

# Integrated Approaches to Controlling Typhoid Fever in Uganda: Synergizing Vaccination, Sanitation, and Antibiotic Stewardship

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## ABSTRACT

Typhoid fever remains a significant public health challenge in Uganda, exacerbated by inadequate water sanitation, antimicrobial resistance (AMR), and limited vaccine coverage. The disease, caused by *Salmonella enterica* serovar Typhi, is primarily transmitted through contaminated food and water, disproportionately affecting urban slums and rural communities. This review explores an integrated approach to controlling typhoid fever by synergizing vaccination, sanitation, and antibiotic stewardship. While typhoid conjugate vaccines (TCVs) offer a promising prevention strategy, their accessibility and implementation face financial and logistical barriers. Water, Sanitation, and Hygiene (WASH) interventions play a crucial role in reducing transmission, yet infrastructural deficiencies hinder their effectiveness. Additionally, the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *S. Typhi* strains necessitates stronger antibiotic stewardship programs to regulate antibiotic use and mitigate resistance. This review underscores the need for a comprehensive, multi-sectoral strategy to combat typhoid fever in Uganda, integrating vaccination programs, improved sanitation infrastructure, and responsible antibiotic use to reduce disease burden and enhance public health outcomes.

**Keywords:** Typhoid fever, *Salmonella Typhi*, Uganda, typhoid conjugate vaccines (TCVs), antimicrobial resistance (AMR)

## INTRODUCTION

Typhoid fever, caused by the bacterium *Salmonella enterica* serovar Typhi (*S. Typhi*), remains a pressing public health challenge in Uganda [1]. The disease is primarily transmitted through the ingestion of food or water contaminated with fecal matter from an infected person. Typhoid fever is endemic in many developing countries, particularly in regions with inadequate water sanitation and hygiene (WASH) infrastructure [2]. Uganda, like many sub-Saharan African countries, has witnessed recurrent typhoid outbreaks, highlighting the continued threat of the disease to public health [3]. Globally, typhoid fever affects millions annually, with an estimated 10–20 million cases and 100,000–160,000 deaths each year [4]. In Uganda, sporadic outbreaks and high endemicity rates underscore the need for sustained efforts to curb its transmission [5]. Urban centers such as Kampala and rural communities with limited access to safe drinking water are particularly vulnerable [6]. The socioeconomic impact of typhoid fever is considerable, affecting workforce productivity, school attendance, and household incomes due to high treatment costs and long recovery periods [7]. The emergence of antimicrobial resistance (AMR) in *S. Typhi* further complicates management strategies. Multidrug-resistant (MDR) strains, resistant to first-line antibiotics such as ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, have been increasingly reported [8]. Additionally, extensively drug-resistant (XDR) strains, which exhibit resistance to even more advanced antibiotics like fluoroquinolones and third-generation cephalosporins, pose a severe challenge to treatment efforts. The growing resistance trend calls for an urgent shift in approach, emphasizing prevention through vaccination, enhanced WASH interventions, and strict antibiotic stewardship to minimize the overuse and misuse of antibiotics [9]. While typhoid conjugate vaccines (TCVs) have shown promise in reducing disease incidence, their adoption

and accessibility remain suboptimal in many parts of Uganda [10]. Effective prevention and control measures require a multi-pronged approach integrating vaccination, improved public health infrastructure, and responsible antibiotic usage. Despite advancements in healthcare and disease prevention, typhoid fever continues to be a significant burden in Uganda [11]. The persistent prevalence of the disease is primarily attributed to inadequate WASH conditions, limited access to clean drinking water, and poor sanitation facilities. Contaminated food and water sources remain major transmission pathways, particularly in informal settlements and rural communities where public health interventions are less effective or poorly implemented. The growing threat of AMR in *S. Typhi* exacerbates the challenge of managing typhoid fever. The increasing resistance to first-line and second-line antibiotics has led to higher treatment failure rates, prolonged hospital stays, and increased mortality risks [12]. With the continued emergence of MDR and XDR *S. Typhi* strains, conventional antibiotic therapy is becoming less reliable, necessitating urgent alternative approaches to disease prevention and control. Current public health strategies in Uganda rely heavily on reactive responses to typhoid outbreaks rather than proactive prevention mechanisms [13]. While vaccination offers a promising solution, coverage remains limited due to logistical challenges, vaccine hesitancy, and resource constraints. Moreover, existing WASH interventions are often inadequately funded or poorly maintained, contributing to recurrent outbreaks. Addressing typhoid fever in Uganda requires a comprehensive approach integrating vaccination, improved WASH conditions, and strengthened antibiotic stewardship programs [14]. Without urgent action, the disease will continue to burden the healthcare system, threaten public health, and contribute to the growing crisis of AMR [15]. This study aims to assess the prevalence and risk factors associated with typhoid fever in Uganda, identify high-risk populations and geographical areas with recurrent outbreaks, examine the role of contaminated water sources, poor sanitation, and food hygiene in disease transmission, evaluate the impact of antimicrobial resistance (AMR) on treatment, and explore the role of vaccination in reducing typhoid fever incidence. The study also evaluates the effectiveness of vaccines, WASH interventions, and community-based interventions in reducing disease transmission. The findings will contribute to the development of more effective disease control measures in Uganda. The public health impact of this study is significant, as understanding the risk factors and epidemiology of typhoid fever will enable policymakers and health practitioners to design targeted interventions for high-risk populations. Identifying the role of AMR in treatment failures will help improve clinical management guidelines and inform appropriate antibiotic use. The study will contribute to disease prevention strategies by evaluating the effectiveness of vaccination programs and highlighting the role of WASH interventions in improving sanitation infrastructure and public health education. Policy and program development will be facilitated by evidence-based recommendations for integrating vaccination, improved sanitation, and antibiotic stewardship into national public health policies. Antimicrobial resistance mitigation strategies will be developed through better antibiotic stewardship programs and promoting awareness of AMR among healthcare professionals and the public [16]. Reducing typhoid fever incidence will alleviate the economic burden on affected households, as families spend less on medical treatment and loss of productivity. Strengthening WASH infrastructure will have broader public health benefits beyond typhoid prevention, including reducing other waterborne diseases such as cholera and dysentery. Future research directions include assessing emerging infectious diseases and vaccine-preventable illnesses in Uganda and using findings on AMR trends to guide further studies on alternative treatment options and novel antimicrobial agents.

