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East Africa Public Health Laboratory Networking Project

Strengthening the Role of Laboratories in Tracking Antimicrobial Drug Resistance in East Africa

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Executive Summary

Antimicrobial resistance (AMR) surveillance is an indispensable component of the response to a rising tide of antimicrobial resistance worldwide. The World Health Organization (WHO) recommends surveillance as part of every AMR national action plan and has developed a global initiative to collect a standard set of AMR data from each country. National-level systems are needed to guide local and national policy, but regional systems can enhance the value of the data, depicting larger patterns and trends. This case study qualitatively examines the benefits, costs, feasibility, and importance of AMR surveillance and assesses the readiness of laboratories supported by the East Africa Public Health Laboratory Networking (EAPHLN) Project to participate in national and, ultimately, regional AMR surveillance.

AMR surveillance is the second consumer of antimicrobial susceptibility testing (AST) results, after the treating clinician. The added value of surveillance is not free, but comes at a relatively low cost, assuming well-functioning laboratories that produce reliable results. Additional costs are largely for information technology, data analysis capacity, personnel time and training, and software. Epidemiologic and general public health expertise are needed to interpret the data for public policy use. Kenya is in the process of establishing a national AMR surveillance system, with an estimated annual budget of approximately $160,000 USD.

AMR surveillance creates value at the facility, national, and global levels. The value at each level includes:

- Facility (local) level: information to guide antimicrobial treatment when laboratory results are analyzed regularly (e.g., monthly) and communicated to clinical staff; early detection of outbreaks of particular AMR strains or hospital-acquired infections generally
- National level: information to update standard treatment guidelines and track trends in AMR, including geographic variations
- Global level: promote understanding of AMR in each country compared to global patterns; helps complete global picture

This case study was intended to determine whether and how the EAPHLN laboratories, located in five neighboring countries, could be leveraged as the backbone of a regional AMR surveillance network. The aim has evolved somewhat to examine the potential contribution of the EAPHLN laboratories to national AMR surveillance systems, which could then later be linked into a regional network. A regional surveillance network would require collaboration between the national governments and would involve entire surveillance systems, not just the EAPHLN-supported laboratories. However, the EAPHLN-supported laboratories could add depth to the country networks and later on, a regional network. A major part of this case study involved assessing the readiness of these laboratories to contribute to national AMR surveillance systems.

The 32 EAPHLN laboratories include a central reference laboratory in each country and satellite laboratories, mainly near country borders. Substantial funds have been spent on upgrading these laboratories, but bacteriology (the portion of microbiology that deals with most bacterial infections) capacity has lagged behind at least some other laboratory services (e.g., hematology), even with significant infrastructure and equipment investments. Most laboratories are underutilized and perform relatively few microbiology cultures and antimicrobial susceptibility tests. A similar pattern is likely to exist in laboratories throughout the region, and possibly in low- and middle-income countries (LMICs) generally. The following are probable causes for this situation, which may vary by facility:

- Lack of demand from clinicians, related to length of time to get results (at least 2 days); lack of trust in results; lack of laboratory capacity for blood cultures, which are needed for many of the most serious, life-threatening infections
- Low priority given to diagnostic supplies by hospitals and other decision makers who control purchasing
- The multi-component nature of bacterial culture and antimicrobial susceptibility testing, which makes it especially vulnerable to weak supply chains and frequent stock outs; results cannot be obtained if essential components are unavailable when testing is needed
- Lack of recognition that microbiology requires dedicated, trained personnel, leading some facilities and/or ministries of health to rotate staff in and out of microbiology
- Few options for automated testing relative to hematology, chemical pathology or HIV testing, which may be more satisfying to staff, leading to low morale
- Requirement for patients to pay out of pocket for diagnostic tests in many countries

The EAPHLN-supported national reference laboratories appear to be better positioned to join national surveillance systems in their initial phases than are non-EAPHLN laboratories. Assuming progress in improving bacteriology capacity, the satellite laboratories could join within a few years. The national systems will set standards for the type and quality of data that they will accept, but those systems are still in development.

The following recommendations for EAPHLN and national AMR surveillance systems are based on the proficiency assessment and other research undertaken for this case study. Although specific to EAPHLN, they should be generalizable to many other low-resource countries.

