Together We Can Take on Typhoid

China

Burden of Typhoid in

Nepal

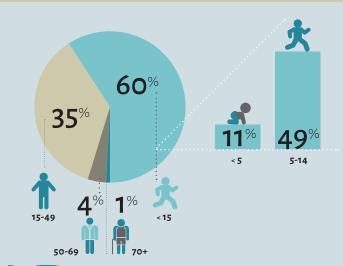
Nepal is a typhoid-endemic country and is estimated to have one of the highest burdens of typhoid in the world. The Global Burden of Disease study estimated that, in 2019, there were at least:

82,449 919 typhoid deaths 68,186

typhoid cases (271 cases per 100,000)

disability-adjusted life-years (DALYs) lost to typhoid¹

Nepa Typhoid incidence per 100,000 - 2019 <50 50-100 101-300 >300



Most typhoid cases occur in children younger than 15 years old.

Bayalpata Hospital, Achham

- Damauli Hospital, Tanahun Dhulikhel Hospital, Kavrepalanchok
- Kirnetar Health Centre, Dolakha

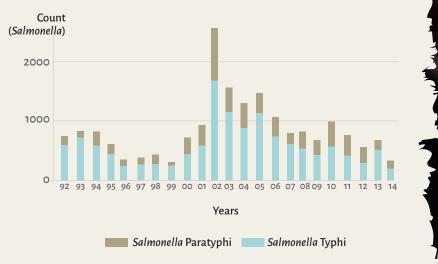




1,000-2,4999

Reported clinical rates of enteric fever (typhoid and paratyphoid) differ by district, with a large burden concentrated in the Eastern hill and mountain regions.²

- » While diagnostic limitations in Nepal mean that typhoid is often misdiagnosed,² laboratory culture-confirmed studies have found a high burden of typhoid.
- » Data from Patan Hospital demonstrate a consistent presence of culture-confirmed typhoid and paratyphoid each year, with occasional outbreaks (e.g. 2002).³



» A surveillance study near Kathmandu found 1,062 cases of typhoid per 100,000 people. The rate of typhoid cases identified from this study was highest in children 5-9 years old.⁴ While typhoid is rarely fatal, the recovery is long and difficult. The disease takes time, money, and productivity from those infected and their families and is associated with numerous long-term complications.

 One study in Kathmandu found that the combined direct and indirect mean costs for hospitalized patients was US\$233approximately one-third of the average Nepali household income (US\$730 annually).⁵

Drug-resistant typhoid strains are a growing problem nationally, regionally, and across the globe.



A qualitative study from Katmandu found that antibiotics are frequently prescribed without accurate diagnostics to positively confirm a typhoid case,⁵ which leads to antibiotic resistance.



A 2002 outbreak of 5963 cases in Bharatpur, Nepal was traced to the city's single municipal water supply. Analysis found that 90% of isolates were resistant to more than one antibiotic.⁶



A study on typhoid treatment in 2014 ended early because it encountered high rates of treatment failure with fluoroquinolones, and concluded that fluoroquinolones should no longer be used for treatment of enteric fever in Nepal.⁷ Ceftriaxone was also suboptimum.



Because other treatments may be costly or inaccessible, the authors recommend prioritzing vaccines and the development of new treatment options for typhoid.⁷



Isolates identified during a recent surveillance study found that 83% were resistant to fluoroquinolone antibiotics. 7% were resistant to azithromycin, one of the last oral antibiotics available for typhoid treatment.⁴

Typhoid conjugate vaccines (TCVs) in Nepal

The World Health Organization (WHO) recommends the introduction of prequalified TCVs be prioritized in countries with a high burden of typhoid disease or a high burden of drug-resistant typhoid. Gavi, the Vaccine Alliance support for introduction is available now.

Prequalified TCVs are highly effective and safe for children as young as 6 months of age. Recent data from a large Phase 3 study in Nepal show that TCV is safe and 79% effective in preventing typhoid.⁸ TCVs:



Require one dose;



