 2022. Emerg Infect Dis. 2023:29(11). https://doi.org/10.3201/eid2911.230499.

[27] Thirumoorthy TP, Jacob JJ, Velmurugan A, Teekaraman MP, Shah B, Iyer V et al. Recent emergence of cephalosporin-resistant *Salmonella* Typhi in India due to the endemic clone acquiring IncFIB(K) plasmid encoding blaCTX-M-15 gene. Microbiol Spectr. 2025:13(5):e00875–24. https://doi.org/10.1128/spectrum.00875-24.

[28] Tharani Priya T, Jacob JJ, Monisha Priya T et al. Genomic insights into the emergence of Carbapenem-Resistant *Salmonella* Typhi harboring *blaNDM-5* in India. medRxiv. 2025. https://doi.org/10.1101/2025.05.20.25327816.

[29] The WHO AWaRe (Access, Watch, Reserve) antibiotic book. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240062382). Licence: CC BY-NC-SA 3.0 IGO.

[30] Gibani MM, Jin C, Sreshtha S, Moore M, Norman L, Voysey M et al. Homologous and heterologous re-challenge with *Salmonella* Typhi and *Salmonella* Paratyphi A in a randomised controlled human infection model. PLoS Negl Trop Dis. 2020;14:e0008783. https://doi.org/10.1371/journal.pntd.0008783.

Ty21a

The Ty21a vaccine is a live attenuated oral vaccine derived from the wild-type Ty2 strain of *Salmonella* Typhi and first licensed in the 1980s. It is administered as enteric-coated capsules in a 3-dose regimen given on alternate days (or 4 doses in some national schedules) and is licensed for use in individuals aged ≥6 years. The vaccine requires storage at 2–8 °C; the previously available liquid formulation is no longer in use.[31]

Ty21a vaccine induces humoral and cell-mediated immune responses to *Salmonella* Typhi antigens but does not induce anti-Vi antibodies.[32,33] Protective immunity following the 3-dose Ty21a regimen is achieved approximately seven days after administration of the final dose.

Evidence from randomized controlled trials indicates moderate efficacy. A systematic review and meta-analysis reported pooled efficacy of approximately 45% (95% CI: 33–55%) over 1–3 years following vaccination.[34] Individual field trials reported efficacy ranging from approximately 33% to 67% at 3 years following vaccination, with variability across epidemiological settings.[35] In a trial conducted in Indonesia under conditions of very high typhoid incidence, lower estimates of efficacy than those generated during previous efficacy trials were observed, with differences between vaccine formulations.[36] Studies in Chile demonstrated sustained protection of around 62–67% for up to 7 years,[37] and population-level effects consistent with herd protection were observed.[38] Field trials indicate that Ty21a provides significant protection against *Salmonella* Paratyphi B disease but not against *Salmonella* Paratyphi A disease.[39]

Revaccination is recommended to maintain protection, with intervals of approximately 3–7 years depending on national guidelines and risk group.

The Ty21a vaccine has a favourable safety profile with predominantly mild and transient adverse events – most commonly gastrointestinal symptoms. In double-blind, placebo-controlled efficacy trials conducted in Chile and Indonesia involving approximately 325 000 school-aged children, rates of diarrhoea, vomiting, fever and rash were not significantly different between vaccinated and control groups. As a live attenuated vaccine, Ty21a is also contraindicated in immunocompromised individuals and should not be administered during pregnancy.

Vi polysaccharide (ViPS)

Vi polysaccharide (ViPS) vaccines consist of purified capsular Vi antigen derived from *Salmonella* Typhi and have been in use since the early 1990s. ViPS vaccines are licensed for use in individuals aged ≥2 years and are administered as a single 0.5 mL dose by intramuscular or subcutaneous injection. Multiple products are available globally in single-dose and multi-dose presentations and are stored at 2–8 °C.[31]

[31] Levine MM, Simon R. Typhoid and paratyphoid (enteric) fever vaccines. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's vaccines. 7th edition. Philadelphia: Elsevier; 2018.

[32] Salerno-Goncalves R, Paseti MF, Sztein MB. Characterization of CD8(+) effector T cell responses in volunteers immunized with Salmonella enterica serovar Typhi strain Ty21a typhoid vaccine. J Immunol. 2002(4);169:2196–203. https://doi.org/10.4049/jimmunol.169.4.2196.

[33] Wahid R, Fresnay S, Levine MM, Sztein MB. Immunization with Ty21a live oral typhoid vaccine elicits crossreactive multifunctional CD8+ T-cell responses against Salmonella enterica serovar Typhi, S. Paratyphi A, and S. Paratyphi B in humans. Mucosal Immunol. 2015;8(6):1349–59. https://doi.org/10.1038/mi.2015.24.

[34] Batool R, Qamar ZH, Salam RA, Yousafzai MT, Ashorn P, Qamar FN. Efficacy of typhoid vaccines against culture-confirmed *Salmonella* Typhi in typhoid endemic countries: a systematic review and meta-analysis. Lancet Glob Health. 2024;12(4):e589–98. https://doi.org/10.1016/S2214-109X(23)00606-X.

[35] Levine MM, Black RE, Ferreccio C, Germanier R, Chilean Typhoid Committee. Large-scale field trial of Ty21a live oral typhoid vaccine in enteric coated capsule formulation. Lancet. 1987;329(1):1049–52. https://doi.org/10.1016/S0140-6736(87)90480-6.

[36] Simanjuntak CH, Totosudirjo H, Haryanto P, Paleologo FP, Punjabi NH, Darmowigoto R et al. Oral immunisation against typhoid fever in Indonesia with Ty21a vaccine. Lancet. 1991;338:1055–1059. https://doi.org/10.1016/0140-6736(91)91910-m.

[37] Levine MM, Ferreccio C, Abrego P, San Martin O, Ortiz E, Cryz S. Duration of efficacy of Ty21a, attenuated salmonella typhi live oral vaccine. Vaccine. 1999;17:S22–7. https://doi.org/10.1016/S0264-410X(99)00231-5.

[38] Levine MM, Ferreccio C, Black RE, Tacket CO, Germanier R. Progress in vaccines against typhoid fever. Rev Infect Dis. 1989;11:S552–67. https://doi.org/10.1093/clinids/11.supplement_3.s552.

[39] Wahid R, Simon R, Zafar SJ, Levine MM, Sztein MB. Live oral typhoid vaccine Ty21a induces cross-reactive humoral immune responses against *Salmonella* enterica serovar Paratyphi A and S. Paratyphi B in humans. Clin Vaccine Immunol. 2012;19(6):825–34. https://doi.org/10.1128/CVI.00058-12.