1. **All five countries should enroll in WHO's Global Antimicrobial Surveillance System (GLASS), which has promised assistance for capacity building, training, and implementation.**

2. Countries should also consider contributing eligible susceptibility data (from invasive isolates) to CDDEP's ResistanceMap, which is currently the largest global repository of susceptibility test data. Currently, few laboratories produce qualifying data.
3. Each laboratory should have computer(s) with appropriate software and sufficient power and storage space for input of AST results and hospital-level analysis. If computer(s) are shared with other laboratory functions, sufficient use time should be allocated to AST results. WHONET (or comparable software) should be installed on the designated computer in every laboratory for this purpose, and a minimum of two microbiology staff members should be trained in its use. WHONET is free and training can be arranged through WHO.
4. Ministries of health should consolidate and prioritize inventories for infectious disease management so that antimicrobials are procured along with diagnostic media and reagents required for the optimal use of the antimicrobials, some of which are very expensive. This strategy would prevent diagnostics stock outs, optimize use, conserve expensive reserve drugs, and work toward the global goal of containing antimicrobial resistance.
5. The need for single-source consumables should be avoided when possible, or long-term agreements for a continuous source of these supplies should be included in equipment purchase agreements.
6. Capacity building energies should be focused on the services that clinicians value most – blood and cerebrospinal fluid cultures – as well as other cultures for critically ill patients and collation and dissemination of local antibiogram information from those cultures to support empiric prescribing at the facility level. This falls into the general category of diagnostic stewardship.
7. Consultant clinical microbiologists should be appointed to the network to enhance communication between laboratories and clinicians. Qualified clinical microbiology pathologists are in short supply in the region and suggest that visiting consultants provide some service to a handful of laboratories until more pathologists can be trained. We recommend recruiting clinicians in training to microbiology residencies, such as that at the Aga Khan University Hospital in Kenya.
8. At the periodic meetings of the network, countries or laboratories involved in surveillance should present summary reports on AMR surveillance, including specimen type and pathogen-antimicrobial combinations.
9. Ministries of health should be discouraged from rotating staff between facilities and specialties when possible. Currently, frequent transfers take place in many facilities.
10. EAPHLN should approach the Clinical and Laboratory Standards Institute (CLSI) for discounted regular access to standard documentation. EAPHLN should then support annual CLSI subscriptions. National reference laboratories take the responsibility of updating CLSI standards for all in country laboratories. In the event that CLSI is unable to offer free or heavily subsidized access to their standards for African countries, we recommend a medium-term plan for switching to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards, which will require considerable staff training.
11. Where the WHO does not offer proficiency testing for antimicrobial susceptibility testing, arrangements should be made to procure in-continent proficiency testing for surveillance. (South Africa and Kenya present potential options.) In the long term, the network should develop capacity to perform within-region proficiency testing at affordable rates.
12. The National Reference Laboratories should facilitate provision of standard microorganisms (ATCC) for internal quality control of media and facilitate participation in external quality assurance (EQA) to all of the sites in order to improve the accuracy of the AST data generated by the laboratories.
13. Countries should source animal blood from in-country veterinary farms or prepare blood agar plates centrally (at national reference laboratories) or regionally to supply laboratories.
14. The EAPHLN laboratories should be encouraged to continue their progress through the WHO Africa scheme for Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) and on to international accreditation, motivating countries to maintain accreditation after the expiration of World Bank support.

Introduction

Rationale for and content of the case study

Antimicrobial resistance (AMR) is increasingly recognized as a major threat to global health and security. In 2016, the World Health Organization (WHO) called upon all countries to adopt national AMR action plans, with five overarching objectives, one of which is to "strengthen the knowledge and evidence base through surveillance and research." The first specific activity listed is to "develop a national surveillance system for antimicrobial resistance" involving both national reference laboratories and functioning clinical laboratories, which are the source of data for AMR surveillance. This case study first explores the nature of AMR surveillance, the types of costs it incurs, and its public health benefits. It then applies this general framework to specific laboratories in sub-Saharan Africa supported under the World Bank funded East Africa Public Health Laboratory Networking (EAPHLN) Project.

