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The Role of Vaccines in Mitigating Antimicrobial Resistance in Uganda

GARP - Uganda Policy Brief

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS AND ACRONYMS

ACT	Artemisinin-based combination therapies
AMC	antimicrobial consumption
AIDS	acquired immunodeficiency syndrome
AMR	antimicrobial resistance
AMU	antimicrobial use
ARI	acute respiratory tract infection
BCG	Bacillus Calmette-Guérin
DALYs	disability-adjusted life years
DPT-Hib-HepB	pentavalent vaccine for diphtheria pertussis, tetanus, Haemophilus influenzae type B and hepatitis B
FQNS	fluoroquinolone nonsusceptible
GDP	gross domestic product
Hib	Haemophilus influenzae type B
HIV	human immunodeficiency virus
IPD	invasive pneumococcal disease
IPV	injectable polio vaccine
LRTI	lower respiratory tract infection
LMICs	low- and middle-income countries
MAAP	Mapping Antimicrobial Resistance and Antimicrobial Use Partnership
MCV	measles-containing vaccine
MDR	multidrug resistant
OPV	oral polio vaccine
PCV	pneumococcal conjugate vaccine
RotaC	rotavirus vaccines (completed dose)
RSV	respiratory syncytial virus
STI	sexually transmitted infection
TB	tuberculosis
TCV	typhoid conjugate vaccine
UTI	urinary tract infection
WASH	water, sanitation, and hygiene
WHO	World Health Organization
YFV	yellow fever vaccine

EXECUTIVE SUMMARY

Antimicrobial resistance (AMR) is a global challenge that threatens to reverse the advances of modern medicine, potentially ushering us into a post antibiotic era. AMR occurs when medicines used to treat infections caused by bacteria, viruses, fungi, and parasites become less effective, often due to factors such as prolonged exposure to antimicrobials or adaptive changes in the organisms over time. Although many factors contribute to the emergence and spread of AMR, the overuse and misuse of antimicrobials are the primary drivers behind the widespread prevalence of resistant strains.

AMR presents a multifaceted challenge, jeopardizing the effectiveness of antimicrobial treatments and compromising our ability to manage infectious diseases. The economic burden associated with treating resistant infections further impacts individuals, health care systems, and national economies. The World Bank projects that AMR might incur an estimated US$1 trillion in additional health care costs by 2050, alongside potential annual gross domestic product (GDP) losses of US$1–3.4 trillion by 2030.

In Uganda in 2021, of the 47,821 deaths due to bacterial infections, 21,258 were associated with six leading drug-resistant pathogens, including *Streptococcus pneumoniae*, *Klebsiella pneumoniae, Escherichia coli,* and *Staphylococcus aureus*, pathogens that contribute significantly to its rising infectious disease burden; 5,616 deaths were directly attributable to AMR. Diseases such as malaria, acquired immunodeficiency syndrome (AIDS), lower respiratory tract infections (LRTIs), tuberculosis, measles, diarrheal diseases, and sexually transmitted infections (STIs) are major contributors to deaths and disability-adjusted life years (DALYs). The rising rates of AMR add to the already high burden of infectious diseases, making treatment more difficult. Poor health care access, limited availability of antibiotics, inadequate water, sanitation, and hygiene facilities, and environmental pollution all contribute to the rise in AMR.

Given the limited progress in developing new antimicrobials, the need for alternative strategies has intensified, making vaccination a cornerstone in the battle against AMR. Vaccines are pivotal in combating AMR and safeguarding public health by preventing infections and providing immunity against diseases. This reduces the reliance on antimicrobial treatments and minimizes the prevalence of resistant pathogens. Increased vaccine coverage reduces infections, dependence on antibiotics, and selective pressure for the emergence of resistant strains.

*Photo source: Braconnier 2017

By preventing infections, vaccines help maintain the effectiveness of antimicrobial treatments and ensure their continued success in managing diverse medical conditions. Vaccination programs also offer a cost-effective means of infection prevention, reducing the financial strain on health care systems. Given the escalating threat of AMR, it is imperative to prioritize and strengthen national immunization programs to achieve widespread coverage and protection against vaccine-preventable diseases. To guide policymakers, this policy brief presents a summary of the essential areas and priority interventions that need to be considered when formulating a national strategy to combat AMR.

Key Recommendations

1. Maintain high coverage of all available vaccines, including the pneumococcal conjugate, rotavirus, Bacillus Calmette-Guérin, measles-rubella, and hexavalent (DPT-Hib-HepB) vaccines.

2. Expedite the approval and rollout of current vaccines and vaccines in development, such as typhoid, malaria, and adult and adolescent tuberculosis vaccines and monoclonal antibodies against the respiratory syncytial virus.

3. Enhance collaborations between institutions and authorities working on AMR and immunization to promote alignment in national strategies for AMR that include vaccination-specific targets and objectives and the generation of AMR and vaccine data through research.

4. Develop and implement a comprehensive communication strategy for AMR and the role of vaccines in mitigating AMR.

COUNTRY PROFILE

Uganda, officially known as the Republic of Uganda, has a population of 48.5 million as of 2023 (World Bank 2023), with 73 percent residing in rural areas (World Bank n.d-a). Life expectancy at birth has steadily increased, reaching 66 years in 2021, up from 48.8 years in 2000 (WHO n.d-b). Despite this progress, in 2019, communicable diseases, along with maternal, prenatal, and nutritional-related conditions, accounted for 52 percent of deaths (World Bank n.d-b); communicable diseases alone were responsible for 36 percent of deaths (WHO Africa Region 2023). By 2021, the leading causes of death were malaria, COVID-19, and neonatal disorders (IHME 2024). These figures highlight the ongoing burden of preventable diseases and emphasize the need for enhanced health care interventions.

Health care expenditure in Uganda provides insight into the financial resources allocated to address these health challenges. In 2021, the annual health care expenditure was 4.67 percent of GDP (WHO n.d-b), with out-of-pocket expenditure at US$15.18 per person (IHME 2024). This is expected to rise to US$23.73 by 2050, reflecting the growing health care costs. Government expenditure on health care was US$11.70 per person in 2021. Despite efforts such as removing user fees to improve health care access, the high incidence of catastrophic health expenditures remains a concern (Nannini et al. 2021), contributing to the under-five mortality rate of 64.6 deaths per 1,000 live births in 2021 (IHME 2024).

