World Health Organization

Briefing Note

Guidance note on the inclusion of activities for AMR surveillance and laboratory strengthening into Global Fund proposals

Antimicrobial resistance (AMR) severely undermines progress against HIV, tuberculosis (TB), and malaria by increasing the risk of treatment failure, mortality, and health system costs due to resistant bacterial and fungal co-infections. By integrating AMR surveillance and laboratory strengthening activities into Global Fund grant proposals countries can support more effective HIV, TB, and malaria disease programs and improve readiness for emerging infectious threats.

What is AMR and why is it important for patients infected with HIV, tuberculosis and malaria?

AMR occurs when bacteria, viruses, fungi, or parasites no longer respond to antimicrobial agents, making common infections harder to treat and routine medical procedures riskier for patients. Focusing on infections caused by bacterial pathogens, an estimated 4·71 million (95% UI 4·23-5·19) deaths in 2021 were associated with, and 1·14 million (1·00-1·28) deaths were the direct result of drug-resistant bacterial infections (1). WHO reported that 1 in 6 laboratory-confirmed infections in 2023 were caused by bacteria resistant to commonly used antibiotics (2).

The burden of drug-resistant bacterial infections is highest in low- and middle-income countries (LMICs), driven by weak water, sanitation and hygiene infrastructure; limited laboratory capacity; low vaccination coverage; and restricted access to essential antibiotics and diagnostics (1-3). In 2023, 1 in 3 infections in the WHO South-East Asia region were caused by bacteria resistant to antibiotics; 1 in 3 in the Eastern Mediterranean region; 1 in 5 in the WHO African region; 1 in 7 in the WHO region of the Americas; 1 in 10 in the WHO European region; 1 in 11 in the WHO Western Pacific region (2).

Given the geographic overlap of the HIV, TB, malaria epidemic with regions bearing the highest AMR burden, and considering the immunocompromised status of these patients and their frequent need for hospitalization, people living with HIV, tuberculosis and malaria are at a particularly high risk of drug-resistant bacterial or fungal co-infections.

Despite the substantial impact of AMR on clinical and public health outcomes, containment efforts have largely remained vertical and disease-specific, without consideration of the impact of resistant bacterial and fungal infection on people with HIV, TB and malaria. Laboratory capacity to diagnose bacterial and fungal infections remains limited in LMICs. Out of 50,000 laboratories

surveyed in 14 African nations, only 1.3% could perform any bacteriological testing, with most lacking capacity to conduct antimicrobial susceptibility testing (4).

Achieving the 2030 targets for ending AIDS, TB and malaria requires urgent investment in microbiology capacity for detecting and monitoring bacterial and fungal infections and for systematic surveillance of antimicrobial resistance. Strengthened laboratory networks – supported by infrastructure, digital health systems, supply chains, and quality management – directly benefit HIV, TB, and malaria programmes while improving pandemic preparedness for emerging infectious threats.

Bacterial resistant infections in people living with HIV

Bacterial infections are the second leading cause of hospitalization for people living with HIV (5). Among this population, infections caused by resistant bacteria occur more often than in people without HIV (6). Compared with HIV-negative individuals, people living with HIV have a 90% higher risk of methicillin-resistant Staphylococcus aureus (MRSA), 128% higher risk of Streptococcus pneumoniae with reduced penicillin susceptibility, and 159% higher risk of third-generation cephalosporin resistance in *Escherichia coli* and *Klebsiella pneumoniae*. Bacterial infections are a leading cause of morbidity and mortality among people with advanced HIV disease, after TB and cryptococcal disease, and the risk of invasive bacterial infections remains elevated even when people living with HIV receive antiretroviral therapy (ART) (7). Furthermore, the introduction of ART as pre-exposure prophylaxis may have contributed to increased incidence of *Neisseria gonorrhoeae* (8). Co-trimoxazole prophylaxis, widely used among people living with HIV, has been shown to drive resistance: for example, 84% of *E. coli* isolates from people living with HIV on co-trimoxazole prophylaxis were resistant to the drug (9). Strengthening countries' capacity to monitor the burden of bacterial resistant infections and manage severe bacterial infections is essential to achieving the goal of ending the AIDS epidemic by 2030 (10).