The EAPHLN, which began in 2010, links national reference laboratories and district (county) level laboratories, most of which are near country borders, in Burundi, Kenya, Rwanda, Tanzania, and Uganda through knowledge sharing and joint activities. Many of the laboratories have been substantially upgraded in their physical plants, and all have benefitted from new equipment and extensive personnel training and mentoring. Unique in Africa, the EAPHLN is itself an appropriate "laboratory" for assessing how and how well these facilities could contribute to national AMR surveillance systems in representative LMICs.

Background on antimicrobial resistance

Antibiotics are essential to modern medicine. They are used to treat and prevent infections in both humans and animals, as well as to promote growth in food animals (1). Reliance on antimicrobials is large and growing: global antibiotic consumption increased by more than 30 percent between 2000 and 2010 (2). However, antimicrobial resistance (AMR) is decreasing the effectiveness of these valuable drugs (1).

Resistant infections lead to higher morbidity and mortality and are more expensive to treat. In the United States, an estimated two million infections and 23,000 deaths per year are attributable to antibiotic resistance (3). In Europe, antibiotic resistance accounts for about 25,000 deaths per year (4). Estimates of the health care costs of antimicrobial resistance vary. The U.S. Centers for Disease Control and Prevention (CDC) estimates that resistance incurs $20 billion USD in direct costs and $35 billion USD in productivity losses each year in the United States (3). The European Centre for Disease Prevention and Control (ECDC) estimates that resistant infections cost about 1.5 billion Euros annually in Europe (4). Understanding the magnitude of the AMR problem in the United States and Europe depends critically on data aggregated in AMR surveillance systems.

Ad hoc studies in East Africa have documented high and increasing resistance to commonly-used antimicrobials (5–7). For instance, in hospital-level studies of *Salmonella* Typhi in Nairobi, Kenya, 60 to 70 percent of samples were multi-drug resistant (8,9). Other studies have observed rapid increases in resistance: in a study of non-typhoidal *Salmonella* in western Kenya, ceftriaxone resistance increased from 6 to 57 percent over a three-year period (6). As in many LMICs, AMR data in East African countries are largely from ad hoc hospital-level studies, which are informative but not a satisfactory substitute for tracking regional rates and trends in resistance (10). Only organized surveillance will provide a clear picture of AMR in the region, even if limited in scope.

In addition to tracking AMR, it is important to understand the patterns and trends in antimicrobial use. Per capita use is generally highest in high-income countries, but is increasing most rapidly in LMICs (2). However, few data have been gathered to indicate the extent of antibiotic resistance in LMICs or to quantify the related health and health care costs (11). LMICs typically have weaker public health systems, fewer resources, and higher burdens of infectious disease. In these countries, antimicrobial resistance is common in community-acquired infections such as pneumonia, diarrheal disease, tuberculosis, malaria, and sexually-transmitted diseases (1). In addition, resistance makes it more difficult to treat patients with HIV/AIDS, which has a high prevalence in many LMICs (1).

In May 2015, the 68th World Health Assembly approved the Global Action Plan on Antimicrobial Resistance (12). The action plan calls for member countries to create national strategies for AMR within two years, centering around five main objectives (13):

1. improving awareness and understanding of AMR;
2. strengthening evidence through surveillance and research;
3. reducing incidence through disease prevention measures such as improved sanitation and hygiene;
4. improving antimicrobial stewardship in humans and animals; and
5. assessing the economic impact of AMR and investments in new drugs and other interventions.

Other initiatives, such as the Global Antibiotic Resistance Partnership (GARP) and the Global Health Security Agenda (GHSA), also aim to assess and improve national capacity for combatting AMR. GARP, a project of the Center for Disease Dynamics, Economics & Policy (CDDEP) supports local creation of AMR policy by providing guidance, tools, and technical support to local researchers and policymakers, and is currently functioning in India, Kenya, Mozambique, Nepal, South Africa, Tanzania, Uganda, and Vietnam (1). The GHSA is a partnership of nearly 50 countries, international organizations,

and other stakeholders working to improve countries' capacity to fight infectious disease. Preventing AMR is one of their main action packages, under which countries develop national plans to strengthen surveillance and laboratory capacity, improve antimicrobial stewardship, and support development of new drugs and alternative treatments (14).

