Antimicrobial Resistance Diagnostic Initiative

Strengthening bacteriology and mycology diagnostic capacity, laboratory systems and service delivery
Acknowledgements

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In May 2023, the World Health Assembly adopted a resolution (1), urging Member States to commit to strengthening diagnostic capacity. This includes addressing various challenges such as local production, streamlining regulatory approaches, and overcoming quality and access barriers, while promoting research and innovation.

To support Member States in addressing their commitments to this resolution, the WHO Strategic and Technical Advisory Group on Antimicrobial Resistance (AMR) recommended WHO to develop and implement the AMR Diagnostic Initiative (2). The aims of the initiative are to strengthen global diagnostic capacity, laboratory systems and service delivery and support access to safe, affordable, and quality-assured diagnostics, in order to improve the diagnosis and management of bacterial and fungal infections and associated antimicrobial resistance.

The goals of the Antimicrobial Resistance Diagnostic Initiative are to:

1. Bring diagnostics to the forefront of the global response to antimicrobial resistance, to support patient management, antimicrobial stewardship, infection prevention and control interventions and to enhance routine surveillance.

2. Achieve equitable access to quality testing for common bacterial and fungal pathogens and associated antimicrobial resistance across all levels of the health system.
To achieve these goals, the Antimicrobial Resistance Diagnostic Initiative encompasses four building blocks:

1. **a strategic and operational framework**, setting out the strategic goals, objectives, implementation considerations and technical guidance and tools to support Member States in strengthening bacteriology and mycology laboratory services;

2. **standardized assessment tools** for monitoring and reporting bacteriology and mycology laboratory services capacity at national and global level;

3. **a global antimicrobial resistance laboratory network**, comprising of WHO-designated laboratories at the national, supranational, and specialized levels; and

4. **research and innovation in diagnostics** to develop new strategies, tools and interventions to address antimicrobial resistance.
Background

Reliable and timely laboratory testing results are crucial for decision-making in health services and to achieve universal health coverage. Laboratory results also play a critical role in public health decisions related to national health security and international agreements, such as the International Health Regulations (3).

However, the current state of diagnostic accessibility is a significant obstacle for nearly half the global population (4), with only 1–2% of clinical laboratories in sub-Saharan Africa undertaking bacteriology testing (5). Moreover, capacity to perform mycology testing is even more limited, exacerbating the challenges in adequate clinical management and diagnostic accessibility (6).

The available data on antimicrobial resistance is mostly from hospital settings and are limited. Low- and middle-income countries may bear the highest burden of antimicrobial resistance, with women, neonates and vulnerable groups being especially affected (7-12). Suboptimal access to early and accurate diagnosis of common bacterial and fungal pathogens is a major contributing factor to high rates of morbidity, disability, mortality, and health care–associated costs, which in turn fuel the emergence and spread of antimicrobial resistance.

In addition, robust diagnostic capacity is critical to effectively respond to global health threats and monitor emerging variants. The Lancet Commission on COVID-19 has highlighted the failure to ensure adequate global supply and equitable distribution of key commodities, including diagnostics during the COVID-19 pandemic (13). Strengthening and sustaining diagnostic capabilities for pandemic preparedness and beyond are therefore imperative. The reported increases in inappropriate use of antibiotics and in the emergence and transmission of antibiotic-resistant gram-negative bacteria during the COVID-19 pandemic highlights the importance of robust antimicrobial resistance surveillance, along with strengthened infection prevention and antimicrobial stewardship measures, to be integrated into pandemic preparedness and response plans (14) (15). The effective implementation of these measures requires the establishment of a robust diagnostic and laboratory system.

Antimicrobial resistance ranks among the top 10 global public health threats. Appropriate and rapid diagnosis of bacterial and fungal infections and associated resistance is of paramount importance for guiding appropriate clinical management and rational selection of antimicrobial therapy, monitoring infections and treatment response, and carrying out antimicrobial stewardship initiatives, infection prevention and control measures, investigating outbreaks and emerging threats, and monitoring the burden of antimicrobial resistance (18).
Strengthening countries’ capacity to diagnose common bacterial and fungal infections and to determine their susceptibility to antimicrobial medicines is critical for protecting populations against infectious disease threats.