Furthermore, considerable disparities exist in access to essential services. In 2022, only 47.1 percent of the population had access to electricity (World Bank n.d-c). In 2019, the mortality rate attributed to unsafe water, unsafe sanitation, and lack of hygiene was 28.1 per 100,000 (World Bank n.d-c). In 2022, just over half (59 percent) of the population used at least basic drinking water services (World Bank n.d-e), and only one-third (30.9 percent) had access to basic handwashing facilities, including soap and water (World Bank n.d-f). Only 18 percent had access to safely managed sanitation services, and 19 percent used safely managed drinking water services (World Bank n.d-g). These statistics emphasize the need for continued efforts to improve the water, sanitation, and hygiene (WASH) infrastructure to enhance public health outcomes. The limitations in access to WASH facilities have been closely linked to the high rates of infectious diseases and the increasing challenge of antimicrobial resistance (AMR) in Uganda (WHO 2023a). Moreover, drug-resistant infections impose a significant health and economic burden in low- and middle-income countries (LMICs) such as Uganda, where poverty is considered an important factor, contributing to partial or delayed access to antibiotics among patients (World Bank n.d-d).

THE BURDEN OF INFECTIOUS DISEASE AND AMR IN UGANDA

Infectious diseases contribute significantly to the mortality rate in Uganda, even though vaccines can prevent many of these (WHO 2019) (Table 1). The pathogens responsible for the majority of the infectious disease burden include *Salmonella typhi*, which causes typhoid fever; *Plasmodium* species, which cause malaria; *Staphylococcus aureus* and *Klebsiella pneumoniae*, which cause respiratory infections; and *Escherichia coli*, which causes diarrheal diseases (IHME 2021; Murray et al. 2022; Nabadda et al. 2021).

Table 1. The Burden of Infectious Disease Ranked Against All Causes of Mortality and Disability in Uganda, 2021

Rank in the Top 10 causes of death	Rank in the Top 10 causes of DALYs	Disease	Percentage of total deaths	Percentage of total DALYs
1	1	Malaria	13.65	17.09
5	2	Neonatal disorders	9.45	13.84
3	3	HIV/AIDS	7.62	7.03
2	4	Lower respiratory infections	4.2	3.51
4	6	Tuberculosis	3.59	2.62
-	9	Diarrheal diseases	2.71	2.98

Source: IHME 2021; WHO 2021a

Disability-adjusted life years (DALYs) describe disease burden in terms of years of life lost prematurely and loss of productive years due to ill health. The rank represents each infectious disease category's contribution to total DALYs, and deaths compared to all other causes. STI = sexually transmitted infection.

The high burden of infectious diseases is compounded by rising levels of AMR, which makes them increasingly challenging to treat. Poor access to health care facilities, weak diagnostic capabilities, substandard antibiotics, inadequate WASH infrastructure, and environmental contamination further impede containing and managing AMR and associated infectious diseases (WHO 2023a).

AMR surveillance data in Uganda show a high prevalence of resistant pathogens that commonly cause urinary tract infections (UTIs). A study conducted in rural hospitals and clinics throughout Uganda and Kenya found that 93 percent of 55 UTI-causing *E. coli* strains and virtually all 19 *K. pneumoniae* strains detected were multidrug resistant (MDR) (Decano et al. 2021). A systematic review of AMR rates in Uganda identified *E. coli* and *S. aureus* as the most frequently reported bacteria for 1995–2020 (Kivumbi et al. 2021). However, the review noted an underrepresentation of rural studies and those from resource-limited settings, skewing the representation of the Ugandan population in AMR-related literature. Retrospective AMR and antimicrobial consumption (AMC) data collected from 16 laboratories between 2016 and 2018 by the Mapping Antimicrobial Resistance and Antimicrobial Use Partnership (MAAP) project provide further insights into the AMR landscape in Uganda (MAAP consortium 2022). Among the 22,349 patient specimens assessed, *Staphylococcus* and *Escherichia* species were the most frequently isolated bacterial organisms.

The 2024 WHO Bacterial Priority Pathogens List categorizes 15 families of antibiotic-resistant pathogens into critical-, high-, and medium-priority levels for research, development, and public health interventions (WHO n.d-c). The MAAP analysis showed moderate to high resistance to antibiotics among bacterial priority pathogens, including third-generation-cephalosporin-resistant *Enterobacterales* (49–55 percent), carbapenem-resistant *Acinetobacter baumannii* (30–54 percent), fluoroquinolone-resistant *Neisseria gonorrhoea* (34 percent), methicillin-resistant *Staphylococcus aureus* (34–36 percent), penicillin-resistant *Streptococcus pneumoniae* (34 percent), carbapenem-resistant *Pseudomonas aeruginosa* (10–22 percent), and fluoroquinolone-resistant *Salmonella* species (5–29 percent). For the WHO priority pathogens assessed in the study, vaccines exist against *Streptococcus pneumoniae* (causing pneumococcal disease) and *Salmonella typhi*, and a vaccine for *Neisseria gonorrhoea* is in late-stage development (Tacconelli et al. 2018; WHO 2021b).

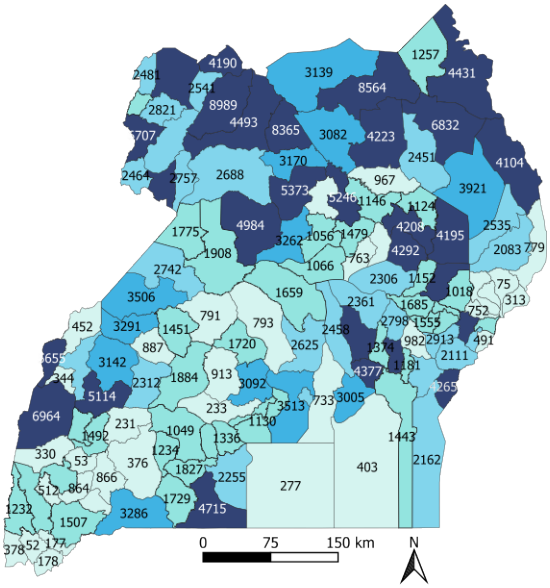
Tuberculosis (TB) is one of the many conditions impacted by rising levels of resistance. MDR-TB management in Uganda has been estimated to cost US$3,722 per patient, which is over nine times more than drug-susceptible TB. This makes the impact of economic insecurity among patients on antibiotics particularly concerning (Muttamba et al. 2020). The total TB incidence in Uganda was estimated to be around 94,000 cases in 2022, with 30,000 of those positive for human immunodeficiency virus (HIV) (29). In 2021, 502 rifampicin-resistant TB or multidrug-resistant tuberculosis (MDR-TB) cases were confirmed in Uganda (World Bank n.d-c). Around 70 percent were diagnosed using the WHO-recommended rapid diagnostics, and 292,090 people were started on TB preventative treatment in 2022 (WHO 2024).