A single dose of ViPS vaccine elicits serum IgG antibodies to the Vi antigen, which wane over time, with substantial decline after approximately 2 years.[40,41,42,43] Hyporesponsiveness following revaccination has been suggested in some studies, although robust data supporting this observation are limited.[44,45,46,47]

A systematic review and meta-analysis reported pooled efficacy of approximately 58% (95% CI: 44–69%) over 1–3 years of follow-up.[34] Vaccine efficacy in pre-licensure trials conducted in endemic settings ranged from approximately 60% to 70% over follow-up periods of up to 2 years.[40,41,48]

Post-licensure effectiveness of ViPS vaccines has been evaluated in cluster randomized trials in India and Pakistan. In Kolkata, India, a cluster-randomized trial offered a ViPS vaccine to all eligible residents aged ≥2 years and found total vaccine effectiveness of 61% (95% CI: 41–75) over 2 years. The trial also demonstrated indirect protection among unvaccinated residents of Vi-vaccine clusters and overall protection at the cluster level, consistent with reduced transmission in vaccinated communities. In age-stratified analyses, protection was observed among children aged 2–4 years and 5–14 years, although the trial was not powered to detect differences in protective effectiveness between age subgroups.[49]

In Karachi, Pakistan, a cluster randomized trial offered ViPS vaccine or hepatitis A vaccine to eligible children aged 2–16 years. Across the vaccine recipients, the adjusted protective effectiveness of ViPS vaccine was 31% (95% CI: −28 to 63) and was not statistically significant. In the prespecified subgroup aged 5–16 years, however, protective effectiveness was 57% (95% CI: 6–81), whereas no protection was observed among children aged 2 to <5 years. The authors suggested that the difference from the Kolkata findings might reflect lower immunogenicity among younger children and less potential for indirect protection, because vaccination in Karachi targeted children aged 2–16 years while the Kolkata campaign targeted all residents aged over 2 years.[50]

Protection provided by ViPS vaccine declines over time, with evidence of waning effectiveness after approximately 2–3 years.[34]

ViPS vaccines have an established safety profile supported by large-scale studies conducted in multiple settings, including data from more than 300 000 recipients, including both children and adults. No serious safety concerns have been identified. Reported adverse events are generally mild and transient. In WHO's updated vaccine safety information sheet on observed rates of reactions to typhoid vaccines, based on a systematic review of studies published from 1980 to 2025, the rate of any serious adverse event following ViPS vaccination was 0.8 per 100 doses. Among the adverse events, the most common local reactions were tenderness (70.7 per 100 doses) and injection-site pain (20.2 per 100 doses), while malaise was the most common systemic reaction (8.9 per 100 doses).[51] The ViPS vaccine has been shown to be well tolerated when co-administered with routine childhood vaccines. Revaccination at intervals of approximately two years has also been shown to be safe, with no increase in reactogenicity compared with primary vaccination. Serious adverse events are rare, and no consistent safety signals have been identified. The WHO Global Advisory Committee on Vaccine Safety (GACVS) has concluded that both ViPS and Ty21a vaccines have favourable safety profiles, with most adverse events being mild and transient and serious adverse events rare.[51]

[40] Acharya IL, Lowe CU, Thapa R, Gurubacharya VL, Shrestha MB, Cadoz M et al. Prevention of typhoid fever in Nepal with the Vi capsular polysaccharide of *Salmonella* Typhi. A preliminary report. N Engl J Med. 1987;317:1101-1104. doi:10.1056/NEJM198710293171801.

[41] Klugman K, Koornhof HJ, Schneerson R, Cadoz M, Gilbertson IT, Robbins JB et al. Protective activity of Vi polysaccharide vaccine against typhoid fever. Lancet. 1987;2:1165–9. https://doi.org/10.1016/S0140-6736(87)91316-X.

[42] Plotkin SA, Bouveret-Le Cam N. A new typhoid vaccine composed of the Vi capsular polysaccharide. Arch Intern Med. 1995;155:2293–9. doi:10.1001/archinte.1995.00430210041007.

[43] Froeschle JE, Decker MD. Duration of Vi antibodies in participants vaccinated with Typhim Vi (Typhoid Vi polysaccharide vaccine) in an area not endemic for typhoid fever. Vaccine. 2009;28:1451–3. https://doi.org/10.1016/j.vaccine.2009.11.051.

[44] Overbosch D, Peyron F, Picot N, Varichon J-P, Dumas R, Chambonneau L et al. Combined typhoid fever and hepatitis A vaccine: comparison of immunogenicity and safety to concomitant monovalent vaccine over 3 years. J Travel Med. 2005;12:319–26. https://doi.org/10.2310/7060.2005.12604.

[45] Keitel WA, Bond NL, Zahradnik JM, Cramton TA, Robbins JB. Clinical and serological responses following primary and booster immunization with *Salmonella typhi* Vi capsular polysaccharide vaccines. Vaccine. 1994;12:195–9. https://doi.org/10.1016/0264-410X(94)90194-5.

[46] Roggelin L et al. Serological response following re-vaccination with *Salmonella typhi* Vi-capsular polysaccharide vaccines in healthy adult travellers. Vaccine. 2015;33:4141–5. https://doi.org/10.1016/j.vaccine.2015.05.080.

[47] Zhou WZ, Koo HW, Wang XY, Zhang J, Park JK, Zhu F et al. Revaccination with locally-produced Vi typhoid polysaccharide vaccine among Chinese school-aged children: safety and immunogenicity findings. Pediatr Infect Dis J. 2007;26:1001–5. doi:10.1097/INF.0b013e31812565bc.

[48] Yang HH, Wu CG, Xie GZ, Gu QW, Wang BR et al. Efficacy trial of Vi polysaccharide vaccine against typhoid fever in south-western China. Bull World Health Organ. 2001;79(7):625–31. https://iris.who.int/handle/10665/268379.

[49] Sur D, Ochiai RL, Bhattacharya SK, Ganguly NK, Ali M, Manna B et al. A cluster-randomized effectiveness trial of Vi typhoid vaccine in India. N Engl J Med. 2009;361:335–44. doi:10.1056/NEJMoa0807521.

[50] Khan MI, Soofi SB, Ochiai RL, Habib MA, Sahito SN, Nizami SQ et al. Effectiveness of Vi capsular polysaccharide typhoid vaccine among children: a cluster randomized trial in Karachi, Pakistan. Vaccine. 2012;30:53895395. https://doi.org/10.1016/j.vaccine.2012.06.015.

[51] Information sheet: observed rate of vaccine reactions – typhoid vaccine. Geneva: World Health Organization; 2026 (https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance/guidance/reaction-rates-information-sheets).

Typhoid conjugate vaccines (TCVs)

Administration, manufacturers' stipulated schedules, and storage TCVs consist of the Vi capsular polysaccharide antigen of *Salmonella* Typhi conjugated to a carrier protein to enhance immunogenicity, particularly in young children. To date, four TCVs have been prequalified by WHO and three additional TCVs have received national licensure.

All currently WHO-prequalified TCVs are administered as a single 0.5 mL intramuscular dose and contain 25 µg of purified Vi capsular polysaccharide conjugated to a carrier protein (indicated below).[52] These TCVs are supplied in single-dose and multi-dose presentations, all with vaccine vial monitors (VVM30) and require storage at 2–8°C. Multi-dose presentations of currently WHO-prequalified TCVs contain 2-phenoxyethanol as a preservative. Typbar-TCV®has demonstrated stability in accordance with WHO's controlled temperature chain guidelines for three days for storage up to 55°C and for seven days for storage up to 40°C. The remaining WHO prequalified TCV products are not licensed for use under controlled temperature chain conditions.