Each of these global efforts highlights the importance of surveillance for detecting and taking steps to prevent resistance (15). However, AMR surveillance networks are uncommon in LMICs for the same reasons that the infectious disease burden is high and not always adequately treated: weak health systems, low laboratory capacity, and lack of appropriate diagnostic tests (16). In particular, few surveillance networks exist in sub-Saharan Africa outside of South Africa (16).

This case study assesses the potential role of the East Africa Public Health Laboratory Networking Project (EAPHLN) laboratories in national surveillance programs. These national systems are now in development in the EAPHLN countries and, in the future, could contribute to a regional AMR profile. Briefly, the EAPHLN was started in 2010 with the objective of providing diagnosis and surveillance of tuberculosis and other infectious diseases to vulnerable populations in border areas of Burundi, Kenya, Rwanda, Tanzania, and Uganda. Twenty-eight laboratories were selected for upgrading and have been serving in a clinical capacity. The project, initially slated to conclude in 2016, was extended to 2020 and expanded to include four additional laboratories.

When they are prepared to contribute data to surveillance networks, the EAPHLN satellite laboratories – due to their locations outside major cities – will add a dimension to these programs that may otherwise be difficult to find. Establishing this capacity could fill one of the largest gaps in the global understanding of the levels and trends in antibiotic resistance, and would contribute directly to local, national, and regional antibiotic policy and guidelines to improve the effectiveness of patient care.

Goal and Objectives

The goal of this case study is to explore the costs, benefits, feasibility, and importance of AMR surveillance in LMICs. This type of surveillance starts with antibiotic susceptibility test results from microbiology laboratories that serve hospitals and other healthcare facilities to aid in patient diagnosis and treatment. The EAPHLN laboratories, which perform this function, were used as a test case for participation in an AMR surveillance system. The cost of establishing a national AMR surveillance system is estimated, and the benefits of surveillance – as understood from the global literature and global experience – are discussed.

The idea initially was to explore using the natural alliance of the network laboratories as the backbone of a regional network, but has evolved toward assessing their capacity to participate in national systems. A regional network could be built later, and should include the entirety of the national networks rather than just EAPHLN laboratories. Forming such a regional network – which would involve data sharing across borders – would have to involve the respective national governments.

With regard to the laboratories in the EAPHLN, this case study has assessed their current performance, physical and human resource capacity, and infrastructure for antibiotic susceptibility testing.

Recommendations relate to improving the functioning of the EAPHLN laboratories for microbiology, including antibiotic susceptibility testing, and for contributing data to nascent national AMR surveillance systems, which are of broader interest to other LMICs.

Status of global AMR surveillance

In 2014, the WHO surveyed its Member States about their efforts in AMR surveillance. They found that AMR among some specific pathogens – such as those that cause tuberculosis, malaria, and gonorrhea – has been tracked globally for many years. Strong networks existed to track AMR among a broad set of pathogens in some regions, but there were major gaps in coverage. Europe and the Americas had the best surveillance coverage and sub-Saharan Africa and Southeast Asia, the least developed. The survey also underscored the lack of international methods and standards for generating and collecting AMR data.

Shortly after the surveillance report was released in 2015, the World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance, which reinforces the importance of AMR surveillance. As a result, with the support of Member States from all regions, WHO developed its Global Antimicrobial Resistance Surveillance System (GLASS) and has issued a call for all Member States to enroll. According to the GLASS Manual for Early Implementation (17):

The goal of GLASS is to enable standardized, comparable, and validated data on AMR to be collected, analyzed, and shared with countries, in order to inform decision-making, drive local, national and regional action, and provide the evidence base for action and advocacy.

