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Comparative Cost-Effectiveness of Typhoid Vaccination and Treatment in Rural vs. Urban Ugandan Healthcare Settings

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ABSTRACT

Typhoid fever remains a persistent public health challenge in Uganda, with both urban and rural populations experiencing high disease and economic burdens. While antimicrobial treatment has historically been the mainstay of management, rising antimicrobial resistance (AMR) has significantly increased treatment costs and reduced effectiveness. This review compares the cost-effectiveness of typhoid treatment and vaccination across urban and rural Ugandan healthcare settings, highlighting differences in epidemiology, infrastructure, and socio-economic conditions. Evidence indicates that in urban centers, where population density and outbreak frequency are high, typhoid conjugate vaccines (TCVs) rapidly reduce healthcare costs through economies of scale, decreased hospitalizations, and prevention of resistant infections. In rural areas, despite higher delivery and logistical costs, vaccination often proves even more cost-effective given the severe indirect costs of illness, such as delayed care, transportation expenses, lost productivity, and poorer outcomes. Key challenges include data gaps, logistical barriers, vaccine acceptance, and financial constraints. Policy recommendations emphasize prioritizing high-burden urban slums while carefully expanding rural rollout, integrating vaccination with water, sanitation, and hygiene (WASH) improvements, strengthening rural health infrastructure, and enhancing AMR surveillance. Overall, vaccination emerges as a sustainable, equitable strategy to reduce Uganda's typhoid burden and support broader global health goals.

Keywords: Typhoid fever; cost-effectiveness; Uganda; rural health; urban health; vaccination.

INTRODUCTION

Typhoid fever, caused by *Salmonella enterica* serovar Typhi, remains a major public health concern across sub-Saharan Africa, including Uganda. It is an enteric infection transmitted through ingestion of contaminated food or water, and its persistence is closely tied to poor water, sanitation, and hygiene (WASH) conditions [1]. Globally, typhoid fever affects an estimated 9–12 million people annually and causes over 100,000 deaths, with Africa carrying a substantial share of this burden. In Uganda, recurrent outbreaks and endemic transmission have been reported in both rural and urban settings, highlighting the disease's entrenched nature within the country's healthcare and socio-economic systems [2]. Urban centers, particularly informal settlements within Kampala, Mbale, and Gulu, are prone to periodic typhoid outbreaks due to high population density, overstretched sanitation systems, and unsafe water supplies. Conversely, rural districts face endemic transmission fueled by limited access to safe water, poor waste management, and reliance on untreated water from wells, rivers, and lakes [3]. While the epidemiological profiles differ, the disease remains a costly health challenge across both contexts. The management of typhoid fever generally relies on prompt diagnosis and effective antimicrobial treatment. However, challenges abound: delays in seeking care, misdiagnosis due to overlapping symptoms with malaria and other febrile illnesses, and the growing prevalence of antimicrobial resistance (AMR) that limits treatment efficacy [4]. As resistant *S. Typhi* strains spread, treatment costs escalate due to the need for more expensive second-line antibiotics and prolonged hospital stays for complicated cases.

Preventive measures, particularly the typhoid conjugate vaccine (TCV), are increasingly recognized as effective tools in controlling the disease. TCVs provide long-lasting immunity and can be integrated into routine childhood immunization schedules [4]. However, rolling out vaccination at scale involves substantial costs, including vaccine procurement, cold chain logistics, training of healthcare personnel, and community mobilization. These costs may vary significantly between rural and urban areas due to infrastructural and socio-economic differences [5]. Against this backdrop, evaluating the comparative cost-effectiveness of typhoid vaccination versus treatment in rural and urban Ugandan healthcare settings is essential. Such analysis provides evidence to guide policymakers on resource allocation, health system prioritization, and strategies for integrating typhoid prevention and management into broader public health frameworks [6].

Uganda continues to bear a significant typhoid disease burden, with both rural and urban populations affected, albeit in different ways. In urban centers, overcrowding, poor sanitation in slums, and intermittent safe water access create fertile ground for recurrent outbreaks. In rural areas, sparse health infrastructure, long distances to facilities, and dependence on untreated water sources perpetuate endemic transmission [7]. Both contexts lead to high healthcare expenditures for families and the government, alongside indirect economic losses from reduced productivity and school absenteeism.