Furthermore, antimicrobial-resistant bacterial and fungal coinfections jeopardize the achievement of the global targets for HIV, TB and malaria by 2030. Individuals infected with multiple pathogens generally have worse outcomes than those infected with a single pathogen, and they may also pose a greater risk of transmission to other people (19) (20).

The limited ability to timely identify bacterial and fungal infections and the associated antimicrobial resistance and the limited access to second- and third-line treatment options in countries with the highest burden of HIV, TB and malaria highlight the need for urgent action. People living with HIV are more susceptible to bacterial and fungal opportunistic infections and have a greater risk of antimicrobial resistance because of frequent health-care visits (21), which have significant implications for treatment outcomes (22). Bacterial coinfection is common in populations with a high prevalence of TB and increases the risk of mortality (23). In sub-Saharan Africa, children with recent or acute malaria have a higher risk of developing severe bacterial infections, which in turn increases the risk of death (24) (25).

Diagnostic capacity and laboratory services for diagnosis of bacterial and fungal infections and associated antimicrobial resistance are essential for implementing the Global Action Plan on Antimicrobial Resistance (26). Equitable access to quality testing and rational use of clinical bacteriology services are pivotal for achieving objective 2 (strengthening antimicrobial resistance surveillance), objective 3 (preventing and controlling the spread of multidrug-resistant bacteria) and objective 4 (rational use of antibiotics and antimicrobial stewardship) of the plan.
The challenges and the needs

When health-care providers face patients presenting symptoms and signs that are consistent with an infectious disease, such as fever, they need to rapidly differentiate between viral, bacterial, parasitic, and fungal illnesses. They also need to rule out non-infectious disease syndromes and determine whether identifying the pathogen and testing for antimicrobial resistance are necessary. However, suboptimal access to high-quality laboratory diagnosis often hinders this rational diagnostic pathway, leading to inappropriate use of antibiotics, poor infection prevention and control practices and unreliable surveillance data, which all contribute to the emergence and spread of antimicrobial resistance.

Bacterial pathogens have traditionally been detected through microscopy, culture and serology. More recently, molecular techniques like polymerase chain reaction and sequencing have become increasingly common. However, laboratories in low-resource settings, especially those in fragile, conflict-affected, and vulnerable areas, often face challenges in implementing even basic routine testing (27).

The provision of essential bacteriology laboratory services is hindered by a variety of barriers, including a shortage of clinical microbiologists and laboratory technologists with adequate training in conventional bacterial and fungal culture. Other challenges include the high cost of supplies and equipment, inadequate infrastructure and equipment maintenance, poor supply chain management, inadequate access to instruments, reagents and consumables, weak bio-risk and quality management systems, failing referral mechanisms and a lack of national strategic planning for laboratory services (18) (28).
Even where bacteriology and mycology diagnostic facilities are available, they are often underutilized (29). Clinicians may lack sufficient knowledge of the value of laboratory diagnostic tests or may perceive laboratory results as non-actionable because of poor quality or prolonged turnaround times (30). Additionally, the high costs of diagnostic tests can contribute to low demand in low-resource settings, creating difficulty in justifying investments in laboratory infrastructure. Further, laboratory services are not often monitored or adequately funded at the national level, exacerbating the existing challenges. It is therefore important to recognize the role of laboratories in national health systems and to invest in developing and strengthening their capacity in low-resource settings.

The need to strengthen national laboratory systems has been recognized by the Maputo Declaration (31) and Freetown Declaration (32) as well as resolution AFR/RC58/R2 (2008) on strengthening public health laboratories in the African Region (33). However, laboratory capacity strengthening programmes and financial support have primarily focused on HIV, TB, and malaria, which have contributed to the sustainable development of laboratory capacity specifically for these diseases. These strengthening measures include adequate supply chain management, pooled procurement of quality consumables for reduced prices, referral mechanisms, digital solutions, and training.

Although disease-specific laboratory capacity-strengthening programmes have contributed to the sustainable improvement of disease-specific responses, they have not sufficiently addressed the need to improve clinical bacteriology and mycology testing access, capacity, and quality management (33) (34). Despite the “decade of remarkable progress” described in the Freetown Declaration, these approaches have not translated into addressing the challenges of clinical bacteriology and mycology testing.