Value of Antimicrobial Resistance Surveillance

Laboratory-based antimicrobial resistance surveillance: How it works

A laboratory-based AMR surveillance network is a partnership between clinicians, microbiology laboratories, and a central organizing body. Clinicians collect and send samples of urine, blood, cerebrospinal fluid, stool, and swabs of pus or secretions from skin, wounds, burns, umbilical cords, throats, eyes, ears, or genitals to clinical laboratories (18). If possible, these samples are annotated with patient information such as age, gender, specimen type, date, and geographic location (17). In the laboratory, technicians culture the specimens, identify bacterial isolates, and test isolates for antimicrobial susceptibility (17,18). There are several methods for testing antimicrobial susceptibility, including disk diffusion, broth dilution, minimum inhibitory concentration (MIC) strips (E-tests®), and automated tests (19). In disk diffusion, the most basic and common method, the bacterial isolate and a control strain of known susceptibility are swabbed onto agar and antimicrobial discs are placed on the inoculated surface. After overnight incubation, a technician measures the diameters of the inhibition zones created around the discs on the bacterial lawn of each plate (Figure 1). Bacterial isolates are categorized as susceptible (S), intermediate (I), or resistant (R) to that antimicrobial (19) based on standardized bug- and drug-specific "break points" in inhibition zone sizes (measured with a ruler). The results of these tests are returned to the clinicians for patient management. Other methods measure the minimum concentration of the drug required to inhibit growth of the test bacterium under set conditions or sequence the genome of the pathogen to detect antibiotic resistance determinants.

Antimicrobial susceptibility testing (AST) results are used by clinicians to aid in developing informed patient treatment plans. These same results and the patient demographic information form the basis of laboratory-based AMR surveillance.

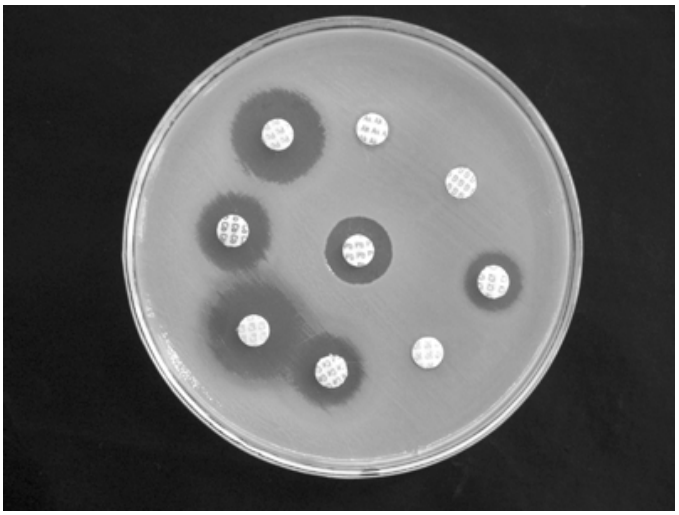


FIGURE 1: Antibiotic susceptibility testing using the disk diffusion method (Source: Wikimedia Commons)

AMR surveillance data management

Once AST data are collected, efficient data management is essential to successfully contribute those data to an AMR surveillance system. Data are entered into a software program to record, analyze, and report results (18). Individual laboratories then share their results with network or national data managers for further analysis of aggregate data (17).

Streamlined, electronic data management systems are the most efficient way to record, collate, and analyze data at the facility, national, and regional levels. Some laboratories record test results manually, but keeping only paper records is a less consistent and more difficult way to store, maintain, and analyze data.

Laboratory use laboratory information systems (LISs) to record and collate data at the facility level from AST and other clinical tests. LISs are computer-based management systems that allow laboratory staff to store test results and patient information for one or more facilities. Some LISs can also be used to analyze data and identify trends. There are several proprietary and open source LISs available, such as LabWare LIMS™.

Some laboratories also utilize a program that can analyze AST results, especially if their LIS does not have his capability. WHONET is a free data management software developed by the WHO specifically for managing and analyzing AST results. WHONET can import data directly from a general LIS through its BacLink function or data can be entered manually. Facility level analysis of AST results is essential for identifying local or hospital-based outbreaks.

Data collected at each participating laboratory is then aggregated at the national level. National AMR surveillance systems include a national database for aggregating surveillance data from participating laboratories and a system for analyzing data to identify trends and outbreaks. For example, CDDEP's ResistanceMap Surveillance Network (RSN) is an open-source software that can store and provide facility- and national-level analysis of resistance data. RSN currently operates only in the United States, but could be adapted for use in EAPHLN and other countries. Future versions of WHONET may also include an online platform and capability for aggregation between facilities. Data managers in each country oversee the national AMR surveillance database and coordinate with epidemiologists for further analysis.