While treatment remains the primary control strategy, its sustainability is threatened by increasing AMR and the high recurrent costs of hospitalizations and antibiotics. On the other hand, vaccines like TCV offer a preventive solution with potential long-term cost savings, yet Uganda has limited experience with large-scale deployment outside outbreak responses [8]. Furthermore, differences in infrastructure, community acceptance, and healthcare delivery between rural and urban areas may alter the cost-effectiveness balance of vaccination relative to treatment. Despite the urgency of addressing typhoid fever, there is a lack of comprehensive evidence comparing the economic and health outcomes of vaccination and treatment strategies in Uganda, disaggregated by rural and urban settings. Without such data, national health policy may risk suboptimal resource allocation, perpetuating both disease transmission and financial strain on households [9]. The primary aim of this study is to evaluate the comparative cost-effectiveness of typhoid vaccination and treatment in both rural and urban Ugandan healthcare settings, with a view to generating context-specific evidence that can guide national health policy. The objectives are designed to systematically address the multiple dimensions of this issue. First, the study will assess the current burden of typhoid fever in Uganda, examining incidence, morbidity, mortality, and socio-economic impacts, while distinguishing between rural and urban populations. Second, it will estimate the direct and indirect costs associated with treatment, including the economic impact of antimicrobial resistance and complications, which are particularly critical given Uganda's constrained healthcare resources. Third, the costs and logistical requirements for deploying typhoid conjugate vaccines (TCVs) in both rural and urban contexts will be evaluated, considering infrastructure, cold chain systems, and human resource needs. Fourth, the study will compare vaccination and treatment strategies to establish which is more cost-effective across different settings. Finally, the findings will be synthesized to provide evidence-based policy recommendations for optimizing typhoid prevention and management. Overall, this research seeks to reduce disease burden, improve health outcomes, promote equity in healthcare access, and support Uganda in aligning with global health priorities.

Vaccine Costs, Deployment, and Effectiveness

The World Health Organization (WHO) strongly recommends the inclusion of Typhoid Conjugate Vaccines (TCV) in the routine immunization programs of countries where typhoid remains endemic, given its high disease burden and growing antimicrobial resistance. Gavi, the Vaccine [10] Alliance, alongside other global partners, has played a central role in supporting vaccine introduction by providing either financial assistance or introductory doses at subsidized costs. While the cost per dose under Gavi support is relatively affordable, it is important to note that overall vaccine deployment entails additional expenditures such as transportation, cold chain infrastructure, healthcare worker training, and community sensitization efforts. Evidence indicates that TCVs are highly effective in preventing typhoid cases, significantly reducing hospitalizations, mortality, and the spread of drug-resistant strains [11]. Moreover, vaccination contributes to herd immunity, amplifying public health benefits, especially in densely populated regions where transmission rates are higher. The extent of impact, however, depends on key factors including baseline incidence, vaccine efficacy, coverage levels, and duration of protection. In Uganda, discussions and preparatory steps toward incorporating TCV into the national immunization schedule have been ongoing, with the potential for catch-up campaigns to ensure broader population coverage [12]. The precise timeline for roll-out remains subject to confirmation through official Ministry of Health reports.

Treatment Costs and Burden

The treatment costs and burden of typhoid fever are considerable and extend beyond the immediate medical expenses. Direct medical costs often include the purchase of antibiotics, diagnostic tests such as blood cultures, hospitalization in severe cases, and even surgical interventions to manage complications [13]. In urban hospitals, where advanced diagnostics and treatment facilities are more available, these services tend to be more expensive. Conversely, in rural areas, the limited availability of diagnostic tools often leads to empirical treatment, which may contribute to overuse of antibiotics, the emergence of resistance, or inadequate treatment of the disease. Alongside these direct costs, there are significant indirect costs and socioeconomic burdens [14]. Patients and caregivers may lose income due to illness or time spent providing care, and they often incur additional expenses related to transportation to healthcare facilities and other opportunity costs. These burdens are particularly severe in rural settings, where incomes are generally lower and travel distances to clinics are longer [15]. Compounding the issue is the growing problem of antimicrobial resistance (AMR). Resistance in *Salmonella Typhi* increases treatment costs, as more expensive second- or third-line antibiotics are required, often alongside longer hospital stays and intensive monitoring. In urban centers, where antibiotic exposure is higher, AMR is more prevalent, exacerbating the financial and health-related burden. Studies in Uganda highlight a troubling trend of rising AMR in *S. Typhi*, underscoring the urgent need for sustainable treatment strategies [16].