Are more effective and may be longerlasting than other typhoid vaccines; and



Can be **co-administered with measlesrubella vaccine.**⁹

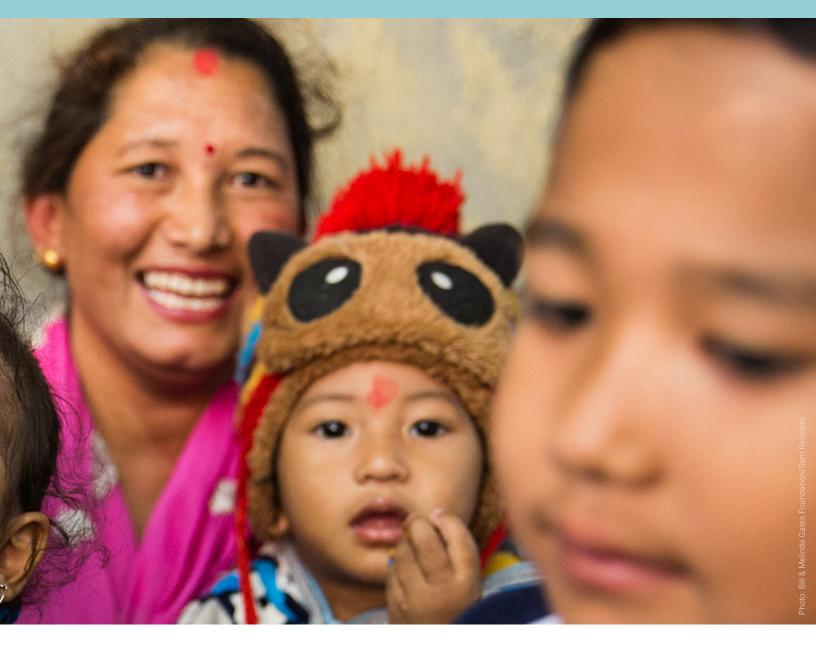


The Government of Nepal has **prioritized typhoid prevention** and control and plans to introduce TCV into its routine childhood immunization program in 2022.

Let's Take on Typhoid in Nepal

- Typhoid is endemic in Nepal, with more than **82,000** cases per year.
- Nepal's burden of typhoid is most heavily borne by children **younger than 15** years of age.
- Data show an increase in *drug-resistant typhoid* in Nepal, regionally, and globally.
- **TCVs** are safe, effective, and WHO-recommended for routine immunization as part of a costeffective, integrated approach to typhoid prevention and control alongside safe water, sanitation, and hygiene interventions.
- Nepal plans to *introduce TCV* into its routine immunization system with *support from Gavi*.

» Findings from an economic analysis predict that, even in the absence of a Gavi subsidy, a catch-up campaign with TCV could be cost-effective in Nepal.¹⁰



- Institute for Health Metrics and Evaluation. Global Burden of Disease. 2019. Accessed via: ghdx.healthdata.org/gbd-results-tool.
- 2. Andrew JR, Vaidya K, Bern C, et al. High rates of enteric fever diagnosis and lower burden of culture-confirmed disease in peri-urban and rural Nepal. *The Journal of Infectious Diseases*. 2017; jix221:S1-S8.
- Karkey A, Arjyal A, Anders KL, et al. The burden and characteristics of enteric fever at a healthcare facility in a densely populated area of Kathmandu. *PLoS One*. 2010;5(11):E13988.
- Meiring JE, Shakya M, Khanam F, et al. Burden of enteric fever at three urban sites in Africa and Asia: A multicentre population-based study. *The Lancet Global Health.* 2021;9(12):E1688-1696.
- Kaljee LM, Pach A, Garrett D, et al. Social and economic burden associated with typhoid fever in Kathmandu and surrounding areas: A qualitative study. *The Journal of Infectious Diseases*. 2017;jix122:S1-S7.
- 6. Lewis MD, Serichantalergs O, Pitarangsi C, et al. Typhoid Fever: A massive, single-point source, multidrug-resistant outbreak in Nepal. *Clinical Infectious Diseases*. 2005;40:554-561.

- Arjyal A, Basnyat B, Nhan HT, et al. Gatifloxacin versus ceftriaxone for uncomplicated enteric fever in Nepal: an open-label, two-centre, randomised controlled trial. *The Lancet Infectious Diseases*. 2016;16(5):535-545.
- Shakya M, Voysey M, Theiss-Nyland K, et al. Efficacy of typhoid conjugate vaccine in Nepal: Final results of a phase 3, randomised, controlled trial. *The Lancet Global Health*. 2021;9(11):e1561-1568.
- 9. Sirima SB, Ouedraogo A, Barry N, et al. Safety and immunogenicity of Vityphoid conjugate vaccine co-administration with routine 9-month vaccination in Burkina Faso: A randomized controlled phase 2 trial. *International Journal of Infectious Diseases*. 2021;108:465-472.
- Blicke J, Antillon M, Pieters Z, et al. Cost-effectiveness of routine and campaign use of typhoid Vi-conjugate vaccine in Gavi-eligible countries: A modelling study. The Lancet Infectious Diseases. 2019;19(7):728-739.