Currently WHO-prequalified TCVs differ in carrier protein, age indications and presentation. TypbarTCV®and ZyVac®TCV use tetanus toxoid as the carrier protein and are licensed for use from 6 months up to 65 years of age. TYPHIBEV® uses CRM197 as the carrier protein and is licensed for use from 6 months of age up to 45 years. SKYTYPHOID® Multi Inj. uses diphtheria toxoid as the carrier protein and is licensed for use from 6 months up to 45 years of age. Typbar-TCV® is available as both single-dose (including prefilled syringe) and multi-dose presentations. TYPHIBEV® is available in both single-dose and multi-dose vial presentations. SKYTYPHOID® Multi Inj. and ZyVac®TCV are currently available in multi-dose vial presentations only.

Immunogenicity, efficacy, effectiveness and impact The conjugation of the Vi polysaccharide antigen to a carrier protein enables T-cell-dependent immune responses. TCVs elicit robust anti-Vi IgG responses, including in infants and young children, with higher and more sustained antibody concentrations than those observed following Vi polysaccharide vaccines.[5,53] Although anti-Vi IgG responses are used as a measure of immunogenicity, no validated correlate of protection has been established. Several TCVs have been licensed on the basis of the demonstration of a non-inferior anti-Vi antibody response to a previously licensed TCV or Vi polysaccharide vaccine in randomized clinical trials. WHO has developed recommendations to guide the evaluation and licensure of TCVs, including the use of immunogenicity endpoints in the absence of a validated correlate of protection.[54]

The first TCV field efficacy data were generated in a trial of Vi-rEPA, a conjugate vaccine consisting of Vi capsular polysaccharide conjugated to recombinant exoprotein A from *Pseudomonas aeruginosa* in Viet Nam. Among children vaccinated at 2–5 years of age, vaccine efficacy of 89% (95% CI: 76–97) was demonstrated through 46 months of follow-up.[55] This vaccine was never commercialized. The first efficacy data for a commercially available TCV came from a controlled human infection model in immunologically naïve volunteers, in which Vi-TT showed 80% efficacy in a modified analysis restricted to symptomatic infection with fever and positive blood culture.[56]

The Typhoid Vaccine Acceleration Consortium (TyVAC) conducted three randomized controlled trials to assess Vi-TT efficacy in epidemiologically diverse endemic settings.[57] In Malawi, an individually randomized Phase 3 trial among children aged 9 months to 12 years demonstrated vaccine efficacy of 83.7% (95% CI: 68.1–91.6) after two years.[58] In Nepal, an individually randomized trial among children aged 9 months to 15 years reported efficacy of 79.0% (95% CI: 61.9–88.5) at 24 months.[59] In Bangladesh, a cluster-randomized trial among children aged 9 months to 16 years reported 85% (97·5% CI: 76–91) total protection over 18 months of follow-up.[60] The Bangladesh trial also estimated overall protection of 57% (95% CI: 45–67) among all residents of vaccine clusters and indirect protection of 19% (95% CI: −12 to 41) among unvaccinated cluster residents. Indirect protection was a secondary endpoint in this trial; this efficacy estimate did not achieve statistical significance.

[52] List of prequalified vaccines. Geneva: World Health Organization (https://extranet.who.int/prequal/vaccines/prequalified-vaccines).

[53] Mohan VK, Varanasi V, Singh A, Pasetti MF, Levine MM, Venkatesan R et al. Safety and immunogenicity of a Vi polysaccharide-tetanus toxoid conjugate vaccine (Typbar-TCV) in healthy infants, children, and adults in typhoid endemic areas: a multicenter, 2-cohort, open-label, double-blind, randomized controlled phase 3 study. Clin Infect Dis. 2015;61:393–402. https://doi.org/10.1093/cid/civ295.

[54] Recommendations to assure the quality, safety and efficacy of typhoid conjugate vaccines. In: WHO Expert Committee on Biological Standardization 72nd and 73rd reports. Geneva: World Health Organization; 2020: Annex 2 (WHO Technical Report Series, No. 1030; https://www.who.int/publications/i/item/9789240024373.

[55] Lanh MN, Bay PB, Ho VA, Thanh TC, Lin FYC, Bryla DA et al. Persistent efficacy of Vi conjugate vaccine against typhoid fever in young children. N Engl J Med. 2003;349:1390–1. doi:10.1056/NEJM2003100234914.

[56] Jin C, Gibani MM, Moore M, Juel HB, Jones E, Meiring J et al. Efficacy and immunogenicity of a Vi-tetanus toxoid conjugate vaccine in the prevention of typhoid fever using a controlled human infection model of *Salmonella* Typhi: a randomised controlled, phase 2b trial. Lancet. 2017;390:2472–80. https://doi.org/10.1016/S0140-6736(17)32149-9.

[57] Meiring JE, Gibani M; TyVAC Consortium Meeting Group. The Typhoid Vaccine Acceleration Consortium (TyVAC): Vaccine effectiveness study designs: Accelerating the introduction of typhoid conjugate vaccines and reducing the global burden of enteric fever. Report from a meeting held on 26–27 October 2016, Oxford, United Kingdom, Vaccine. 2017;35(38):5081–8. https://doi.org/10.1016/j.vaccine.2017.08.001.

[58] Patel PD, Patel P, Liang Y, Meiring JE, Misiri T, Mwakiseghile F et al., Safety and efficacy of a typhoid conjugate vaccine in Malawian children. N Engl J Med. 2021;385(12):1104–15. doi:10.1056/NEJMoa2035916.

[59] Shakya M, Colin-Jones R, Theiss-Nyland K, Voysey M, Pant D, Smith N et al. Phase 3 efficacy analysis of a typhoid conjugate vaccine trial in Nepal. N Engl J Med. 2019. 381(23):2209–18. doi:10.1056/NEJMoa1905047.

[60] Qadri F, Khanam F, Liu X, Theiss-Nyland K, Biswas PK, Bhuiyan AI et al. Protection by vaccination of children against typhoid fever with a Vi-tetanus toxoid conjugate vaccine in urban Bangladesh: a cluster-randomised trial. Lancet. 2021;398:675–84. https://doi.org/10.1016/S0140-6736(21)01124-7.

Post-campaign assessments show substantial effectiveness under programmatic and outbreak-response conditions, with effectiveness against blood culture–confirmed *Salmonella* Typhi generally ranging from approximately 70% to >90% across diverse settings.[61,62,63,64]

Post-introduction evaluations in Fiji, Malawi, Nepal, Pakistan and Samoa further demonstrated reductions in typhoid incidence at population level in vaccinated age groups, with findings broadly consistent with efficacy estimates from randomized trials, although follow-up duration in programme settings remains shorter than in long-term clinical trial extensions.[64,65,66,67,68,69]

Duration of protection

Evidence on the duration of protection following a single dose of TCV is derived from the three TyVAC randomized controlled trials and extended follow-up analyses conducted in diverse epidemiological settings, indicating heterogeneity in duration of protection.

In Malawi, which was a high-incidence setting,[70,71] follow-up of the Phase 3 trial demonstrated cumulative vaccine efficacy of 83.4% (95% CI: 60.1–94.3) after one year, 80.7% (95% CI: 63.8–90.5) after two years, 80.1% (95% CI: 65.0–89.4) after three years, 77.1% (95% CI: 63.7–86.1) after four years and 78.3% (95% CI: 66.3–86.1) through 4.61 years of follow-up.[72] A meta-regression of the interval-specific estimates found no statistically significant decline in efficacy over time, although estimates for the later individual follow-up intervals were imprecise.

