

Typhoid + Drug Resistance



Key Messages



Drug-resistant typhoid poses a serious risk to health, with widespread prevalence of multidrug-resistant and increasing identification of extensively drug-resistant typhoid strains that are resistant to multiple classes of antibiotics.



It is only a matter of time until typhoid becomes untreatable, raising the urgency for prevention through proven interventions including vaccination with typhoid conjugate vaccines (TCVs) and improvements in water, sanitation, and hygiene.



We can't afford to wait for typhoid to become untreatable when we have tools available now to prevent infections. TCVs are a safe and effective tool that countries can use now to protect children from typhoid and slow the spread of drug-resistant typhoid strains.

Drug resistance is a multifaceted, complex global issue that not only impacts health systems, it also affects agricultural, ecological, and economic sectors.

Antimicrobials are medications used to treat different types of infections caused by any type of microbe, from viruses to bacteria to fungi to parasites. Drug resistance—when the microbe is unaffected by the medication—undermines the treatment of many diseases. For typhoid, which is caused by a bacteria, there is growing resistance to many available antibiotics. Tackling drug-resistant typhoid will require effective prevention through vaccines and safe water and sanitation systems. As the world moves toward universal health coverage and achieving the Sustainable Development Goals, it is imperative that global and national leaders take a multisectoral approach to curtail the impact of drug resistance on communities and health systems in countries and identify ways to collaborate across sectors to reduce its effect.

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Typhoid

Typhoid is a serious and potentially life-threatening enteric fever spread through contaminated food and water.

While largely eliminated in industrialized countries, it remains a substantial public health issue that disproportionately affects children and adolescents in low- and middle-income countries. The Global Burden of Disease study estimates that in 2019 there were **more than 9 million cases and more than 110,000 deaths due to typhoid worldwide**. However, the burden is likely underestimated due to difficulties with surveillance and diagnostics.

Research shows that the burden of typhoid goes beyond physical illness and mortality. Even with prompt treatment with antibiotics, **typhoid infections can force children to miss school for weeks**, impacting attendance and performance. **A child's illness has broader economic impacts on the family** due to medical and transport expenses, and time lost from work to care for a sick child.

Improved water quality, sanitation, and hygiene are the major ways to break the typhoid transmission cycle in the long term. However, until these investments can be made in all countries, vaccination with TCV is an important and effective way to prevent typhoid.

Expanded use of TCVs through routine immunization will allow children to remain healthy, stay in school, and for families to continue to work and prosper, preventing the socioeconomic burden from typhoid. It also has the potential to reduce the need for antibiotics and slow further emergence of drug-resistant typhoid.



Drug resistance

Antibiotics are medicines used to treat bacterial infections.

Since their discovery and use, bacteria have naturally evolved and adapted, usually through genetic changes, in response to the constant use of these medicines. When that happens, the bacteria can protect itself from the antibiotic, rendering it ineffective in the treatment of disease and leading to drug resistance.

Drug resistance is occurring everywhere in the world, and the problem is increasing. A growing list of infections—such as pneumonia, tuberculosis, and typhoid—are becoming harder, and sometimes impossible, to treat as available antibiotics become less effective. **Each year, at least 700,000 people die from drug-resistant infections, and that number is expected to rise to 10 million deaths per year by 2050 if nothing is done to reverse course.** Without urgent, coordinated action, we are heading for a post-antibiotic era in which common infections will once again kill people.

Given the severity and potential consequences of inaction, the World Health Organization has developed the Global Action Plan on Antimicrobial Resistance to prioritize national-level action to improve awareness, strengthen surveillance and research, and provide a framework for action.



Appropriate antibiotics are the only effective way to treat typhoid.

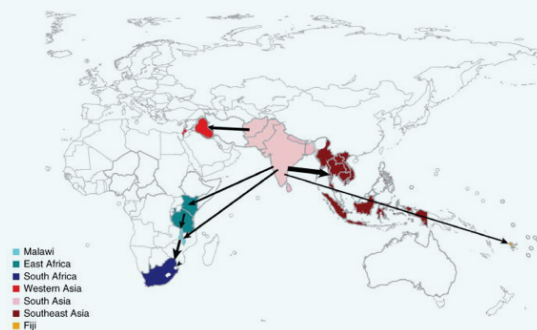
Unfortunately, typhoid has evolved and developed to survive antibiotics. The original first-line antibiotics to treat typhoid were chloramphenicol, ampicillin, and cotrimoxazole; however beginning in the 1970s, strains resistant to these three drugs—multidrug resistance (MDR)—appeared and since spread globally. **MDR typhoid is prevalent in many parts of Asia and sub-Saharan Africa where typhoid has the largest burden.**

The maps to the right demonstrate how MDR typhoid strains have spread across countries in multiple regions. The first shows the transfer of H58-type MDR typhoid, which is predominant in southeast Asia and in eastern and southern Africa. The second map shows the three MDR typhoid types prevalent in Africa—H58 is identified in eastern and southern Africa, while a different type is prevalent in Western Africa, highlighting the organic development of strains independent of each other.