Bacterial and fungal resistant infections in people with tuberculosis

Bacterial co-infections are common in TB patients, with prevalence ranging from 10% in Cambodia to 34% in Indonesia (11, 12). Misdiagnosis of TB frequently leads to unnecessary prescription of antibiotics, which in turn drives the emergence of AMR (13). The use of repurposed antibiotics for the treatment of both drug-susceptible and drug-resistant TB also contributes to the selection of multidrug-resistant bacteria, including MRSA and extended-spectrum beta-lactamase (ESBL) producing strains (14). Screening for bacterial pathogens that are not susceptible to anti-TB medicines is essential for ensuring successful treatment outcomes in pulmonary TB patients (15). Overall, TB patients are at increased risk of co-infection with other

multidrug-resistant bacteria due to antimicrobial selection pressure and nosocomial transmission.

Fungal infections present an additional diagnostic challenge in TB patients. Approximately 1 million people recovering from TB develop fungal infections annually, yet up to 80% of them are misdiagnosed as having recurrent TB (16, 17). In Africa and Asia, up to a quarter of people with pulmonary TB are estimated to have a *Candida* co-infection (17). Histoplasmosis is frequently underdiagnosed or mistaken for tuberculosis, with case fatality in Latin America reported to range from 10% to 53% (18). Other invasive fungal infections (e.g., aspergillosis, cryptococcosis, coccidioidomycosis) can also mimic TB, resulting in misdiagnosis and mismanagement. This highlights the need to equip laboratories with appropriate fungal diagnostic tools and to ensure quality through participation in external quality assessment schemes and targeted training for laboratory professionals (16, 18).

Bacterial resistant infections in people with malaria

Treatment of malaria with sulfadoxine/pyrimethamine may promote respiratory tract carriage of trimethoprim/sulfamethoxazole-resistant *Streptococcus pneumoniae* (19). Bacterial co-infections, including those with ESBL *Klebsiella pneumoniae*, more than doubles the risk of death in children with severe malaria, increasing case fatality from 10% to 24% (20-22). The introduction of malaria rapid diagnostic tests has also had an impact on antibiotic use in this population; in some settings, up to 70% of people with negative malaria rapid diagnostic test results are prescribed antibiotics, often inappropriately, which further drives the emergence of resistance (23, 24).

What AMR activities are eligible for inclusion in Global Fund grant proposals?

Countries are encouraged to include core AMR-related interventions in their Global Fund grant applications, consistent with the commitments made in the 2024 AMR Political Declaration, WHO guidance and Global Fund strategy (25).

Activities fall into two areas: (1) strengthening AMR surveillance and (2) reinforcing diagnostic capacity for bacteriology and mycology testing for improved monitoring.

Priority Area 1: Strengthening AMR surveillance

a. National AMR surveillance system

National AMR surveillance systems provide important strategic information to inform policies and interventions for clinical management, antimicrobial stewardship, and infection prevention and control of bacterial and fungal infections, including among people living with HIV, TB, and malaria. Countries must invest in improving the coverage, representativeness, and quality of data generated by these systems.

National AMR surveillance systems are encouraged to comply with WHO standards and recommendations. WHO provides guidance on the essential components of a national AMR surveillance system, including a National Coordinating Centre (NCC), a National Reference Laboratory (NRL), representative sample of surveillance sites selected by level of care and geographic distribution, a functioning laboratory network supported by external quality assurance, and a functional information system.