Across the full follow-up period, vaccine efficacy was 70.6% (95% CI: 6.4–93.0) among children vaccinated before 2 years of age, 79.6% (95% CI: 45.8–93.9) among those vaccinated at 2–4 years, and 79.3% (95% CI: 63.5–89.0) among those vaccinated at 5–12 years. Age-specific estimates of durability of protection over time were not reported.

In Nepal, which was a very-high-incidence setting,[70,71] extended follow-up was conducted following unblinding and cross-over vaccination. This was delayed due to COVID-19 restrictions, resulting in crossover vaccinations occurring from 2020 to 2021. Participants were therefore analysed as previous Vi-TT vaccinees vaccinated in 2017 and 2018, or recent Vi-TT vaccinees vaccinated during crossover in 2020 and 2021. Using a test-negative analysis, vaccine effectiveness was estimated at 77% (95% CI: 46–90) at 1–5 years after vaccination among recent vaccinees and 53% (95% CI: 8–76) at 4–8 years after vaccination among previous vaccinees.[73] These overlapping time windows reflect the staggered timing of crossover vaccination rather than discrete non-overlapping follow-up periods. Age-stratified analyses suggested more rapid decline in protection among children vaccinated at younger ages. At later time points, protection was not statistically significant among children vaccinated at younger ages, whereas protection remained evident among those vaccinated at age ≥10 years.

[61] Lightowler MS, Manangazira P, Nackers F, Van Herp M, Phiri I, Kiuwenyi K et al. Effectiveness of typhoid conjugate vaccine in Zimbabwe used in response to an outbreak among children and young adults: a matched case control study. Vaccine. 2022;40:4199–210. https://doi.org/10.1016/j.vaccine.2022.04.093.

[62] Hoffman SA, LeBoa C, Date K, Haldar P, Harvey P, Shimpi R et al. Programmatic effectiveness of a pediatric typhoid conjugate vaccine campaign in Navi Mumbai, India. Clin Infect Dis. 2003;77:138–44. https://doi.org/10.1093/cid/ciad132.

[63] Batool R, Yousafzai MT, Qurechi S, Ali M, Sadaf T, Mehmood J et al. Effectiveness of typhoid conjugate vaccine against culture-confirmed typhoid in a peri-urban setting in Karachi: a case-control study. Vaccine. 2021;39(40):5858–65. https://doi.org/10.1016/j.vaccine.2021.08.051.

[64] Background paper to SAGE on typhoid policy recommendations. Geneva: World Health Organization; 2026 (https://terrance.who.int/mediacentre/data/sage/SAGE_eYB_March26.pdf).

[65] Tamrakar D, Shahi SB, Jung E, Naga SR, Shrestha B, Raka PB et al., Effectiveness of the TYPHIBEV® (Vi-CRM197 conjugate) vaccine introduction in Nepal: a test-negative, case-control study. medRxiv. 2025. https://doi.org/10.1101/2025.11.20.25340644.

[66] Tamrakar D, Naga SR, Jungh E, Shrestha B, Raka PB, Pokharel R et al. Impact of the COVID-19 pandemic and typhoid conjugate vaccine introduction on typhoid fever in Nepal. PLOS Negl Trop Dis. 2026;20(1):e0013242. https://doi.org/10.1371/journal.pntd.0013242.

[67] Driscoll AJ, Liang Y, Patel P, Jafali J, Meiring J, Ndeketa LO et al. Effectiveness of typhoid conjugate vaccine for typhoid fever prevention in Malawi – MITIMA study results. Am J Trop Med Hyg. 2025;113(5 Suppl): Abstract Book, ASTMH 2025 Annual Meeting, Toronto, Canada, 9–13 November 2025. Abstract 7038 (https://d1lx8xdon3af7k.cloudfront.net/ASTMH_2025_Annual_Meeting_Abstract_Book_56833b3855.pdf).

[68] Driscoll AJ, Liang Y, Patel PD, Jafali J, Meiring J, Ndeketa LO et al. Typhoid conjugate vaccine effectiveness in Malawi. Presented at: 14th International Conference on Typhoid and Other Invasive Salmonelloses; 24–26 March 2026; Phnom Penh, Cambodia.

[69] Bristow P, Sikorski MJ, Sia CM, Fatupaito G, Tupua S, Wit V et al. Evaluating the Samoa Typhoid Fever Control Program: surveillance, vaccination, and progress toward elimination. Presented at: 14th International Conference on Typhoid and Other Invasive Salmonelloses; 24–26 March 2026; Phnom Penh, Cambodia.

[70] Meiring JE, Shakya M, Khanam F, Voysey M, Phillips MT, Tonks S et al. Burden of enteric fever at three urban sites in Africa and Asia: a multicentre population-based study. Lancet Glob Health. 2021;9:e1688–96. https://doi.org/10.1016/S2214-109X(21)00370-3.

[71] Typhoid fever incidence is classified as follows: Very high incidence: ≥500 cases per 100 000 population per year High incidence: 100 to <500 cases per 100 000 population per year Medium incidence: 10–<100 cases per 100 000 population per year Low incidence: <10 cases per 100 000 population per year These classifications are based on estimated incidence of symptomatic typhoid fever after appropriate adjustments for blood culture sensitivity, testing practices, and healthcare-seeking behaviour. They should not be applied to crude, unadjusted typhoid surveillance data such as national disease registries based on laboratory-confirmed cases. In the absence of direct data in settings where typhoid incidence data are unavailable, countries may make inferences about probable incidence and severity using alternative data. Vaccination is estimated to be cost-effective in medium-incidence settings with case fatality ratio ≥ 0.5% in community-based studies where ambulatory cases are included. A document to support countries defining their incidence levels and case fatality ratio can be found here: https://cdn.who.int/media/docs/default-source/immunization/typhoid/typhoid_incidence_cfr_definitions_document.docx?sfvrsn=49d81058_1

[72] Patel PD, Liang Y, Meiring JE, Chasweka N, Patel P, Misiri T et al. Efficacy of typhoid conjugate vaccine: final analysis of a 4-year, phase 3, randomised controlled trial in Malawian children. Lancet. 2024;403(10425):459–68. https://doi.org/10.1016/S0140-6736(23)02031-7.

[73] Pant D, Basile FW, Shakya M, Kelly S, Gurung M, Shrestha S et al. Eight-year vaccine protection following a single dose of Vi-tetanus toxoid conjugate vaccine in Nepali children: extended follow-up of the TyVAC Nepal randomised controlled trial. SSRN, 2026. doi:10.2139/ssrn.6327745.

In Bangladesh, which was also a very-high-incidence setting,[70,71] a nested test-negative case-control analysis among children vaccinated during the main TyVAC campaign in 2018 showed an overall decline in vaccine effectiveness over seven years, from 91% (95% CI: 84–95) in year 1 and 86% (95% CI: 76–92) in year 2 to 50% (95% CI: 8–73) in year 5, with imprecise estimates of 39% (95% CI: −7 to 65) and 44% (95% CI: −29 to 75) in years 6 and 7, respectively.[74] Age-stratified analyses demonstrated that waning was most pronounced among children vaccinated at younger ages – particularly those vaccinated before 2 years of age, among whom declines in both antibody responses and vaccine effectiveness were more rapid.