### The Role of Vaccination

Typhoid fever is a highly prevalent disease, with typhoid conjugate vaccines (TCVs) being a highly effective and long-lasting intervention. TCVs offer broad immunogenicity across different age groups and reduce dependence on antibiotic treatments, mitigating the threat of antimicrobial resistance (AMR) [17]. They have demonstrated superior efficacy compared to earlier-generation vaccines, such as the polysaccharide vaccine, which provided only short-term immunity and required booster doses. TCVs elicit a strong immune response, conferring long-term protection and effectively reducing the incidence of typhoid fever. The World Health Organization (WHO) strongly advocates for the integration of TCVs into routine immunization schedules in countries with high typhoid fever prevalence, such as Uganda and sub-Saharan Africa and South Asia. Targeted mass vaccination campaigns have proven effective in controlling outbreaks in high-risk communities. The widespread use of TCVs reduces the need for antibiotic treatments, limiting the emergence of antibiotic-resistant *Salmonella Typhi* strains. This reduction in antibiotic use preserves the effectiveness of existing treatments and decreases the economic burden associated with prolonged hospital stays and medical care [18]. The implementation of typhoid vaccination programs, particularly with the introduction of TCVs, represents a transformative step in global public health efforts to combat typhoid fever.

### **Challenges in Vaccine Implementation**

Vaccine implementation faces several challenges, including limited vaccine coverage due to financial and logistical constraints, public skepticism, and the need for continuous funding [19]. In low- and middle-income countries (LMICs), the high cost of vaccine procurement, storage, and distribution often strains national healthcare budgets. Additionally, logistical challenges such as inadequate cold chain infrastructure, inefficient supply chain management, and poor transportation networks further hinder vaccine distribution, especially in rural and hard-to-reach areas. Inadequate health worker training and workforce shortages also contribute to delays in vaccine rollout and administration. Public perception and misinformation play a critical role in vaccine acceptance, with some individuals fearing potential side effects or believing in conspiracy theories. Inadequate health education and poor communication strategies from healthcare authorities contribute to low public awareness about the benefits and safety of vaccines. Language barriers, low literacy levels, and the influence of social media in spreading false information further exacerbate vaccine hesitancy. Addressing these concerns requires targeted public health campaigns, community engagement, and transparent communication from trusted healthcare professionals [20]. Sustained government and international funding is essential for the successful implementation of vaccination programs. Many immunization initiatives, particularly in developing countries, rely heavily on external funding from agencies like WHO, Gavi (the Vaccine Alliance), and UNICEF [21]. Without sustained financial commitment, vaccine programs may face setbacks, increasing the risk of outbreaks of preventable diseases. Vaccine implementation faces multiple challenges, including financial and logistical limitations, public skepticism, and the need for continuous funding. Addressing these issues requires a multi-faceted approach that includes strengthening healthcare infrastructure, improving public awareness, ensuring adequate financing, and fostering international collaboration.