In Uganda, malaria contributes significantly to morbidity and mortality attributable to infectious diseases every year (Figure 1). According to the WHO World Malaria Report from 2022, Uganda ranks third globally in malaria burden, accounting for 5.1 percent of cases. Uganda had the fifth highest burden of deaths due to malaria, 3.2 percent of the global total (Severe Malaria Observatory n.d.; WHO 2023c). Between 2019 and 2021, it recorded an estimated 1.7 million malaria cases (WHO 2023c). The high prevalence of drug-resistant *Plasmodium falciparum*, the dominant parasite, intensifies this burden. It is estimated to cause 9.31 cases and 4.31 deaths per 1,000 persons in the nation (Hamilton et al. 2023). Malaria control interventions, such as insecticide-treated nets, indoor residual spraying, combination medications, and rapid diagnostic tests, are already in place, although sustainable access varies across regions (Gibson 2023; Ministry of Health, Government of Uganda 2019). The complex nature of malaria control globally emphasizes the role of vaccinations. Since 2019, the malaria vaccine RTS, S/AS01 has been trialed in Ghana, Kenya, and Malawi and had positive results in reducing the disease burden (WHO n.d-d).

Lower respiratory tract infections (LRTIs) have also been reported to significantly impact public health and contribute to the burden of AMR. LRTIs, such as pneumonia and influenza, are among the leading causes of death, accounting for 4.2 percent of total deaths and 3.51 percent of total disability-adjusted life years (DALYs) (IHME 2021). They are often caused by pathogens such as *S. pneumoniae* and *H. influenzae,* which have shown increasing resistance to commonly used antibiotics (Jansen et al. 2021). This resistance complicates treatments and increases the risk of prolonged illness, higher hospitalization rates, and health care costs.

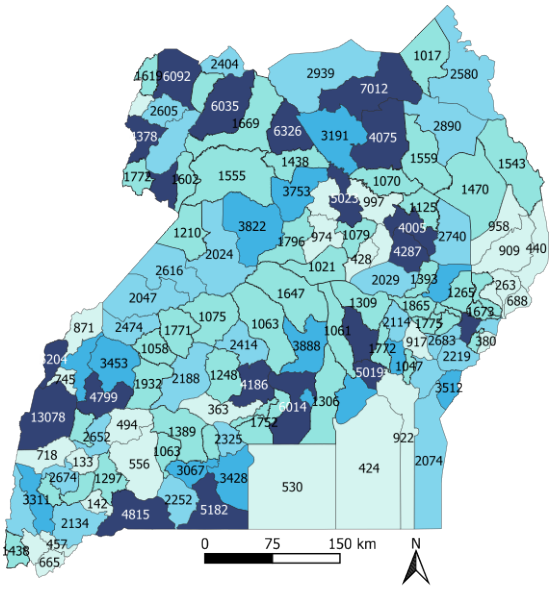
Diarrheal diseases, which account for 2.71 percent of total deaths and 2.98 percent of DALYs in Uganda, are primarily caused by pathogens such as *E. coli,* rotavirus, and *Shigella spp*. (IHME 2021). Inadequate WASH facilities intensify their effects, and the spread of resistant strains of these bacteria further challenges the treatment landscape, making the management of these diseases more complex and expensive.

Antibiotic-resistant genes have also been detected in *Salmonella* strains linked to unsanitary wastewater treatment and poultry slaughterhouses in Uganda, suggesting environmental and zoonotic transmission (Afema et al. 2016). Despite the extensive use of antibiotics in livestock across the country, studies have found promise for prophylactic chicken vaccination in reducing disease by 59.6 percent, suggesting other avenues for combating AMR that have yet to be thoroughly exploited (Emes et al. 2023).



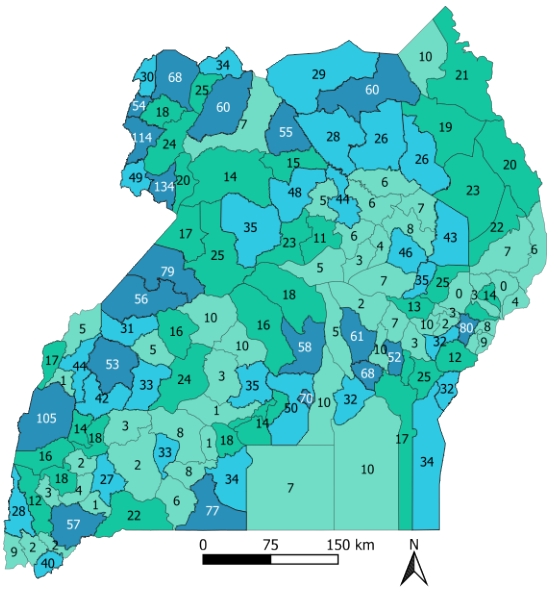
Legend
Average Annual Cases
0 - 1000 | 1001 - 2000 | 2001 - 3000
3001 - 4000 | >4000

A - Under five average malaria cases per district



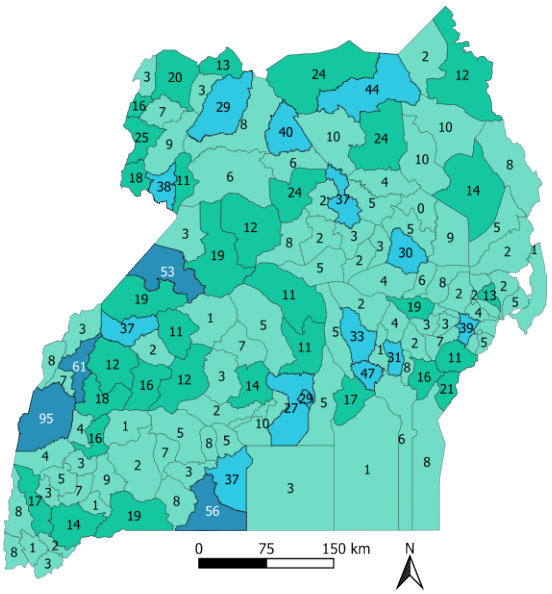
Legend
Average Annual Cases
0 - 1000 | 1001 - 2000 | 2001 - 3000
3001 - 4000 | >4000

B - Five and above average malaria cases per district



Legend
Average Annual Deaths
0 - 10 | 11 - 25 | 26 - 50 | >50

C - Under five average malaria deaths per district



Legend
Average Annual Deaths
0 - 10 | 11 - 25 | 26 - 50 | >50

D - Five and above average malaria deaths per districts

Figure 1. Subnational Spatial Distribution of Malaria Cases and Deaths Among Populations Under Five Years of Age, 2015–2021

Source: Ministry of Health, Government of Uganda (2020a, 2021)

NATIONAL IMMUNIZATION PROGRAM - UGANDA

Vaccines effectively reduce antimicrobial use (AMU), the burden of infectious diseases, and the risk of AMR nationally and globally. Uganda's national childhood immunization program includes nine vaccines that protect against several infectious diseases (Ministry of Health, Government of Uganda n.d.) and are part of the Expanded Program on Immunization, which targets approximately two million children each year (GAVI 2023). The schedule includes Bacillus Calmette-Guérin (BCG) vaccine for tuberculosis; oral polio vaccine; pentavalent DPT-HepB-Hib for immunity against diphtheria, tetanus, whooping cough (pertussis), hepatitis B, and *Haemophilus influenzae* type b (Hib); pneumococcal conjugate vaccine (PCV); injectable polio vaccine (IPV); measles-containing vaccine (MCV); rotavirus vaccine (RotaC); measles vaccine; and yellow fever vaccine (Table 2). The immunization schedule also includes human papillomavirus and tetanus-diphtheria vaccines for women of childbearing age (Question and Answer booklet on routine immunization n.d.).