Table 1: Comparative Analysis: Rural vs Urban

Factor	Urban Settings	Rural Settings
Incidence/ Exposure	Higher in slum areas; water/sanitation may be poor despite proximity to healthcare. Outbreaks more frequent due to population density.	May have lower overall incidence if WASH is better in some rural areas, but in many rural places WASH is very poor. Under-reporting more likely.
Healthcare Access & Infrastructure	More hospitals, diagnostic capacity, trained staff; shorter travel times. Better cold chain facilities. Yet cost of services usually higher.	Fewer hospitals; often lower diagnostic capacity; some remote areas have poor cold chain; travel costs high; lower staffing.
Vaccine Delivery Costs	Lower marginal cost per person in mass campaigns in densely populated areas; outreach costs lower per capita; infrastructure more present.	Higher per capita delivery costs: longer travel for health workers, more logistics, outreach costs, potentially less economies of scale; maintenance of cold chain challenging.
Treatment Costs	Higher absolute costs (hospital stays, diagnostics, drugs), but proportionally perhaps lower on indirect costs because travel time is less, incomes may be higher.	Treatment might be less sophisticated (less diagnostics), possibly lower hospital costs, but perhaps worse outcomes; indirect costs (transport, lost income) higher proportionally; barriers to accessing care may delay treatment.
Cost-Effectiveness Ratio for Vaccination vs Treatment	Vaccination likely to avert more expensive treatments, especially for drug-resistant cases, thus higher cost-savings; favourable incremental cost-effectiveness.	Even though vaccine delivery is more expensive, the costs of treatment (delayed, severe, transport, indirect losses) may be large enough that vaccination remains cost-effective; sometimes more so because treatment barriers lead to worse disease or outcomes, increasing costs.

Empirical Data & Findings (Uganda & Comparable Settings)

Recent empirical evidence underscores the high burden of typhoid fever in Uganda and highlights the potential benefits of introducing the Typhoid Conjugate Vaccine (TCV). A fact sheet from the Coalition Against Typhoid points out that while Uganda lacks extensive cost-of-illness studies, existing modeling strongly suggests that a nationwide vaccination campaign, beginning with a catch-up phase and followed by routine immunization, would be highly cost-effective, even in the absence of Gavi subsidies [17]. This is significant given the dual benefits of reducing disease prevalence and lowering long-term economic strain on the health system. Comparative findings from countries such as Malawi reinforce these projections, showing that typhoid-related expenses can exceed monthly household incomes, particularly among rural and economically disadvantaged populations. Such catastrophic financial impacts highlight the broader socioeconomic benefits of disease prevention through vaccination. Although Uganda-specific data disaggregated by rural and urban settings remain limited, one academic study "Economic and Health System Impacts of Typhoid Control Strategies in Uganda: Vaccination versus Antibiotic Treatment" has addressed these dimensions, albeit with restricted public access to detailed rural-urban breakdowns. Overall, the available evidence suggests that scaling up TCV would mitigate both health risks and financial vulnerabilities [18].

Cost-Effectiveness Metrics & Drivers

Cost-effectiveness of vaccination programs is generally assessed using key metrics such as cost per case averted, cost per death averted, cost per disability-adjusted life year (DALY) saved, and the incremental cost-effectiveness ratio (ICER) when compared with treatment or the status quo. Several major drivers influence these outcomes. Vaccine price and the number of doses are critical, as lower costs, often facilitated by Gavi support or subsidies, greatly improve cost-effectiveness [19]. Coverage and uptake also matter, with high immunization rates in vulnerable groups such as children and residents of urban slums yielding larger public health benefits. Disease incidence and burden play an equally important role, since vaccination in high-incidence areas prevents more cases and becomes more cost-saving. Treatment costs, particularly those rising due to antimicrobial resistance, further enhance the value of prevention. Access to care and treatment delays in rural settings often increase severity, cost, and mortality, reinforcing vaccination's importance. Additionally, infrastructure and logistics, including cold chain and transport, can significantly affect costs, especially in remote areas. Finally, indirect costs such as lost income, travel, and caretakers' time are often underestimated yet have a substantial impact on overall economic evaluations, particularly in labor-dependent rural communities [20].