Taken together, these data indicate heterogeneity in the duration of protection across settings. There is consistent evidence from very-high-incidence settings in Nepal and Bangladesh that protection declines over time following a single dose – particularly among children vaccinated at younger ages. In contrast, in a high-incidence setting in Malawi, protection remained stable up to 4.61 years of follow-up with no data on age-related differences. Differences in durability may reflect variation in transmission intensity, force of infection, age at vaccination and duration of follow-up.

Vaccine safety

Evidence from randomized controlled trials, systematic reviews and post-licensure surveillance indicates that TCVs have a favourable safety profile.

A 2025 Cochrane systematic review of randomized trials – including 394 790 participants from 19 studies that included multiple TCV platforms – found little to no difference in the risk of adverse events between TCVs and control vaccines or placebo (risk ratio [RR] 0.91, 95% CI: 0.76–1.09).[75] Serious adverse events were not more frequent among TCV recipients than controls (RR 0.83, 95% CI: 0.71–0.97), although some comparisons were limited by small numbers of events and wide confidence intervals.

A recent WHO-commissioned meta-analysis of 130 studies reported low pooled rates of serious adverse events across TCV platforms, with estimates of 1.2 per 100 doses for Vi-TT, 0.5 per 100 doses for Vi-CRM197, 0.6 per 100 doses for Vi-DT and 0.1 per 100 doses for Vi-rEPA.[51] Comparative analyses within the review did not indicate an increased risk of serious adverse events for TCVs compared with comparator vaccines or placebo, and showed similar frequency of serious adverse events between TCVs and unconjugated ViPS.[51]

In a review of 1554 suspected adverse event reports submitted by national pharmacovigilance systems across multiple countries to VigiBase, WHO's global database, most were classified as non-serious while 84 (5.4%) reports were marked serious.[64] The most frequently reported events included fever, vomiting and seizures. However, VigiBase data are subject to the limitations of passive surveillance and do not establish causality.

Previous reviews by GACVS similarly did not identify safety signals for early TCV use.[76]

Available data indicate that TCV repeat dosing and booster doses are well tolerated, with no increase in serious adverse events and similar reactogenicity profiles compared with primary vaccination.[77]

Interchangeability

Direct evidence on the interchangeability of different TCVs within vaccination schedules is limited. WHO guidance for the evaluation of TCVs indicates that, in the absence of pre-licensure efficacy studies, the efficacy of a candidate Vi conjugate vaccine may be inferred through demonstration of non-inferiority based on immunogenicity (anti Vi IgG titres) compared to a licensed TCV.54 Licensed TCVs have therefore demonstrated comparable immunogenicity on the basis of standardized immunobridging criteria and are considered interchangeable for programmatic use.[52] There is no validated correlate of protection.

Data from heterologous boosting studies support interchangeability across TCV products. In Nepal, an observational study of children previously vaccinated with Vi-TT showed that boosting 2–4 years later with a Vi-CRM197 vaccine elicited substantially higher antibody responses than a single dose of Vi-CRM197 alone, with stronger responses observed at longer intervals between doses.[78] In Burkina Faso, a randomized study in school-aged children demonstrated that priming with a Vi-TT vaccine in early childhood followed by boosting 5–6 years later with a Vi-CRM197 vaccine resulted in persistent anti-Vi IgG prior to boosting and a marked increase in antibody concentrations after the booster, with geometric mean titres higher than in age-matched children receiving a first dose and near-universal seroconversion.[79]

[74] Zhang Y et al. (25 March 2026). Durability of protection following a single dose of Vi-tetanus toxoid conjugate vaccine: 7-year follow-up of a cluster-randomised trial in Bangladeshi children [Oral presentation]. TyVAC Annual Meeting. Phnom Penh, Cambodia.

[75] Gloeck NR, Leong TO, Mthethwa M, Iwu-Jaja CJ, Katoto PDMC, Wiysonge CS et al. Typhoid conjugate vaccines for preventing typhoid fever (enteric fever). Cochrane Database Syst Rev. 2025. https://doi.org/10.1002/14651858.CD015746.pub2.

[76] See No. 2, 2017:13–20.

[77] Nampota-Nkomba N, Nyirenda OM, Datta S, Mapemba V, Patel PD, Misiri T et al., Immunogenicity and reactogenicity of a booster dose of a typhoid conjugate vaccine (TCV) in Malawian pre-school children. EClinicalMedicine. 2025;81:103100. https://doi.org/10.1016/j.eclinm.2025.103100.

[78] Zhang Y SS, Feaheny F, Pant D, Shakya M, Bijukcheb S, Gehlhaar A et al. TyVAC Nepal Study Team. Impact of dosing interval on immunogenicity following a heterologous typhoid conjugate vaccine booster in Nepalese children: an observational study. SSRN, 2026. http://dx.doi.org/10.2139/ssrn.6148141.

[79] Sawadogo JW, Hema A, Amidou D, Kaboré JM, Hien D, Kuraogo L et al. Immunogenicity and tolerability of booster typhoid conjugate vaccine (TCV) five to six years after initial dose in Burkinabe Children. medRxiv, 2026. doi: https://doi.org/10.64898/2026.04.19.26351224.

Co-administration

Available co-administration data indicate that TCVs can be administered concomitantly with selected routine childhood vaccines, including measles-containing vaccines (measles or the measles, mumps and rubella combination [MMR]) and meningococcal group A conjugate vaccine, without evidence of interference or safety concerns.[5,80]

ViPS vaccines can be co-administered with routine childhood vaccines and with other vaccines that are relevant for international travellers, such as yellow fever and hepatitis A vaccines.[31] The Ty21a vaccine may be given simultaneously with other vaccines, including live vaccines against polio, cholera and yellow fever, as well as the MMR vaccine.[31]

Vaccine use in special populations

Immunocompromised and HIV-infected persons Data on the use of TCVs in persons living with HIV are limited. In a Phase 3 RCT conducted in Malawi, a setting with high HIV prevalence, children living with HIV were included; HIV status was solicited verbally and confirmed by health passport where possible. No vaccine-related serious adverse events were observed, and overall safety profiles were comparable between groups.[58]

Additional data from an open-label study in Malawi among HIV-exposed uninfected and HIV-unexposed uninfected infants aged 9-11 months indicate that TCV is well tolerated, with predominantly mild local reactions and similar rates of adverse events between groups.[81]

In a prospective cohort study in Pakistan including 336 children aged 6 months to 15 years receiving a single dose of TCV and living with PCR-confirmed HIV infection, immune responses were elicited across age groups but more rapid waning and lower geometric mean titres were noted in younger children and in those with more advanced disease or poor nutritional status.[82] Long-term immunogenicity and duration of protection in children living with HIV remain uncertain.

ViPS vaccines are safe in individuals living with HIV, although immunogenicity may be reduced.[83] As Ty21a is a live-attenuated vaccine, it is not recommended for use in individuals with impaired cell-mediated or humoral immune responses.