Table 2. Immunization Coverage Estimates in Uganda, 2023

Vaccine	Target pathogen/disease	Required dosage	Official coverage estimates (%)
National childhood immunization schedule			
BCG	Tuberculosis	1	95
DPT-HepB-Hib	Diphtheria, pertussis, tetanus, hepatitis B, *Haemophilus influenzae* type b	3	95 (1st dose) 91 (3rd dose)
PCV	Pneumococcus	3	91
OPV	Polio	4	89 (3rd dose)
IPV	Polio	2	96 (1st dose)
MCV	Measles	2	93 (1st dose) 21 (2nd dose)
RotaC	Diarrhea attributable to rotavirus	2	86 (1st dose)
YFV	Yellow fever	1	39

Source: WHO/UNICEF Immunization dashboard Uganda (GAVI 2023; WHO 2023b).
BCG = Bacillus Calmette-Guérin; DPT-HepB-Hib = pentavalent vaccine for diphtheria pertussis, tetanus, Haemophilus influenzae type B and hepatitis B; PCV = pneumococcal conjugate vaccine; OPV = oral polio vaccine; IPV = inactivated polio vaccine; MCV = measles-containing vaccine; YFV = yellow fever vaccine

ROLE OF VACCINES IN MITIGATING AMR

Vaccines play a pivotal role in curbing the burden of infectious diseases and slowing the emergence of AMR. They reduce the incidence and transmission of infections, thereby reducing the need for treatment and indirectly tackling a critical driver of AMR: overconsumption of antibiotics (Figure 2) (Vekemans et al. 2021).

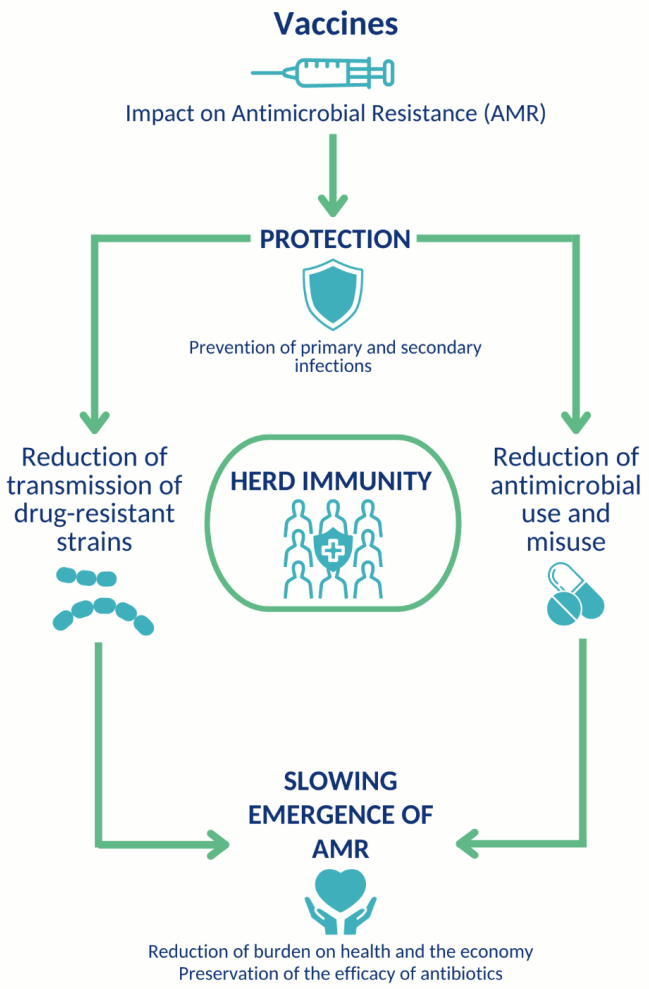


Figure 2. How Vaccinations Can Reduce AMR Incidence
Source: Kalanxhi et al. 2023

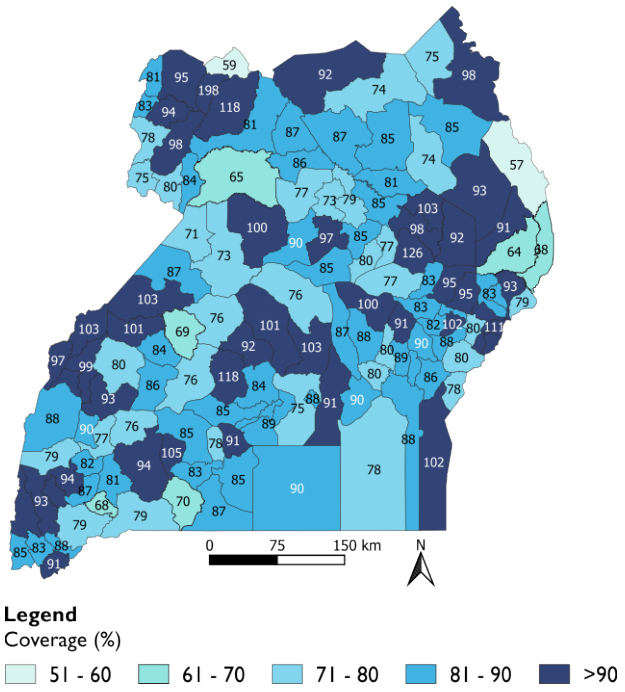
Recent evidence has quantified the impact of vaccines on the health and economic burden imposed by AMR. A study across 18 LMICs found that PCV and rotavirus vaccines prevented 19.7 percent of antimicrobial-treated acute respiratory tract infections (ARIs) in children aged 24–59 months and 11.4 percent antimicrobial-treated diarrhea cases in children under two (Lewnard et al. 2020). The study also analyzed the incidence of ARI and diarrheal disease from 2006 to 2018 and reported that PCV could avert 23.8 million episodes of antimicrobial-treated ARI and 13.6 million episodes of antimicrobial-treated diarrhea annually in children under five. Achieving universal coverage for both vaccines could prevent an additional 40 million episodes of antimicrobial-treated illness (Lewnard et al. 2020).

