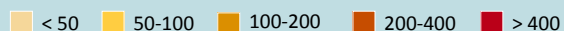


Typhoid in Nepal

Typhoid burden

- Nepal is estimated to have one of the highest burdens of typhoid in the world.
- It is estimated that there were 351 typhoid cases per 100,000 people in 2017.¹

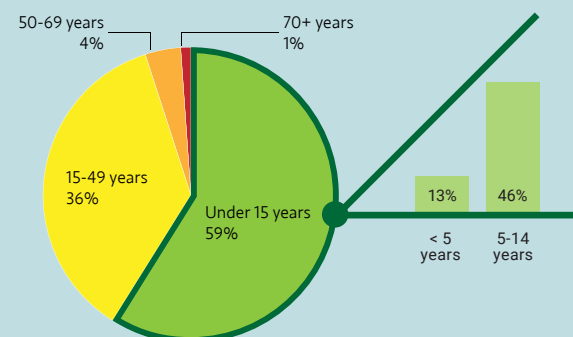
Typhoid incidence per 100,000 - 2017



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

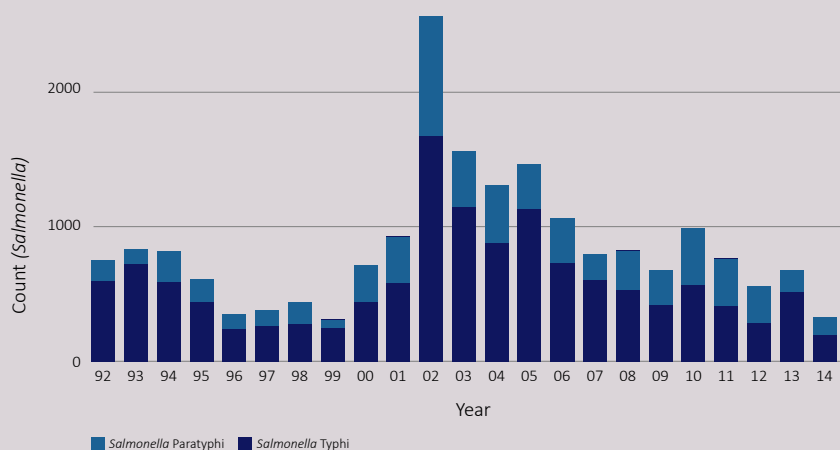
In 2017 there were an estimated:¹

- 105,026 total cases**, 59% among children under 15 years of age.
- 1,042 deaths**, 59% among children under 15.



Typhoid surveillance

- 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



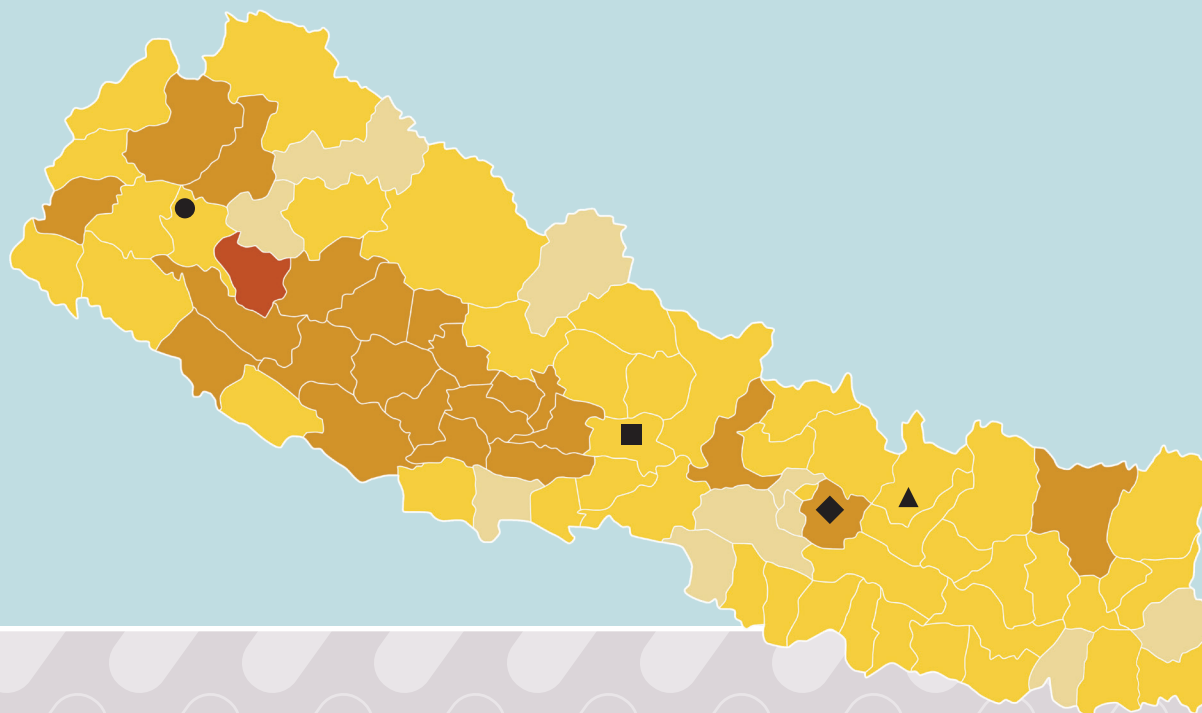
- A surveillance study near Kathmandu found 599 cases of typhoid per 100,000 people.**⁴