Pregnant and lactating women Direct safety data on the use of TCVs in pregnant and lactating women are limited. Unpublished passive surveillance data from TyVAC Bangladesh identified 10 pregnancies during follow-up, including seven among TCV recipients. Five participants were vaccinated while pregnant, with pregnancy recognized later, and five became pregnant after vaccination. All identified pregnancies were followed to completion and were reported to result in healthy term live births.[64] Although data are generally lacking on typhoid vaccine use in pregnant and lactating women, there are no theoretical safety concerns for ViPS vaccines and TCV.

Population impact, cost-effectiveness and economic impact

Typhoid transmission dynamic and economic modelling was conducted independently in the context of a multi-model comparison.[64,84] Two of the transmission models were compartmental and two were agent-based. All models incorporated susceptible, infectious and recovered states, chronic carriage, and vaccine-induced immunity with age-dependent waning. Model outputs were linked to decision-analytic economic frameworks estimating costs and DALYs.

Routine vaccination was evaluated, with the primary dose administered at 9 months, 2 years, or 5 years of age; introduction was accompanied by a catch-up campaign in children from the age of primary vaccination up to 15 years of age. Additionally, a booster scenario was evaluated with routine vaccination at 9 months and an additional dose at 5 years of age. Analyses were conducted under slow- and fast-waning assumptions (based on the vaccine efficacy data from Malawi and Bangladesh, respectively) and across medium-, high- and very-high-incidence settings. The assumed procurement cost of a single dose of TCV was US$1.50.

Compared to routine vaccination at later ages, vaccination at 9 months produced larger initial reductions in incidence because routine coverage was higher and the catch-up campaign targeted a broader age range. However, under the fast-waning assumption, all modelling groups projected a rebound in incidence over time, which was greatest in the very-high-incidence setting. A larger rebound was predicted when routine vaccination was administered at 9 months due to faster waning associated with younger age at vaccination. Routine vaccination at 5 years produced lower initial impact but more sustained reductions under

[80] Sirima SB, Ouedraogo A, Barry N, Siribie M, Tiono A, Nébié I et al. Safety and immunogenicity of co-administration of meningococcal type A and measles-rubella vaccines with typhoid conjugate vaccine in children aged 15–23 months in Burkina Faso. Int J Infect Dis. 2021;102:517–23. https://doi.org/10.1016/j.ijid.2021.05.061.

[81] Nampota-Nkomba N, Nyirenda OM, Mapemba V, Masonga R, Patel PD Misiri T et al. Single and two-dose typhoid conjugate vaccine safety and immunogenicity in HIV-exposed uninfected and HIV-unexposed uninfected Malawian children. Hum Vaccin Immunother. 2024;20(1):2384760. https://doi.org/10.1080/21645515.2024.2384760.

[82] Batool R, Yousafzai MT, Mir F, Muhammad F, Shaikh SA, Memon S et al. Longevity of serologic responses following a single dose of typhoid conjugate vaccine among children living with HIV in Pakistan: a prospective cohort study. Vaccine. 2024;42(22):126009. https://doi.org/10.1016/j.vaccine.2024.05.057.

[83] Kroon FP, van Dissel JT, Ravensbergen E, Nibbering PH, van Furth R. Impaired antibody response after immunization of HIV-infected individuals with the polysaccharide vaccine against Salmonella typhi (Typhim-Vi). Vaccine. 1999;17:2941–5. https://doi.org/10.1016/S0264-410X(99)00167-X.

[84] Wenger CGC, Grantz KH, Menkir TF, Muellenmeister AM, Pithawala Z, Hutubessy R et al. Evaluating the impact and cost-effectiveness of typhoid conjugate vaccine schedules across diverse settings: a multi-model comparison. medRxiv, 2026. https://doi.org/10.64898/2026.03.09.26346651.

the fast-waning assumption. The addition of a booster at 5 years produced a small incremental benefit under the slow-waning assumption but reduced the projected rebound under the fast-waning assumption.

Under higher case fatality and higher cost assumptions,[85] vaccination in medium-incidence settings (~50 cases per 100 000 person-years) may be cost-effective above a willingness-to-pay threshold of approximately US$1250 per DALY averted. Delaying routine vaccination to 2 or 5 years was identified as the most cost-effective strategy due to the older age of peak incidence in these settings. In high-incidence settings (~200 cases per 100 000 person-years), vaccination was likely to be cost-effective above a willingness-to-pay threshold of ~US$100 per DALY averted. Routine vaccination at 9 months was generally the preferred strategy under the slow-waning assumption, but delaying vaccination to 2 years of age was more cost-effective under the fast-waning assumption. In very-high-incidence settings (~1500 cases per 100 000 person-years), vaccination was cost-saving, and the addition of a booster was cost-effective above a willingness-to-pay threshold of US$500 per DALY averted.

Under lower case fatality and cost assumptions, vaccination in medium-incidence settings was not cost-effective. In high-incidence settings, vaccine introduction may be cost-effective above a willingness-to-pay threshold of ~US$700 per DALY averted, with routine vaccination at 2 years generally predicted to be the preferred strategy. In very-high-incidence settings, routine vaccination at 9 months (under the slow-waning assumption) or 2 years (under the fast-waning assumption) was again predicted to be cost-saving, while adding a booster dose was cost-effective at willingness-to-pay thresholds ranging from US$1000 to US$1800 per DALY averted, which was equivalent to approximately 0.5–1 times the GDP per capita in most LMIC settings.[86]

Programmatic and health systems considerations

An expert elicitation survey was conducted to inform deliberations on programmatic considerations for TCV use and focused on three areas, namely: 1) the introduction of TCV in countries that have not yet adopted it; 2) the feasibility and acceptability of delaying the age of first TCV administration; and 3) the feasibility and acceptability of a booster dose in countries following TCV introduction.[64]

Across settings, respondents consistently identified financing, competing immunization priorities and the strength of supporting epidemiological evidence as the primary drivers of decision-making, rather than concerns related to vaccine safety, cold chain capacity or public acceptance.

In countries that have not introduced TCV, uncertainty was based on affordability, programme fit and the need for stronger data on disease burden and impact. Respondents indicated that the feasibility and acceptability of delaying the first dose would depend on the rationale for delayed administration, potential effects on caregiver acceptability, the risk of typhoid disease in early life, and routine immunization coverage at older ages. In countries that have introduced TCV, perspectives on booster dosing were contingent on evidence of the duration of protection, incremental benefit of the booster dose, and the feasibility of delivery – particularly if booster vaccination would require delivery through platforms not already established through the national immunization programme.

WHO recommendations

Vaccination strategies

WHO recommends the use of typhoid vaccines for the control of typhoid fever. All typhoid vaccination programmes should be implemented as part of a comprehensive strategy to prevent typhoid fever and its complications. This includes health education; improvements in water, sanitation and hygiene (WASH) and food safety; and the training of health professionals in diagnosis and treatment of typhoid fever, including the management of chronic carriers and drug-resistant infections.

WHO recommends the use of typhoid conjugate vaccines (TCV) for routine immunization programmes in typhoid-endemic countries. TCV is recommended at all eligible ages in view of its improved immunological properties as compared to ViPS and Ty21a vaccines, its suitability for use in younger children, its longer duration of protection and programmatic advantages.

Vi polysaccharide (Vi-PS) and Ty21a vaccines are licensed typhoid vaccines with shorter durations of protection and programmatic limitations compared with TCV. For these reasons, they are not recommended for routine use in typhoid-endemic countries and are primarily used for travellers and other targeted indications where TCV is not available.