Another modeling study predicted that introducing TCV for infants in 73 GAVI-eligible countries could prevent up to 53.5 million cases of drug-resistant typhoid fever over a 10-year period (Birger et al. 2022). The influenza vaccine has also been shown to curb infection-associated antibiotic use; a 10 percent increase in influenza vaccination coverage in the United States was associated with a 6.5 percent decrease in AMU, equivalent to 14.2 fewer antimicrobials per 1,000 individuals (Klein et al. 2020).

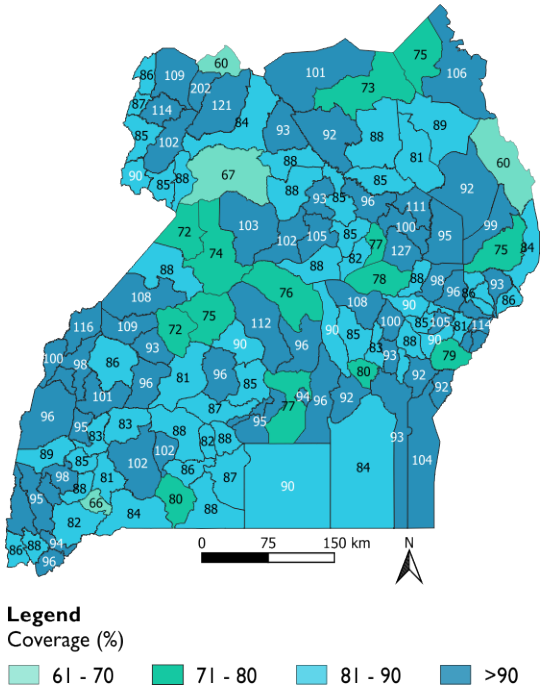
A modeling study published in 2023 estimated that the M72 Mycobacterium tuberculosis vaccines, when administered with 70 percent coverage and 50 percent efficacy and followed by a booster dose every 10 years, could provide protection for 10 years and avert 10,799 deaths and 446,653 DALYs attributable to AMR in the WHO Africa region (Kim et al. 2023).

A WHO action framework leveraging vaccines as a tool for AMR highlights the importance of prioritizing the uptake of available PCV, TCV, Hib, and influenza vaccines (Vekemans et al. 2021). It also emphasizes the development of prophylactics for malaria, HIV, respiratory syncytial virus (RSV), and group A *Streptococcus* to reduce drug-resistant disease and AMU (Vekemans et al. 2021). However, vaccine coverage in countries in Africa and Asia is declining, and the number of zero-dose children has increased, particularly during the COVID-19 pandemic (Rachlin 2022). Despite the overall high coverage levels in the routine immunization schedule, disparities persist at the subnational level (Figure 3). In addition to financial gaps and service

delivery challenges, vaccine uptake is hindered by low education levels, sociocultural and religious beliefs, inadequate information on vaccinations, poverty, and poor access to health care (Jammeh et al. 2023; Malande et al. 2019). These factors must be overcome through concerted efforts by governments, policymakers, health care providers, and society, exemplifying the One Health approach.



Average Rota 2nd dose vaccine coverage (2020-2022)



Average PCV 3rd dose vaccine coverage (2020-2022)

Figure 3. Subnational Rotavirus and Pneumococcal Conjugate Vaccine Coverage in Uganda
Source: Ministry of Health, Government of Uganda 2022, 2023

In Uganda, PCV has been estimated to prevent 8.4 cases (80 percent) of antibiotic-treated ARI per 100 children under 5 (Table 3) (Lewnard et al. 2020). Similarly, rotavirus vaccinations have been shown to avert 7.6 cases (56 percent) of antibiotic-treated diarrhea per 100 children aged 0–23 months (Table 3) (Lewnard et al. 2020).

Table 3: Estimates of the Impact of Routine Childhood Immunizations on Antimicrobial-Treated Infections in Children Under Five in Uganda

Vaccine	Age (Months)	Antibiotic-treated cases per 100 children, estimate for IPD (95% CI)	Antibiotic-treated infections preventable by direct vaccine effects per 100 (95% CI)
		ARI attributable to Streptococcus pneumoniae	
PCV	24–59	20.9 (3.8–46.9)	16.8 (3–36.8)
	0–59	10.5 (-1.5–24.7)	8.4 (-1.2–19.2)
		Diarrhea attributable to rotavirus	
Rotavirus	0–23	13.5	7.6 (2.5–13.4)

Source: Lewnard et al. 2020
ARI = acute respiratory infection; PCV = pneumococcal conjugate vaccine; IPD = invasive pneumococcal disease.

In 2021, enteric infections led to 9,716.55 deaths in Uganda, with typhoid fever accounting for 731.46 of these. Despite its efficacy, typhoid conjugate vaccine (TCV) has not been included in Uganda's national immunization schedule. Introducing it is expected to reduce antibiotic use and AMR significantly. A modeling study by Birger and colleagues (2022) predicted that a successful TCV campaign could avert 75.2 percent of fluoroquinolone nonsusceptible (FQNS) cases and 71 percent of FQNS deaths over 10 years and 75.9 percent of multidrug resistant (MDR) cases and 73.1 percent of MDR deaths (Table 4). The TCV program includes a catch-up campaign for unvaccinated infants up to 15 years of age, aiming to prevent around 94,000 FQNS typhoid cases, 490 deaths, and 25,000 DALYs and 230,000 MDR typhoid cases, 1,239 deaths, and 64,000 DALYs (Table 4) (Birger et al. 2022).

Table 4. The Estimated Effect of Typhoid Conjugate Vaccine on AMR Cases, Associated Deaths, and DALYs for Uganda, Sub-Saharan Africa Regions, and Lower-Income Countries

Vaccine	Averted AMR cases		Averted deaths		Averted DALYs
	Number	%	Number	%	
TCV (10-year prediction)	*Fluoroquinolone nonsusceptible (FQNS) typhoid fever*[a]				
Uganda	94,000	75.2	490	71	25,000
Sub-Saharan Africa	6,819,000	68.8	65,762	65.8	3,093,000
Lower-income countries[b]	42,515,000	61	506,026	59.6	27,923,000
TCV (10-year prediction)	*Multidrug-resistant (MDR) typhoid fever*[a]				
Uganda	230,000	75.9	1,239	73.1	64,000
Sub-Saharan Africa	14,392,000	68	173,735	65.9	8,019,000
Lower-income countries[b]	21,218,000	65.8	342,725	71.5	16,508,000

[a] Uganda-specific estimate of typhoid conjugate vaccines (TCVs) on FQNS and MDR typhoid fever, from Birger et al. (2022).

[b] Average for 73 GAVI-eligible lower-income countries (Birger et al. 2022).

ECONOMIC VALUE OF THE MALARIA VACCINES

Highlighting the impact of malaria vaccines in reducing cases and deaths, a recent study predicted that routine childhood malaria vaccines with 40 percent efficacy over 10 years could avert 611.13 cases, 3.38 resistant cases, and 1.56 deaths per 1,000 children (Hamilton et al. 2023). The model assumes that children would receive three doses of the vaccine in their first year of life and anticipates the benefits to be even greater if the vaccine is implemented alongside improved malaria diagnosis, treatment, and vector control measures.

