

POLICY UPDATE

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As part of our [series](#) on current policy issues regarding antimicrobial stewardship and the threat of antimicrobial resistance (AMR), this update focuses on rapid diagnostic testing in low-resource settings to optimize the use of antimicrobial agents and prevent the spread of drug resistance. It highlights recent global policy initiatives aimed at accelerating the development and deployment of robust, accurate, and inexpensive diagnostic methodologies to support antimicrobial stewardship in low- and middle-income countries. We welcome your feedback on any of the issues addressed in this series. If you have comments or suggestions, please share your thoughts with CIDRAP's ASP project team via Twitter at [@CIDRAP ASP](#) or email at asp-cid@umn.edu.

--Julie Ostrowsky, MSc, CIDRAP Research Associate

Antimicrobial Stewardship and Rapid Diagnostic Testing in Low-Resource Settings

The availability of diagnostic testing—particularly in regions of the world with high rates of infectious disease and weak healthcare systems—is a critical but often overlooked aspect of global efforts to combat antimicrobial resistance (AMR). Accurate and timely diagnosis provides the means to determine appropriate antimicrobial therapy, control further spread of infectious disease, and monitor the emergence of drug-resistance through population-based surveillance programs ([AMS 2017](#); [Sokhna 2017](#); [Review on AMR 2015](#)). Recent advances in the development of novel rapid diagnostic methodologies (summarized in [CIDRAP 2017](#)) suggest the potential to enhance the effective treatment and control of a broad range of bacterial, viral, fungal, and parasitic infections that make up the global burden of infectious disease. The complexity and cost of many of the novel, rapid diagnostic approaches, however, effectively limit their use to high-income countries and centralized reference laboratories.

In low- and middle-income countries (LMICs), especially those with insufficient laboratory services, diagnostic and antimicrobial susceptibility testing is often unavailable, unreliable, or unaffordable. Accordingly, clinical management of suspected infection often starts with empiric antibiotic treatment as an easier or cheaper approach, contributing to the overuse of commonly available antibiotics, poor outcomes for many patients, and continued transmission of disease ([Merrett 2016](#)). In addition, local and national AMR surveillance data, needed to identify trends in the prevalence of drug-resistant disease and inform treatment selection ([Ayukekbong 2017](#)), may be scarce. A recent study noted that AMR surveillance data are unavailable in more than 40 percent of countries in sub-Saharan Africa ([Tadesse 2017](#)).

A key challenge for antimicrobial stewardship is the development of new diagnostic methodologies that address the needs in low-resource settings, such as robust, inexpensive, and low-complexity tests implemented without centralized laboratory facilities, temperature-sensitive reagents, or trained personnel. Automated or hand-held devices designed to deliver sample-to-answer results in less than an hour at the point of care are examples of new rapid technologies being developed to supplement laboratory services ([Cox 2017](#); [Bissonnette 2017](#); [Raichgot 2017](#)). Priorities for the development of new diagnostics aimed at enhancing antimicrobial stewardship in LMICs include the following ([NASEM 2017](#); [AMS 2017](#); [AdvaMedDx 2017](#); [Mendelson 2016](#); [Drain 2014](#)):

- Triage tools to rapidly distinguish between bacterial and nonbacterial (viral, fungal, or parasitic) causes of infection
- Multiplex devices and multiuse diagnostic platforms for syndromic diagnosis
- Methodologies that combine AMR detection (eg, resistance genes) with pathogen identification
- Rapid methods for antimicrobial susceptibility testing

In addition, the assessment of diagnostic test efficacy, including effects on clinical decision-making, clinical outcomes, performance characteristics in the field, and cost-effectiveness, is critical for identifying high-value diagnostics and determining the business case for their development ([Drain 2014](#)). Other key initiatives to ensure successful development of diagnostics targeted to the needs of LMICs may include expedited regulatory pathways and financial incentives (such as prepurchase agreements) to offset costs of product development and evaluation.

Policy Initiatives

Several recent policy initiatives, summarized below, address key barriers in the development and deployment of rapid diagnostics in LMICs relevant to antimicrobial stewardship.