Reported clinical rates of enteric fever (typhoid and paratyphoid) differ by district, with a large burden concentrated in the Eastern hill and mountain regions²

Subnational perspective

- Bayalpata Hospital, Achham
- Damauli Hospital, Tanahun
- ◆ Dhulikhel Hospital, Kavrepalanchok
- ▲ Kirnetar Health Centre, Dolakha

Cases per 100,000 population



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

Drug resistance

- Global data show that the multidrug-resistant (MDR) H58 typhoid strain prevalence has increased dramatically since 1992.⁵
- A qualitative study from Katmandu found that antibiotics are frequently prescribed without accurate diagnostics to positively confirm a typhoid case,⁶ 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.⁷
- 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.⁸ Ceftriaxone was also suboptimum.
- **Because other treatments may be costly or inaccessible, the authors recommend prioritizing vaccines and the development of new treatment options for typhoid.⁸**

- One study in Kathmandu found that the combined direct and indirect mean costs for hospitalized patients was US\$233—approximately **one-third of the average Nepali household income** (US\$730 annually).⁶
- TyVAC will conduct an additional study to assess the household and provider costs of typhoid disease in Nepal.

- A recent economic analysis estimates that **routine immunization of children at 9 months of age, including a catch-up campaign among children up to 15 years of age, is the preferred strategy, and is likely to be cost-effective in Nepal even absent Gavi support.**⁹
- TyVAC will conduct an additional study to assess the cost-effectiveness of typhoid vaccination in Nepal.

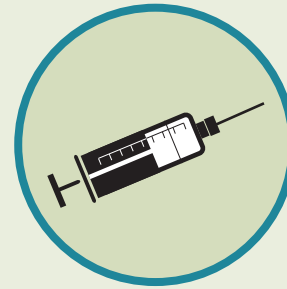
- For **a campaign, Gavi will fully finance the cost of vaccine and injection supplies** and will contribute toward operational costs.
- For **routine immunization, Gavi will provide a vaccine introduction grant and support the cost of the vaccine.** As an Initial Self-Financing country, Nepal will be responsible for co-financing of \$0.20 a dose, injection supplies, and introduction/routine costs.
- Vaccine program cost estimates can be generated upon request.

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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.
3. 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.
4. Results are from SEAP preliminary data as of September 15, 2018.
5. Wong VK, Baker S, Pickard DJ, et al. Phylogeographical analysis of the dominant multidrug-resistant H58 clade of *Salmonella* Typhi identifies inter- and intracontinental transmission events. *Nature Genetics*. 2015;47(6):632-639.
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8. 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.
9. Bilcke J, et al. Cost-effectiveness of typhoid conjugate vaccine delivery strategies in Gavi-eligible countries: a modelling study. *Submitted*.



A new typhoid conjugate vaccine (TCV) offers:

- Longer-lasting protection compared to other available typhoid vaccines.
- Fewer required doses.
- Suitability for children 6 months of age and older.
- Opportunity for inclusion in routine childhood immunization programs.



The World Health Organization encourages:

- TCV introduction prioritized in countries with highest typhoid burden or high burden of drug-resistant typhoid.
- Programmatic administration at same time as other vaccine visits at 9 months of age or in second year of life.
- Catch-up vaccination campaigns up to 15 years of age.
- Use in response to confirmed outbreaks of typhoid.



Typbar-TCV:

- Is manufactured by Bharat Biotech International Limited.
- Can be administered to adults, children, and infants 6 months of age and older.
- Offers long-lasting protection with a single 0.5mL dose injected intramuscularly.
- Presents as ready-to-use liquid in a 5-dose vial with 36-month shelf life when stored at 2-8°C.



Expanded use of TCVs can:

- Reduce the need for antibiotics.
- Slow further emergence of drug-resistant typhoid.
- Decrease prevalence of disease.
- Save lives.