Building on this model (Hamilton et al. 2023), recent projection data suggest significant health and economic benefits from malaria vaccine implementation over 3-, 5-, and 10-year periods in Uganda. The analysis considers varying malaria vaccine efficacy levels (0–80 percent) and assumes an immunization schedule with annual vaccinations for children aged 0–12 months (Table 5). The projected impact is evaluated under two scenarios: one with constant resistance levels and a "crisis" where resistance to artemisinin-based combination therapies (ACTs) increases linearly to 80 percent over a decade.

Over a three-year period, the vaccination program is projected to avert 68,000–82,000 cases of catastrophic health care expenditures, saving approximately

US$76.7–115.7 million in societal costs and US$8.3–12.6 million in monetized DALYs. Over five years, it could prevent at least 82,000 cases of catastrophic health expenditures, societal costs of US$89.4–125.2 million, and US$9.4–13.2 million in DALY-associated costs. After 10 years, these benefits expand significantly, with the program projected to prevent 95,000–153,000 cases of catastrophic expenditures, societal costs of approximately US$96.6 million (even with low vaccine efficacy), and US$9.6–14.7 million in DALY-related costs (Figure 4).

Table 5. Model Malaria Vaccine Efficacy Rates Across Different Scenarios

Year	Baseline	Scenario 1	Scenario 2	Scenario 3
Year 1	0%	40%	80%	40%
Year 2	0%	40%	60%	40%
Year 3	0%	40%	40%	40%
Year 4	0%	40%	20%	40%
Year 5	0%	40%	0%	40%
Year 6+	0%	0%	0%	40%

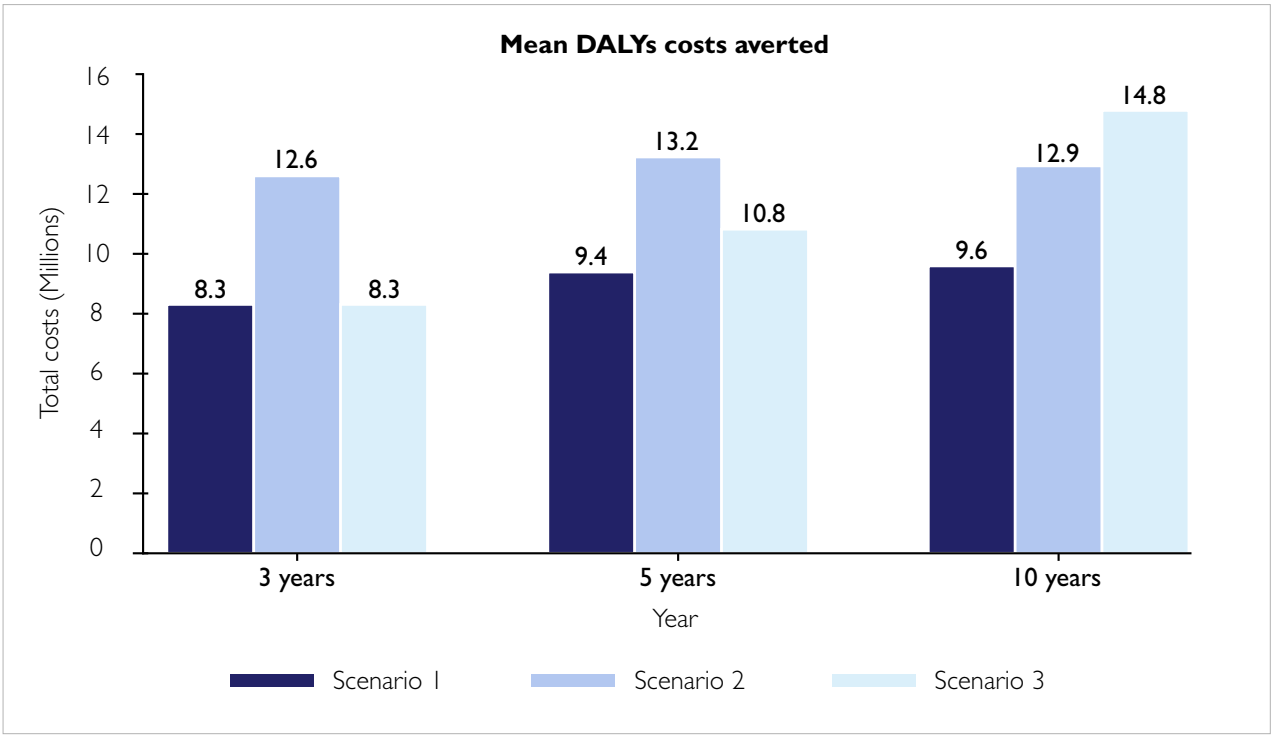


Figure 4a. Averted Health and Economic Costs Across Varying Vaccine Efficacy Scenarios