The first step in developing a national AMR surveillance system is a comprehensive assessment of the existing surveillance system, as well as broader diagnostic and clinical services. This assessment identifies facilitators and barriers to national surveillance, evaluates available resources, and pinpoints gaps and needs. Findings from the assessment inform a national AMR surveillance strategy, supporting stepwise expansion of surveillance across health system levels, clinical syndromes, and 14 bacterial and fungal priority pathogens of WHO's Global Antimicrobial Resistance and Use Surveillance System (GLASS) (26, 27).

b. Genomic AMR surveillance

Pathogen genomic data complement AMR surveillance by identifying determinants and mechanisms of resistance, enabling tracking the emergence and transmission of pathogens and AMR. These data support the development and standardization of treatment guidelines, outbreak investigation, and infection prevention and control measures. Genomic surveillance for AMR also deepens understanding of the biology and evolution of AMR and accelerates the development of new diagnostics.

c. Nationally representative surveys of AMR

WHO standardized protocols for nationally representative surveys measure the prevalence, mortality, and economic burden of AMR in bloodstream infections in hospitalized patients, including those with HIV, TB, or malaria (28). These surveys are particularly valuable in countries with limited routine bacteriology and mycology testing. Findings provide critical evidence on the resistance profiles, health, and economic burden of AMR, informing national empirical antibiotic treatment guidelines, stewardship, IPC programs, and policies. They also strengthen diagnostic referral networks, supply management systems, and health worker capacity, laying the

foundations for routine AMR surveillance. Additionally, these surveys can generate nationally representative genomic datasets linked with phenotypic, demographic, and clinical data through whole-genome sequencing (29). Through technical assistance mechanisms, WHO supports Member States in developing and implementing AMR surveys.

e. Technical assistance

Through technical assistance mechanisms, WHO supports Member States in developing, implementing, and strengthening national AMR surveillance systems to ensure reliable, representative, and actionable AMR data for decision-making.

Priority Area 2: Reinforcing diagnostic capacity and networks for bacteriology and mycology

a. Laboratory capacity assessment

NRL and the wider national laboratory system are assessed using WHO standardized assessment tools (30). These assessments help map AMR diagnostic capacity across different tiers of the health system, identify gaps, and provide recommendations to strengthen infrastructure, workforce, and biosafety.

b. Strengthening NRL and laboratory network

Strengthening the NRL and broader laboratory network involves upgrading infrastructure; implementing biosafety and biosecurity measures; ensuring adequate staffing; and strengthening forecasting and supply chain management for uninterrupted procurement of essential supplies including culture media, pathogen identification tools, antimicrobial susceptibility testing (AST) materials, biosafety supplies, and specimen transport items. To improve access to diagnostic and laboratory services across the health system, the national essential diagnostics list should include WHO-recommended comprehensive package of *in vitro* tests for bacteriology, mycology, and antimicrobial resistance testing across primary, secondary, and tertiary levels of the health system.

c. International and national external quality assessment (EQA) programs

National External Quality Assessment (EQA) programmes following WHO specifications provide objective evaluations of surveillance laboratories' test results and are integral to the quality improvement cycle. They identify gaps, recommend corrective actions, and facilitate capacity building through technical mentorship. Participation in international EQA programmes ensures comparability of results across countries and supports GLASS reporting.

d. Specimen referral systems

Specimen referral systems connect lower-tier laboratories with higher-tier facilities, including the NRL, to ensure access to diagnostic testing, AST, and biobanking. These systems are

essential in LMICs where only a few laboratories have the capacity for culture, identification, and AST. Strengthening referral systems includes reliable transport logistics, cold chain management, and secure data transfer.

e. Information systems and data management

Laboratory information management systems (LIMS) capture, manage, and transmit AMR data in real time across surveillance sites, referral laboratories, and the NRL. Systems should facilitate timely reporting to national AMR surveillance systems and GLASS, support data quality checks, and enable linkage with genomic data where available.

f. Biorepository

Biorepositories store well-characterized bacterial and fungal isolates for reference, research, and genomic studies. Nationally representative collections support outbreak investigations, AMR trend analysis, and development of diagnostic assays and new therapeutics. Proper storage and cataloguing of isolates with associated clinical and demographic metadata ensures long-term utility.

g. Technical assistance

Through technical assistance mechanisms, WHO supports Member States in developing, implementing, and strengthening laboratory systems for bacteriology, mycology and AMR

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