Global Alliance for Medical Diagnostics Initiative (GAMDI)

In 2017, a team of researchers proposed the formation of the Global Alliance for Medical Diagnostics Initiative (GAMDI) ([Mugambi 2017](#)) based on the successful [GAVI](#) model, the public-private partnership established in 2000 to improve access to new and underused vaccines in the world's poorest countries. GAMDI is aimed at enhancing the development, implementation, and accessibility of rapid diagnostic testing in LMICs. It focuses on developing the business case for diagnostic product development and delivery, particularly by coordinating the supply and demand for high-priority diagnostic services to minimize costs and create a predictable and sustainable long-term financing structure. GAMDI's primary goals are to:

- *Accelerate the uptake and use of diagnostic services* (aligned with consensus development of a list of essential diagnostics, an activity that has been proposed but not yet completed—see below)
- *Strengthen healthcare services in LMICs*, including laboratory systems and governance structures, in collaboration with nongovernmental organizations and local stakeholders
- *Increase the predictability of global financing for diagnostics*, eg, by enhancing coordination among existing funding organizations
- *Create sustainable product markets*, eg, via coordinating mechanisms for market forecasting

Essential Diagnostic List

Schroeder and colleagues highlighted the need for a model list of essential in vitro diagnostics ([Schroeder 2016](#)) to provide guidance regarding diagnostic testing in resource-limited settings. They urged the World Health Organization (WHO) to lead the development of an Essential Diagnostics List (EDL), a priority-setting tool similar to the WHO's [Essential Medicines List](#). The EDL would identify diagnostic tests, including point-of-care and laboratory-based methodologies, that should be available to countries as needed, based on local disease epidemiology and population characteristics. Use of the EDL would help to achieve the following goals: (1) identify priorities for diagnostics R&D; (2) reduce the costs of purchasing diagnostic methodologies; and (3) develop logistical solutions for increasing access to diagnostic testing in low-resource settings.

In January 2017, the WHO issued a proposal for developing the EDL ([WHO 2017a](#)), aimed at providing evidence-based guidance for countries to customize their own national lists of essential diagnostic tests. Via increased access to relevant in vitro diagnostics, the EDL is intended to facilitate the appropriate use of antimicrobials, improve patient care, and reduce the risk of AMR. In June 2017, the WHO began forming a [Strategic Advisory Group of Experts on In Vitro Diagnostics \(SAGE IVD\)](#) to guide EDL development and advise on global diagnostic policies, working in conjunction with the WHO Expert Committee on Selection and Use of Essential Medicines.

Diagnostic Test Development

The need for improved diagnostics to inform the treatment of acute febrile illness in malaria-negative patients is considered an urgent global-health priority and a key challenge for antimicrobial stewardship in LMICs ([Escadafal 2017](#)). Collaborative efforts have recently focused on accelerating the development of rapid, affordable diagnostics through comprehensive analysis of specific needs and requirements, which are summarized in detailed Target Product Profiles (TPPs) intended to guide diagnostics research and commercial development. Examples include the following:

- *Diagnostic testing to differentiate bacterial from nonbacterial infections.* A collaborative group of experts in global health and infectious disease diagnostics recently developed a TPP to inform the development and validation of an initial assay to distinguish bacterial from nonbacterial infections in patients with acute febrile illness in resource-limited settings ([Dittrich 2016](#)). The group conducted an expert consensus process to define minimal and optimal characteristics and diagnostic performance requirements of the assay. The goal is to reduce inappropriate antimicrobial use and, following additional diagnostic tests to identify specific pathogens and antimicrobial susceptibilities, ensure appropriate treatment for febrile patients with bacterial infections.
- *Multiplex multianalyte diagnostic platform.* In December 2017, the WHO released a draft TPP for public review regarding the accelerated development of a novel diagnostic approach, the multiplex multianalyte diagnostic platform (MMAPDx), which is envisioned to consist of an instrument platform with self-contained, disposable assay cartridges designed for rapid detection of multiple pathogens based on the measurement of nucleic acids and serologic markers. Developers of the MMAPDx concept (Médecins Sans Frontières and the Foundation for Innovative New Diagnostics, in collaboration with the WHO) also proposed a business model and economic incentives to support the involvement of multiple platform and cartridge manufacturers. The final TPP, expected in 2018, for the MMAPDx platform will serve as the basis for an additional TPP for the development of an assay cartridge specific to the diagnosis of severe febrile illness ([WHO 2017b](#)).

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