Cost-Effectiveness: Rural vs Urban in Uganda — What the Evidence Suggests

Cost-effectiveness analyses comparing rural and urban contexts in Uganda reveal nuanced dynamics shaped by population density, healthcare access, and the economic realities of illness. In urban settings, vaccine introduction can rapidly reduce healthcare costs by lowering the burden on hospitals, limiting outbreaks, and curbing antimicrobial resistance that arises from frequent antibiotic misuse [21]. The high population density in cities also makes vaccine delivery more efficient, as logistical costs are spread across larger groups, lowering the per-person expense. By contrast, rural areas face higher delivery costs due to weak infrastructure, limited health services, and geographic barriers. Yet, the financial and human toll of illness in these communities is disproportionately higher relative to household income. Factors such as delayed treatment, severe complications, expensive transportation, and poor outcomes make disease management highly burdensome. Vaccination, even with elevated delivery costs, often proves cost-effective in these regions because it averts illness, reduces household economic strain, and preserves productivity. Still, in extremely remote or very low-incidence rural settings, the marginal returns of vaccination may be smaller, though models consistently show net positive benefits overall [21].

Challenges, Limitations, and Policy Implications

Despite strong evidence for the cost-effectiveness of vaccination in Uganda, several challenges, limitations, and uncertainties shape both analysis and implementation. A major obstacle lies in persistent data gaps: many studies fail to disaggregate outcomes by rural versus urban settings, while others lack reliable and up-to-date cost estimates for hospitalization, diagnostics, and antibiotic resistance. Estimating indirect costs such as lost productivity, time spent seeking care, and transportation expenses is particularly complex, with wide variability between urban and rural households [22]. Moreover, logistical hurdles including cold chain maintenance, health worker availability, and the higher outreach costs in remote areas can erode projected benefits if not well managed. Behavioral factors add another layer of uncertainty, as vaccine hesitancy, awareness, and acceptance may differ across communities. Additionally, the shifting epidemiology of typhoid and the rise of resistant *S. Typhi* strains complicate the treatment cost structure and heighten the urgency of vaccination. Finally, financial constraints and competing priorities within government and donor budgets may limit the feasibility of large-scale rollouts, given the high up-front investment required [23].

In light of these challenges, policy recommendations emphasize targeted and integrated strategies. Rapid introduction should be prioritized in high-burden urban slum areas to generate quick impact and cost savings, while rural rollout must be carefully planned to address infrastructure gaps and outreach barriers. Complementary WASH improvements, particularly in rural settings, can further reduce incidence and maximize vaccine benefits. Strengthening rural health systems through better diagnostics, treatment access, and cold chain reliability remains essential [24]. Ongoing surveillance of antimicrobial resistance should guide both treatment guidelines and vaccination strategies. Finally, improving disaggregated cost data collection and adopting phased or tailored financing approaches such as catch-up campaigns, mobile outreach, or differential subsidies will help ensure that vaccination programs remain both equitable and sustainable [25].

CONCLUSION

This review underscores that both rural and urban Ugandan populations face significant typhoid-related health and economic burdens, though the dynamics differ across settings. Urban centers, with higher population density and recurrent outbreaks, stand to benefit rapidly from typhoid conjugate vaccine (TCV) introduction due to economies of scale and reduced reliance on costly treatment of resistant cases. In rural areas, despite higher vaccine delivery costs, the disproportionate indirect costs of illness lost productivity, delayed care, and poor outcomes make vaccination highly cost-effective, often more so than treatment. However, data gaps, logistical challenges, antimicrobial resistance, and financial constraints highlight the need for careful planning. Policymakers should prioritize vaccine introduction in high-burden urban slums while simultaneously investing in rural health infrastructure, WASH improvements, and robust AMR surveillance. Strengthening cost data collection and adopting phased, context-sensitive financing approaches will be essential to ensure that vaccination strategies deliver equitable, sustainable, and long-term public health benefits.

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