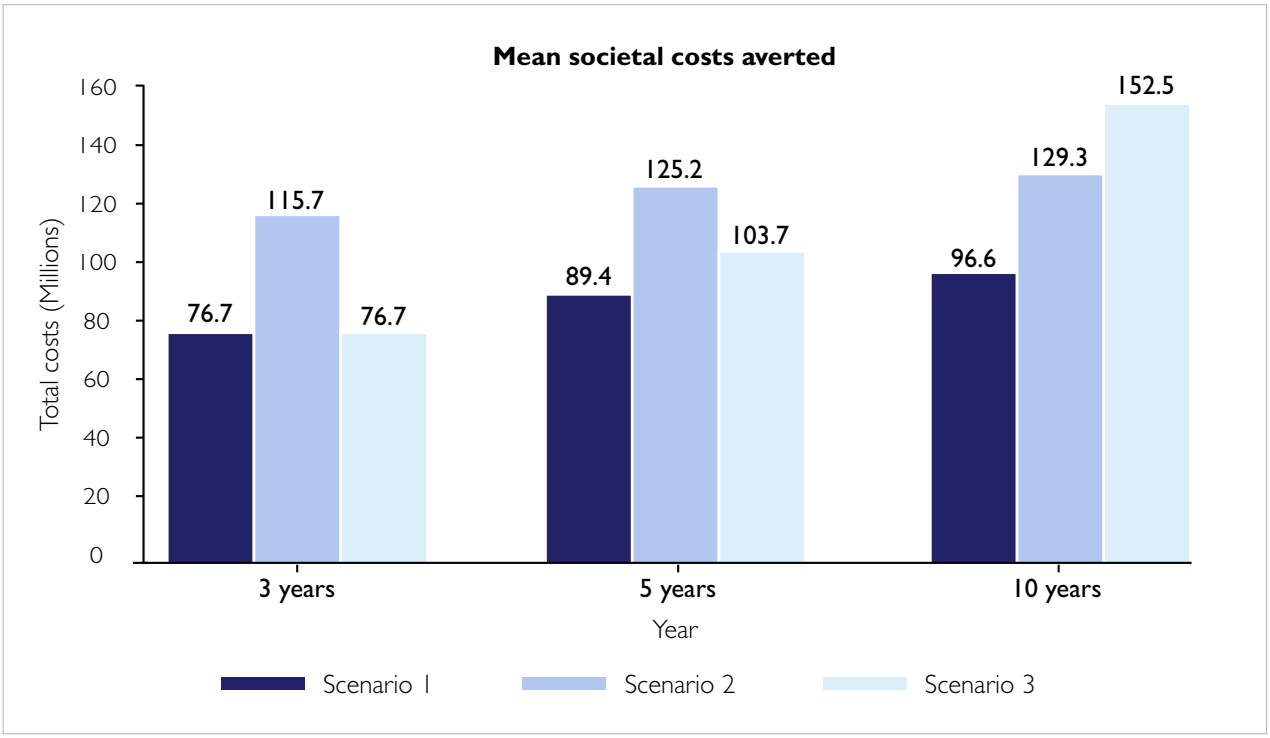


Figure 4b. Averted Health and Economic Costs Across Varying Vaccine Efficacy Scenarios

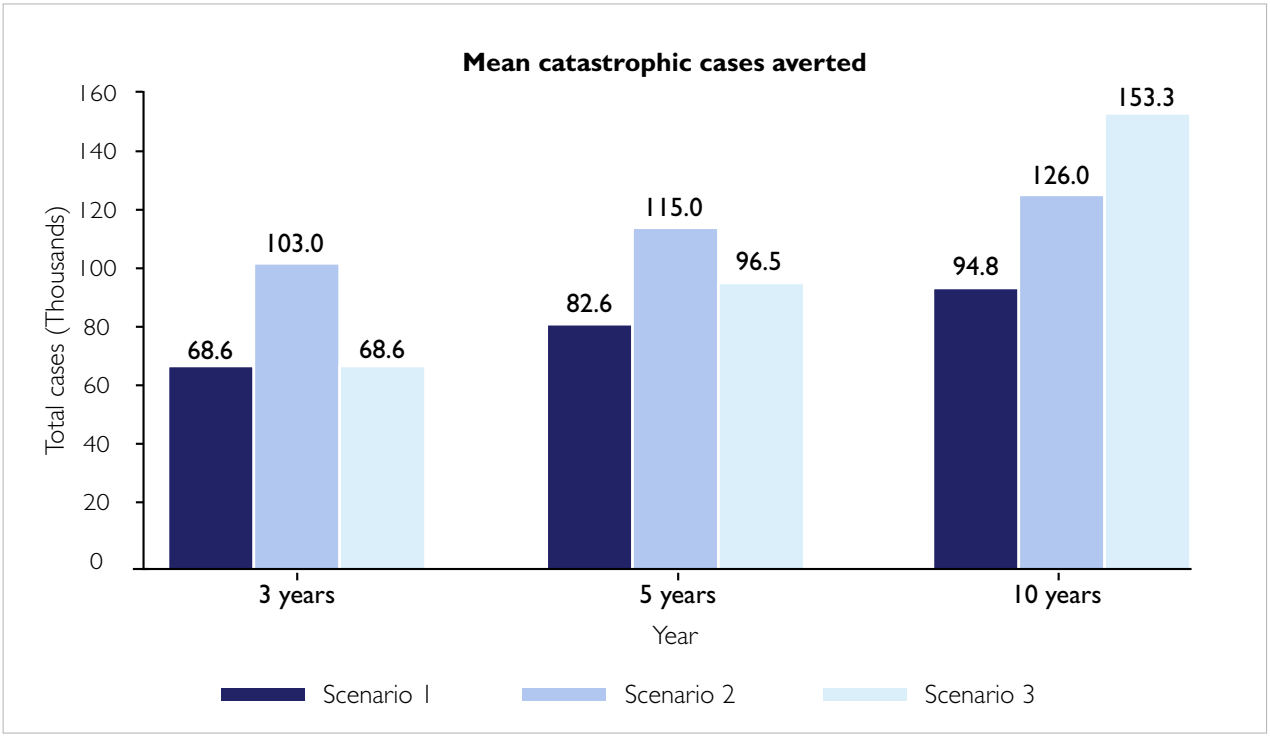


Figure 4c. Averted Health and Economic Costs Across Varying Vaccine Efficacy Scenarios

Catastrophic health care expenditure—defined as exceeding 10 percent of daily household income—disproportionately affects low-income households, often forcing them to forgo essential needs, such as food, housing, water, electricity, or fuel for cooking and heating. The vaccine program is projected to mitigate this financial burden, particularly in the crisis scenario. Out-of-pocket expenditures associated with resistant malaria could be reduced by up to US$1.5 million, further emphasizing the economic and public health value of vaccine implementation (Figure 5).

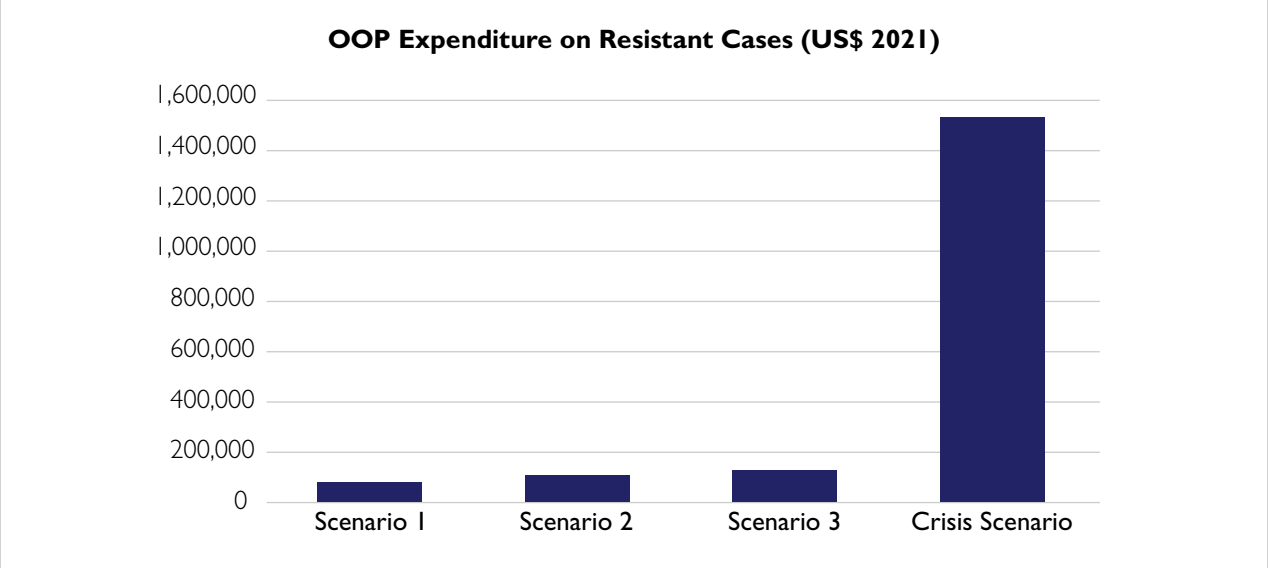


Figure 5. Avertable Out-Of-Pocket Expenditures on Resistant Cases in Varying Vaccine Efficacy Scenarios