Surveillance data from laboratories can be aggregated for analysis on the local, national, and regional levels to identify resistance levels and trends. For example, the National Antimicrobial Resistance Monitoring System (NARMS) in the United States aggregates data at the state and national levels and produces annual reports documenting trends in antibiotic resistance. These data are then fed back into clinical case management to improve patient outcomes. For instance, aggregate resistance data can improve initial therapy choices where prescribers must empirically select a drug before susceptibility data for that patient are available. NARMS

data are also used by government and non-government researchers to study specific aspects of AMR. In addition, the CDC hosts the "NARMS Now: Human Data" interactive online tool that displays and maps resistance data collected through NARMS. Data from multiple surveillance networks can also be combined to facilitate research, visualization, and mapping of global trends in resistance. CDDEP's ResistanceMap online tool summarizes national and subnational antimicrobial use and resistance and is the largest such repository in existence (20). Users can create maps and charts of antibiotic resistance to specific combinations of pathogens and antibiotics.

Antimicrobial resistance testing, like many aspects of medical care and research, is benefiting from the revolution in genetic technology. Detecting genetic markers of resistance, and ultimately whole genome sequencing of bacterial isolates, will allow a more precise understanding of resistance at the molecular level and its spread. These methods still require that bacteria be isolated, however, which is a limiting factor in most of the EAPHLN laboratories. Nonetheless, sequence-based methods are becoming cheaper and easier to perform on site, and some laboratories in the network should be able to use these methods once bacterial culture and susceptibility-based surveillance has been strengthened.

What do laboratory-based AMR surveillance data tell us?

Amassing data from clinical laboratories is the global norm for AMR surveillance for reasons outlined in this report. The data are available at low cost because their primary function is to aid in patient management. It is important to consider what these data actually represent, however, when interpreting them as they represent national surveillance.

The aggregated results of laboratory antibiotic susceptibility testing are not necessarily representative of the level of antibiotic resistance in the population: they represent cultures from people who were sick enough to seek medical care, either as outpatients or hospital inpatients, and whose treating physicians ordered a test. In the EAPHLN context, almost all isolates are from inpatients, representing the most severe illnesses. The proportion of inpatients for whom a culture and sensitivity test is done is also an indication of how representative the data are: the smaller the proportion tested, the higher the likelihood that they represent the most extreme, i.e., the most resistant, infections. This is because clinicians may wait until one or more treatments have failed before ordering the test.

In the United States and other high-income countries, a large proportion of hospitalized patients with suspected infections will have samples taken for laboratory analysis shortly after admission, even after starting a course of antibiotics. In a recent study, about 60 percent of patients started on an antibiotic had a sample taken and cultured (21). No corresponding figure for EAPHLN laboratories is available, but we know that annual laboratory records suggest less than one culture per day, which likely represents only a small proportion of patients with a suspected infection.

Thus, antibiotic resistance rates reported from laboratory-based surveillance systems are likely to be higher than among all patients, and certainly higher than in the non-hospitalized population, both with and without infections. Within a hospital, if the proportion of patients tested remains steady – even though the absolute rate may be unrepresentatively high – the trend can be informative. Within hospitals, for instance, clusters of the same antibiotic-resistant organism can warn of an outbreak of a hospital-acquired infection. If practices are changing, interpretation is more difficult. For instance, resistance levels may vary even if true resistance rates are largely constant. If practices change quickly over time (as they are likely to do in EAPHLN laboratories) because of improvements in infrastructure and demand from clinicians, these changes will affect the validity of data trends.

In the EAPHLN countries (as in most LMICs), national reference laboratories are among the best provisioned and most reliable laboratories, and are likely to be in the first wave of laboratories included in national surveillance systems. However, the data they provide may be even less representative than data from individual hospitals. National reference laboratories typically do not conduct routine tests for patient care. Rather, they accept samples from unusual cases for analysis from hospitals around the country and are used extensively to analyze samples from outbreaks. From the assessment carried out as part of this case study, for example, the national reference laboratory in Tanzania conducted 468 antimicrobial susceptibility tests, of which 452 were on cholera samples. Similarly, the Kenya national reference laboratory conducted 804 ASTs, of which 800 were for cholera.