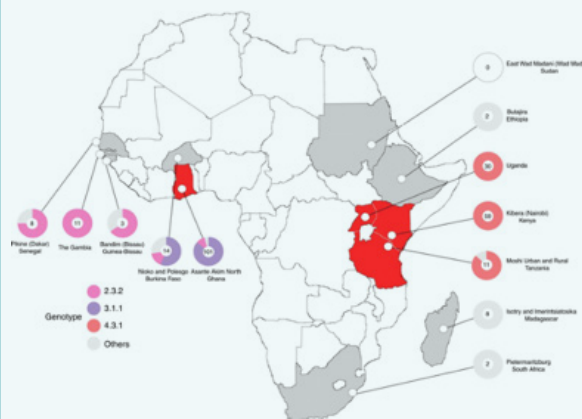
In response, a new class of antibiotics, called fluoroquinolones, became the preferred treatment for MDR typhoid in the 1990s. As treatment with fluoroquinolones increased, however, typhoid again adapted, making these drugs less effective. **Researchers are now observing typhoid strains that are classified as extensively drug-resistant (XDR), meaning they do not respond to five different classes of antibiotics used to treat typhoid, which leaves only one oral antibiotic left.** In Pakistan, an ongoing outbreak of XDR typhoid has sickened more than 15,000 people since 2016. Researchers have also identified XDR strains in Bangladesh that are distinct from the Pakistan strain, which greatly enhances the potential for the rapid, global spread of XDR typhoid.

Drug resistance is a major threat to health across the globe, raising the urgency for prevention through proven interventions including vaccination and access to clean water, safe sanitation, and proper handwashing. Each prevented infection is a case that does not require antibiotic treatment. **TCVs, which can be given to children as young as six months, can play a major role in both decreasing the burden of typhoid and reducing the spread of drug-resistant typhoid strains.** By protecting those most vulnerable from getting sick, we not only keep children healthy so that they can grow and thrive, we also limit the opportunities for typhoid to spread and develop resistance to our remaining antibiotics, allowing treatment options to remain effective for those who do fall ill. TCVs are safe, effective, and available for countries to introduce into their routine childhood immunization schedules.

Major geographic spread of H58-type MDR typhoid¹



Prevalence of MDR typhoid strains in Africa²



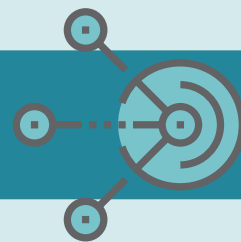
Given typhoid's ability to adapt and evolve to treatment options, it is not a matter of if but when the last oral antibiotic will fail. Once that happens, intravenous antibiotics will be required, which are costly, difficult to administer, and typically unavailable in low- and middle-income countries.



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1. 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.
2. Park SE, Pham DT, Boinett C, et al. The phylogeography and incidence of multi-drug resistant typhoid fever in sub-Saharan Africa. *Nature Communications*. 2018;9(1):5094.

Take Action Now!



- **Call out typhoid specifically within country national action plans** on drug resistance to ensure that it is recognized and included within country policy and plans. Further, health and finance ministries should work together to ensure that these action plans are properly funded.
- **In the short term, prioritize the introduction of TCV** to prevent typhoid infections and slow the spread of drug-resistant typhoid strains, particularly

in areas with high prevalence of drug-resistant typhoid. In addition, countries should invest in improvements to water and sanitation infrastructure to use all the prevention tools available to take on typhoid.

- **Improve access to intravenous antibiotic options** to treat typhoid in low- and middle-income countries to ensure equitable treatment opportunities.



Additional Resources

- **Take on Typhoid website**
- **World Health Organization antimicrobial resistance website**

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a program of the Sabin Vaccine Institute

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Visit www.takeontyphoid.org for the complete series, which includes information about:

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- Drug Resistance
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