In alignment with these predictions, a pilot program of the newly approved RTS, S/AS01 malaria vaccine in Ghana, Kenya, and Malawi has shown a 30 percent reduction in severe cases since 2019 (Gibson 2023). Vaccines may help slow the rapidly inclining rates of antimalarial resistance in Africa (Kozlov 2021). RTS, S/AS01 is set to be rolled out and included in the Ugandan national schedule before 2025 (WHO n.d-a).

The implementation of malaria vaccines plays a critical role in addressing AMR by reducing reliance on antimalarial drugs, particularly in areas where resistance to ACTs is rapidly increasing. By preventing malaria infections and severe cases, vaccines reduce the frequency of treatment with ACTs and other antimalarial therapies, thereby slowing the development and spread of drug-resistant malaria.

NEW VACCINATION STRATEGIES TO TACKLE AMR

Available and new vaccine candidates capable of reducing the burden of infectious diseases and AMU should be prioritized in vaccine regulatory and policy mechanisms (Vekemans et al. 2021). Promising candidates include vaccines or monoclonal antibodies, as for RSV, which causes significant infant morbidity in Uganda (IHME 2021; Weary et al. 2024). Late-stage trials of RSV vaccines and monoclonal antibodies have demonstrated a safe reduction of the viral disease burden and associated antibiotic use due to secondary bacterial infections (GSK 2020; Griffin et al. 2020). Findings from a recent randomized control trial show that the RSV vaccine given to pregnant people in LMICs reduced antimicrobial prescribing by 11 percent for

infants up until three months old (Lewnard et al. 2022). *Mycobacterium tuberculosis* causes a significant disease burden despite available vaccines targeting infants and young children. Therefore, vaccines developed for alternative age groups or pathogen strains could significantly contribute to the fight against TB. A stage-two trial of a postexposure TB vaccine (M72) for adolescents and adults with active TB in Kenya and South Africa demonstrated a 50 percent reduction in symptomatic TB (Tait et al. 2019). A phase-two trial of the TB booster vaccine (MVA85A) for adolescents in Uganda showed a significant increase in antimycobacterial antibody levels, holding promise for further development of booster TB vaccines (Wajja et al. 2017).

RECOMMENDATIONS FOR LEVERAGING VACCINATION TO ADDRESS AMR

To harness the full benefits of vaccines, it is essential to optimize and expand coverage rates, ensure appropriate regulatory mechanisms, and strengthen health care provision and access. Sharing comprehensive data on how vaccines impact AMR with stakeholders and policymakers can significantly enhance advocacy efforts (Table 6).

Table 6. Vaccination Targets to Avert Infectious Disease and Reduce AMR in Uganda

Vaccine	Target	Projected effect on AMR for target
Ensure and maintain universal uptake		
PCV	Pneumococcal ARI in children under five	Prevent 80% of antibiotic-treated cases (per year)
RotaC	Rotavirus diarrheal cases in children under two years old	Prevent 80% of antibiotic-treated cases (per year)
Incorporate into national immunization schedule		
TCV	Typhoid fever cases in infants from 9 months old	Prevent 75.2% and 71% of FQNS cases and deaths and 75.9% and 73.1% of MDR cases and deaths (over 10 years)
Malaria vaccine	Malaria cases from childhood to adulthood	Prevent 611.13 cases and 1.56 deaths per 1,000 children (over 10 years)

Source: Lewnard et al. 2020; Birger et al. 2022; Hamilton et al. 2023
FQNS = fluoroquinolone nonsusceptible, MDR = multidrug-resistant, PCV = pneumococcal conjugate vaccine, TCV = typhoid conjugate vaccine

Key Recommendations

1. **Maintain high coverage of all available vaccines:** Increased coverage of childhood vaccines, such as the PCV, rotavirus, BCG, MCV, and hexavalent DPT-Hib-HepB vaccines, can reduce the incidence of infections in Uganda and the associated AMU.

2. **Expedite the approval and rollout of new vaccines and those in development:** The Ministry of Health should expedite the rollout of approved vaccines to alleviate the burden of infectious diseases in the country. Introducing new vaccines and related prophylactic interventions, such as typhoid and malaria vaccines, adult and adolescent tuberculosis vaccines, and monoclonal antibodies for RSV, to the national immunization schedule would help establish preventative measures and provide herd immunity to the population.

3. **Enhance collaborations:** Increase collaborative initiatives between authorities and institutions working on AMR and immunization to align national strategies, include vaccination-specific targets and objectives in the national action plan for AMR, and generate local data on AMR and vaccines. These collaborations would provide a holistic approach to targeting AMR and reducing the associated health and economic burden.

4. **Develop and implement a comprehensive communication strategy:** A comprehensive communication strategy would help raise awareness about AMR, its burden on individuals and health systems, and the invaluable role of vaccines in mitigating it.

CONCLUSION

Vaccines can prevent infections and the need for treatment with antimicrobials, thereby slowing the development and spread of AMR. In addition to significantly impacting the health and well-being of populations, vaccines can reduce the costs associated with the treatment of drug-resistant infections. They are invaluable interventions to combat AMR and its associated health and economic burden, and AMR is an important metric for vaccine evaluation and prioritization. To inform context-specific public health policies and strategies to address AMR in Uganda, interdisciplinary collaborations and data generation activities must be increased in the intersections between AMR and immunization fields.

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Initiated in 2008, the Global Antibiotic Resistance Partnership (GARP) has played a critical role in advancing country-led national strategies and policies to address antimicrobial resistance (AMR) in several countries in Africa and Asia.

GARP's current focus is generating cross-disciplinary evidence highlighting the impact of vaccines on AMR in country-specific contexts.

This policy brief lays out the situation in Uganda and recommends policy measures to use vaccines as tools to control AMR in the country.

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The findings and conclusions contained within are those of the authors and do not necessarily reflect the positions or policies of OHT, Gates Foundation, or partnering institutions. Related research and additional information on vaccines and antimicrobial resistance are available at onehealthtrust.org.

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