Sustainable Development Goal 3.8 is to achieve universal health coverage. This includes providing access to essential health-care services, safe and effective medicines and vaccines that are of high quality and affordable to everyone.

To support achieving this goal by 2030 and tackling antimicrobial resistance, WHO – through the Antimicrobial Resistance Diagnostic Initiative and in collaboration with partners and stakeholders – is committed to support Member States in strengthening their laboratory systems and diagnostic service delivery with the goal of improving the diagnosis and management of bacterial and fungal infections. Without equitable access to quality-assured diagnostics and laboratory services, antimicrobial resistance will be allowed to spread silently within and across countries.
The Antimicrobial Resistance Diagnostic Initiative: the four building blocks

1. A strategic and operational framework to set standards and provide implementation guidance

The strategic and operational framework aims to set out strategic goals, objectives, activities, and implementation considerations to strengthen bacteriology and mycology laboratory services. Building on the existing WHO model list of essential in vitro diagnostics (35), the framework supports the rational allocation of bacteriology and mycology diagnostic tests and services across the different tiers of the laboratory system and highlights the required capacity and competencies for personnel.

In addition, the framework references a package of technical guidance and tools for pre-analytical, analytical, and post-analytical procedures to support the rational use of quality-assured testing for bacterial and fungal infections and associated antimicrobial resistance. The strategic and operational framework aims to provide guidance and resources to strengthen governance, ensuring equitable access to bacteriology and mycology diagnostic services across the entire health system, while upholding high-quality standards and optimizing the utilization of bacteriology and mycology diagnostic tests.

2. Standardized assessment tools for monitoring and reporting national and global capacity on antimicrobial resistance and bacteriology and mycology diagnostics and laboratory services

A set of standardized assessment tools are used to evaluate and monitor the progress of both national bacteriology and mycology laboratory systems, as well as the capacity of national reference laboratories for bacteriology and mycology. These tools will be instrumental to conduct global surveys and identify areas for improvement, funding requirements and technical assistance needs by WHO or other stakeholders.
Global laboratory networks play a critical role in supporting national, supranational, and specialized laboratories to generate accurate test results. Building on the successes of other global laboratory networks, such as those for TB (34), HIV (36), polio (37), measles and rubella (38), influenza (39) and COVID-19 (40), the global antimicrobial resistance laboratory network aims:

- to strengthen global laboratory capacity to identify bacteria and fungi as well as associated antimicrobial resistance, to improve clinical management and expand routine antimicrobial resistance surveillance;
- to support the standardization and quality of laboratory testing procedures for bacterial and fungal infections and associated antimicrobial resistance across settings and WHO regions;
- to ensure high-quality testing standards, assessed and demonstrated through a standardized WHO global external assurance programme; and
- to support research, innovation, and validation of newer diagnostic modalities.

The global antimicrobial resistance laboratory network comprises specialized, supranational, and national antimicrobial resistance laboratories that are equipped and dedicated to fulfilling specific tasks and responsibilities in accordance with WHO specifications. These laboratories are identified by health ministries and designated by WHO through a standardized process based on agreed performance criteria and network requirements.
Research and innovation in antimicrobial resistance diagnostics

Research and innovation are the cornerstone principles that drive the advancement of diagnostic tests in bacteriology, mycology, along with susceptibility testing. These innovations aim to achieve improved precision, speed, and usability of diagnostic tools — factors that are paramount for the effectiveness of targeted treatment and containment strategies.

WHO works in partnership with Member States and stakeholders to:

- identify research priorities, including research and development, and advocate for their implementation to address critical knowledge gaps in AMR;
- conduct landscape analyses of current and developing bacterial and fungal diagnostics;
- support the development and introduction of new and innovative diagnostic tools and technologies, through the development of target product profiles and supporting of real-world evaluation studies with a focus on translating research into clinical use recommendations and informing policy;
- set global standards and specifications for bacterial genomic data, including for the interpretation of molecular information to predict antibiotic resistance in selected pathogens of public health importance; and
- promote digital health solutions, including software and connectivity tools for interconnected diagnostic networks, referral mechanisms and supply chain management, and result reporting and interpretation.
References