### **Sanitation and Water Hygiene Interventions**

Typhoid fever is a significant public health concern in Uganda, with poor sanitation and contaminated water sources being the primary drivers of disease transmission [22]. Effective Water, Sanitation, and Hygiene (WASH) interventions can play a critical role in reducing infection rates and improving public health outcomes. Key WASH interventions include expanding access to clean drinking water, improving water treatment processes, expanding water distribution networks, and encouraging household-level water purification techniques. Enhancing sanitation infrastructure is essential for preventing human waste from contaminating water sources, reducing the spread of typhoid bacteria. Key strategies include constructing and maintaining latrines and toilets in both rural and urban areas, implementing proper sewage disposal systems, and promoting community-led total sanitation programs. Promoting hygiene education and behavioral change is essential for minimizing typhoid transmission. Educational programs should focus on regular handwashing with soap, teaching safe food handling and storage techniques, and raising awareness about the risks of consuming untreated water and promoting safe alternatives [23]. However, challenges to WASH implementation in Uganda include inadequate funding, infrastructure deficiencies, rural-urban disparities, and behavioral and cultural barriers. Strengthening WASH interventions is crucial in mitigating the spread of typhoid in Uganda, and a multi-sectoral approach involving government agencies, NGOs, and community participation is essential to address funding gaps, expand infrastructure, and promote sustainable behavioral change. Investing in WASH not only reduces typhoid transmission but also enhances overall public health and economic productivity.

### **Antibiotic Stewardship and Combatting Resistance**

The overuse and misuse of antibiotics in treating typhoid fever have led to the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Salmonella Typhi* strains [24]. These strains pose a significant public health challenge, limiting the effectiveness of conventional antibiotics and increasing morbidity and mortality. To combat antibiotic resistance, a robust antibiotic stewardship framework is needed. This involves regulating antibiotic prescription and administration through policies, guidelines, and monitoring systems. Key strategies include strengthening diagnostic capabilities, implementing national treatment guidelines, and improving surveillance systems. Accurate and timely diagnosis is crucial to ensure antibiotics are prescribed only when necessary. Standardized treatment protocols should be based on the latest evidence and resistance patterns, emphasizing first-line antibiotics and restricting last-resort drugs to severe or resistant cases [25]. Effective antimicrobial resistance monitoring is essential for tracking emerging resistance trends, informing public health policies, and adapting treatment guidelines. Public awareness campaigns, healthcare provider training, and regulatory policies limiting over-the-counter antibiotic sales are complementary measures to curb antibiotic misuse. By implementing comprehensive stewardship initiatives, countries can slow the spread of MDR and XDR *Salmonella Typhi* strains, ensuring typhoid remains a treatable disease with effective antibiotic options in the future.

### Economic Considerations

Typhoid fever is a significant economic burden on individuals, families, healthcare systems, and national economies. Direct costs include hospitalization and outpatient care, diagnostic tests and laboratory investigations, and medication and treatment costs. These costs can be catastrophic for low-income households, forcing them to incur debt or forgo essential expenses like food and education [26]. Indirect costs include loss of productivity, long-term complications, and impact on caregivers. Individuals suffering from typhoid fever often experience prolonged illness, leading to absenteeism from work or school, reduced productivity, and economic losses for employers and businesses. Chronic complications can lead to long-term disabilities, further reducing an individual's ability to work and contribute to economic development. Caregivers may also face additional financial losses when their children or family members fall ill. Investing in preventive measures, such as vaccination programs, improved sanitation, and clean water supply, is a cost-effective approach to reducing the economic burden of typhoid fever [27]. Studies have shown that vaccination campaigns significantly reduce the incidence of typhoid fever, leading to decreased healthcare expenditures and improved productivity. Investment in water, sanitation, and hygiene (WASH) infrastructure reduces exposure to contaminated water and food, preventing outbreaks and saving long-term public health costs. Governments and stakeholders must prioritize sustainable funding for typhoid fever prevention and control efforts through public-private partnerships, integration of typhoid vaccination into national immunization programs, international donor support and development aid, and economic policies that allocate resources efficiently toward disease prevention rather than reactive treatment. By addressing the economic burden of typhoid fever through proactive investments, governments can enhance public health, reduce financial strain on healthcare systems, and promote long-term economic productivity.

### CONCLUSION

Typhoid fever remains a significant public health issue in Uganda, exacerbated by inadequate water, sanitation, and hygiene (WASH) infrastructure, limited vaccine coverage, and the growing threat of antimicrobial resistance (AMR). To control and prevent the disease, a comprehensive approach is needed. Vaccination, particularly through typhoid conjugate vaccines, has shown potential in reducing disease incidence and limiting antibiotic reliance. However, barriers like logistical constraints, vaccine hesitancy, and financial limitations must be addressed through governmental and international support, improved healthcare infrastructure, and public awareness campaigns. Strengthening WASH interventions, such as expanding access to clean drinking water, enhancing sanitation facilities, and promoting hygiene education, is crucial for reducing typhoid transmission. Antibiotic stewardship is also vital in combating the rise of MDR and XDR strains of *Salmonella Typhi*. A synergistic approach integrating vaccination, improved sanitation, and responsible antibiotic use is essential for effective control. Policy reforms, increased funding, and multi-sectoral collaboration are crucial for overcoming existing challenges and ensuring sustainable disease prevention efforts.

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