[85] Harmonized assumptions were applied across all models. Medium incidence was defined as an annual incidence of 52 cases per 100 000 person-years, with peak incidence in the 10–15-year age category. High incidence was defined as annual incidence of 214 cases per 100 000, with peak incidence in the 2–4-year age category. Very high incidence was defined as annual incidence of 1255 cases per 100 000 person-years with peak incidence in the 2–4-year age category. Assumed case fatality risk was 0.81% in Africa (95% CI: 0.10%, 6.22%) and 0.16% in Asia (95% CI: 0.07%, 0.40%); these estimates were drawn from available country-level surveillance and costing cohort data from each region. Assumed cost of treatment was age, treatment and region-specific.

[86] Ozawa S, Mirelman A, Stack ML, Walker DG, Levine OS. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: a systematic review. Vaccine. 2012;31:96–108. doi:10.1016/j.vaccine.2012.10.103.

Primary vaccination schedule

WHO recommends the use of TCV in settings with: 1) high or very high incidence[71] or 2) a high case fatality ratio[87] or 3) a high burden of antimicrobial resistant *Salmonella* Typhi.[88] The first dose is recommended at 9–24 months of age.

In settings with medium incidence,[71] TCV introduction may be considered, particularly if disease is associated with a high CFR or there is a high burden of AMR. In such settings, the first dose may be administered at ≥ 2 years of age. The first dose may be delayed up to 5 years of age on the basis of local epidemiology and feasibility.

Decisions on the age at TCV administration, the target population and the delivery strategy for routine and catch-up vaccination should be based on the local epidemiology of typhoid fever and programmatic considerations.

Routine programmatic administration is encouraged at the same visit as for other vaccines or public health interventions in the targeted age group.

Vaccination of older children and adults may also be considered on the basis of local epidemiology and product licensure.

When ViPS vaccine is used, a single dose of vaccine should be administered intramuscularly or subcutaneously from 2 years of age.

For Ty21a vaccine, a 3-dose oral immunization schedule, given every second (alternate) day, is recommended in those aged ≥ 6 years.

Catch-up vaccination

WHO recommends catch-up vaccination with TCV at the time of vaccine introduction.

The age range for catch-up vaccination should be guided by epidemiological data and programmatic feasibility. On the basis of a substantial burden of disease and programmatic feasibility, children aged <15 years are often targeted for catch-up vaccination. The available evidence on indirect protection shows that catch-up vaccination of multiple age cohorts at the time of vaccine introduction is likely to accelerate the disease impact of vaccination.

Booster doses

Countries with very high typhoid incidence should consider a booster dose at around 5 years of age for children who received a primary TCV dose at 9–24 months of age.

In high-incidence settings, a booster dose at around 5 years of age may be considered if there is evidence of waning of protection.

In other epidemiological settings where the primary dose of TCV is administered before 24 months of age, a booster dose may also be considered if any evidence of waning protection is observed in vaccinated cohorts.

National decisions on a booster dose should be based on an assessment of typhoid incidence,[71] typhoid case fatality ratio,[87] antimicrobial resistance patterns,[88] cost-effectiveness, and programmatic feasibility.

WHO recommends that efforts should be made to maintain a minimum interval of one year between primary vaccination and the booster dose. The booster dose may be safely administered even if the exact date of the primary vaccination dose is not known. The timing of a booster dose should be adapted to programmatic and operational contexts.

If a booster dose is introduced, delivery may occur through health facilities, schools or community outreach activities, using approaches aligned with existing infrastructure and ensuring affordability and sustainability.

In medium- or high-incidence settings or in contexts where limited waning of protection is observed, a booster dose may not be needed, particularly if the primary dose is administered at ≥ 2 years of age.

If administering a booster dose is a significant barrier, this should not preclude the introduction and use of TCV without a booster in these settings.

When ViPS or Ty21a vaccine is used, revaccination is recommended every 3 years for ViPS vaccine, and every 3–7 years for Ty21a vaccine, or every 1–7 years for travellers from non-endemic to endemic areas, depending on national policies.

Vaccination in typhoid outbreaks

WHO recommends that countries experiencing typhoid fever outbreaks should consider TCV introduction or strengthening of existing routine TCV immunization programmes.

Limited data are available on the use of TCV for outbreak response vaccination. In addition, there are no official definitions of an outbreak or the threshold of cases that warrants TCV use in outbreak response. However, the use of TCV in outbreak response campaigns may be considered in large or prolonged outbreaks.

[87] Case fatality ratio (CFR) – i.e. the proportion of individuals with typhoid fever who die – is a key metric for implementing WHO recommendations. CFR can be estimated using published or unpublished country data, meta-analysis or modelled estimates, national or subnational disease surveillance data, or hospital and health facility records. A CFR of 0.5% or higher (for community-based studies) is considered "high" in the context of the WHO recommendations.

[88] The burden of antimicrobial resistance (AMR) in typhoid reflects the extent to which circulating *S.* Typhi organisms are resistant to antimicrobial agents that are currently available, and in routine use locally. In such cases, resistance to these antimicrobial agents constrains effective case management and increasing reliance on alternative, parenteral, more costly or last-resort therapies and may negatively affect clinical outcomes.

Important considerations for the use of typhoid vaccines in outbreak control include vaccine availability, logistics and costs, as well as the characteristics of the outbreak – such as the antimicrobial resistance pattern,[88] the outbreak size and duration, and the age groups affected, including adults. The use of vaccines for outbreak control should be implemented in conjunction with other control measures, including case management and improvements in WASH.

Fragile, conflict-affected and vulnerable settings

Typhoid vaccination may be considered in fragile, conflict-affected and vulnerable settings where the risk of typhoid fever is high. In vulnerable settings where interventions such as improvements in WASH may be limited or difficult to implement rapidly, vaccination may represent an important intervention.

However, vaccination should be implemented as part of a more comprehensive response that includes additional appropriate public health measures.

WHO has developed a framework and tool to assist in deliberate, ethical and rational determination of whether the delivery of one or more vaccines to specific target populations during humanitarian emergencies would result in an overall saving of lives and a reduction in the population burden of disease.[89]

Vaccination of special populations

Pregnancy and breastfeeding

Data are currently lacking on the use of typhoid vaccines in this population. However, there are no theoretical safety concerns on the use of TCV and ViPS vaccines. Therefore, TCV (or ViPS vaccines where TCV is unavailable) may be used. Use of the live attenuated Ty21a vaccine during pregnancy should be avoided because of theoretical safety concerns about the potential adverse effects of live vaccines for the pregnant woman or foetus.

For women who are breastfeeding, where consideration is given to vaccination, TCV (or ViPS where TCV is unavailable) may be used. This is based on the following considerations:

- Breastfeeding offers substantial health benefits to breastfeeding women and their breastfed children.
- Data are not available on the potential benefits or risks of TCV and ViPS vaccines to breastfed children. However, they are biologically and clinically unlikely to pose a risk to the breastfeeding child.
- WHO does not recommend discontinuing breastfeeding because of vaccination.

Immunocompromised persons Immunocompromised persons,[90] including those living with HIV, should receive TCV; ViPS vaccines may be used where TCV is unavailable. The live attenuated Ty21a vaccine should not be used in persons with uncontrolled HIV but may be administered to persons living with well-controlled HIV with a CD4 count $\geq$200 cells/µl.

Immunocompromised persons include those with active cancer, transplant recipients, immunodeficiency, and in active treatment with immunosuppressive agents. They also include people living with HIV with a current CD4 cell count of <200 cells/µl. For persons with malignancy or planned immunosuppressive therapy, vaccination should be timed according to immune status and treatment schedule. Where feasible, non-live vaccines should be administered before immunosuppression or after immune reconstitution.[91]

Health workers and laboratory personnel Laboratory personnel with a recognized risk of occupational exposure to *Salmonella* Typhi should be offered vaccination against typhoid. Other health-care workers with a recognized risk of occupational exposure to *Salmonella* Typhi may also be offered vaccination against typhoid.

Travellers from non-endemic areas to endemic areas

Travellers to typhoid-endemic areas should adhere to safe food and water practices and good hygiene to reduce their risk of infection. Typhoid vaccination could be considered for travellers using any of the available licensed vaccines – including TCVs, ViPS vaccines, or Ty21a vaccines. Where available, licensed typhoid-containing combination vaccines with hepatitis A may also be used for travellers.

Professional food-handlers

In typhoid-endemic areas, professional food-handlers should be vaccinated against typhoid.

[89] Vaccination in acute humanitarian emergencies. A framework for decision making. Geneva: World Health Organization; 2017 (http://apps.who.int/iris/bitstream/10665/255575/1/WHO-IVB-17.03-eng.pdf).

[90] Moderate or severe immunocompromise refers to clinically significant impairment of immune function caused by congenital disorders, disease or immunosuppressive therapy that reduces the ability to mount effective immune responses or control infection.

[91] Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis.* 2014;58:e44–100 (https://doi.org/10.1093/cid/cit684)

Contraindications and precautions

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

Co-administration

Based on several co-administration studies of TCV and inferred from co-administration studies of other vaccines, TCV may be given concomitantly, or at any time before or after other vaccines – including live attenuated, inactivated, adjuvanted or non-adjuvanted vaccines. When administered concomitantly, the vaccines should be injected in separate sites and preferably at different extremities.

Interchangeability of vaccines

On the basis of immunobridging data, licensed TCVs are considered interchangeable. Any recommended TCV may be used for the primary and booster doses.

Monitoring and surveillance

In many endemic settings, systematic and comprehensive surveillance and reporting for typhoid fever remain limited or absent, thus constraining accurate assessment of disease burden and trends.

WHO recommends that countries where typhoid fever is endemic should implement and strengthen surveillance systems to support evidence-based decision-making and to guide the introduction and evaluation of vaccination strategies. Robust surveillance should include blood culture or PCR-confirmed typhoid detection, supported by epidemiological data collection. Such systems are essential for monitoring vaccine impact and effectiveness over time – including the early identification of potential waning of immunity. In addition, sustained surveillance is critical for detecting the emergence of AMR, as well as shifts in circulating *Salmonella* Typhi strains and patterns of antimicrobial resistance.

Countries are encouraged to integrate typhoid surveillance into existing national surveillance frameworks in order to improve efficiency and sustainability. The adoption of electronic reporting systems should be promoted to enhance data timeliness, completeness and accessibility for public health action. Close linkage with *Salmonella* Typhi AMR surveillance platforms – including participation in broader AMR surveillance systems such as the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) – is strongly recommended to ensure coordinated monitoring of resistance trends. When capacity is available, genomic surveillance can complement these efforts.

To complement routine surveillance and inform policy decisions, particularly in settings with limited data, countries may consider using additional tools such as the Typhoid Fever Burden Reduction Assessment Tool (BRAT) to consolidate existing data.[92] Other methods for making inferences about the incidence of typhoid fever, including from sentinel site bloodstream infection data[93] or seroepidemiological studies, may also be used. Seroepidemiological approaches based on antibody responses to *Salmonella* Typhi antigens, particularly haemolysin E (HlyE), may support the estimation of typhoid incidence in settings where blood culture surveillance is limited.[94] Where capacity is available, genomic surveillance of *Salmonella* Typhi can be used to monitor the emergence and spread of drug resistance.[24,95]

Research priorities

Further validation of seroepidemiological approaches is needed across geographical settings and age groups. Priorities include paired clinical and serological incidence studies, further assessment of cross-reactivity, and standardization of assays, antibody decay models and methods for estimating and interpreting seroincidence.[94]

Further research is also needed to clarify the relationship between seroincidence and symptomatic typhoid fever, particularly among children aged <2 years, and to develop practical guidance for field implementation, assay selection and the interpretation of results. The effect of TCV introduction on serological markers should also be evaluated. Further evaluation of wastewater and environmental surveillance is needed to determine its utility for estimating typhoid transmission and for informing vaccination decisions.

TCVs are expected to contribute to the reduction of antimicrobial resistance through the prevention of drug-resistant *Salmonella* Typhi infections and reduced incidence of febrile illness and associated antimicrobial use. This may lead to decreased selection pressure, thus slowing the emergence and spread of antimicrobial resistance.[93] WHO recommends further research to quantify

[92] The Burden and Risk Assessment of Typhoid (BRAT) is a methodology for countries to assess available data on the burden and risk of typhoid fever. Geneva: World Health Organization and TechNet-21; 2026 (https://www.technet-21.org/en/resources/tool/burden-and-risk-assessment-of-typhoid-brat-a-methodology-for-countries-to-assess-available-data-on-the-burden-and-risk-of-typhoid-fever, accessed 17 June 2026).

[93] Hagedoorn NN, Murthy S, Marchello CS, Williman J, Ahmmed F, Andrews JR et al. Predicting *Salmonella* Typhi incidence using prevalence metrics from sentinel studies of community-onset bloodstream infections: a secondary analysis. Vaccine. 2026;85:128691. https://doi.org/10.1016/j.vaccine.2026.128691.

[94] Laurens MB, Ackah E, Agyapong F, Aiemjoy K, Awab GR et al. (2026). Typhoid seroepidemiology for TCV decision-making: meeting report of the 18 July 2025 expert consultation [version 2]. VeriXiv [preprint]. 3:245. https://doi.org/10.12688/verixiv.3487.2

[95] Nampota-Nkomba N, Carey ME, Jamka LP, Fecteau N, Neuzil KM. Using typhoid conjugate vaccines to prevent disease, promote health equity, and counter drug-resistant typhoid fever. Open Forum Infect Dis. 2023;10:S6–12 (2023). https://doi.org/10.1093/ofid/ofad022.

these effects, including development of standardized methods for measuring impacts on antimicrobial prescribing, use and resistance outcomes. Genomic surveillance may be used to monitor any potential changes in the population structure of *Salmonella* Typhi following TCV introduction.

Additional evidence gaps to be addressed include the duration of protection following a single dose of TCV, the impact of booster doses of TCV, and the optimal timing of booster doses across different epidemiological settings.

There is a need for a standardized definition of an outbreak. The impact and cost-effectiveness of TCV use in outbreak response scenarios should be evaluated.

Studies to identify and evaluate immunological correlates of protection are also recommended to support evaluation of new vaccines and optimization of vaccination schedules.