Even data that are not entirely representative of the national situation can provide valuable information. A single result can signal the first instance of a particular strain of antibiotic-resistant organism in a country, in a region, or in the world. It alerts governments and healthcare providers to plan for the new organism and provide for its treatment. A large number of samples from an outbreak or epidemic can guide national treatment guidelines.

Eventually, a reasonably steady state in the proportion of patients whose samples are cultured should be reached, as it has in the United States and Europe. Before that time, data can still provide useful information and should be collected, aggregated, examined, and interpreted, but extra caution is needed to interpret levels and trends.

[1] Uninfected individuals harbor trillions of non-pathogenic bacteria in the gut, on the skin, and elsewhere, many of which may carry antibiotic resistance genes.

BOX 1: Six-Month Pilot Program of an Antimicrobial Resistance Surveillance Network in Ghana

Antimicrobial resistance surveillance is particularly important in resource-limited settings, where infectious disease burden is typically higher and low-quality and counterfeit drugs are more prevalent. In Ghana, data on antimicrobial resistance are scarce and no continuous surveillance network exists. In 2014, a six-month pilot program established a laboratory-based national surveillance network to generate baseline resistance data and evaluate current capacity (23).

The study included a three-day workshop where scientists from 24 laboratories were trained to identify bacterial isolates and perform antimicrobial susceptibility testing using the disk diffusion method. During the study period, scientists from each laboratory recorded test results and sent data sheets and isolates to a central location each week. A research assistant at the central laboratory then performed quality control tests, MIC tests, and extended-spectrum beta-lactamase (ESBL) tests, and entered data into WHONET for analysis (23).

Over the six-month period, 1606 isolates from 18 laboratories serving both inpatient and outpatient settings were submitted. Samples included blood, urine, swabs, stool, and sputum. Bacterial isolates were identified as *E. coli, Pseudomonas spp., S. aureus, Streptococcus spp., Salmonella enterica* Typhi, nontyphoidal *Salmonella, Citrobacter* spp., and *Vibrio cholerae*. Susceptibility testing showed that existing antimicrobials are not as effective as previously thought. Eighty percent of isolates were resistant to older antibiotics such as ampicillin, tetracycline, chloramphenicol, and trimethoprim/sulfamethoxazole (co-trimoxazole). In addition, more than 50 percent of isolates were resistant to third generation cephalosporins and quinolones. Further, most isolates tested were multi-drug resistant and 80 percent were ESBL-producing (23).

These results highlighted the need for continued surveillance of antimicrobial resistance in Ghana and corresponding changes in treatment guidelines. For example, the pre-existing Ghana Standard Treatment Guidelines recommended ciprofloxacin for urinary tract and bloodstream infections, which was ineffective against most isolates tested. The study also highlighted the need for capacity-building. Twenty-five percent of participating laboratories – including two of three participating public health reference laboratories – did not submit samples due to poor microbiology facilities, managerial problems, and lack of samples from clinicians. Also, none of the participating laboratories had the capacity for anaerobic cultures, which are standard for resistance surveillance in high-income countries (23).

Existing AMR Surveillance Systems

AMR surveillance now takes place in large parts of the world (Figure 2). Although most are in high-income areas, some low- and middle-income countries are already supporting surveillance systems. However, creating comprehensive, effective systems is more challenging due to weak laboratory and communications infrastructure; lack of trained laboratory and clinical personnel; and higher prevalence of counterfeit and substandard antibiotics and diagnostics (22,23). A 6-month surveillance program through 24 laboratories in Ghana recently demonstrated the feasibility of establishing surveillance in this lower-middle-income country, producing evidence of higher than expected resistance rates (see Box 1) (23).

Benefits of antimicrobial resistance surveillance

National and regional surveillance networks are essential for monitoring antimicrobial resistance, creating and evaluating evidence-based policies and interventions, formulating guidelines for antimicrobial use, and conducting effective public health research. Table 1 outlines the benefits of AMR surveillance.

Increasing knowledge about antimicrobial resistance

National surveillance networks allow countries to monitor trends in antimicrobial resistance (16,25,31), which correspond to trends in the effectiveness of particular antibiotics and antibiotic classes. For instance, AMR surveillance in South Africa in 2011 showed emerging fluoroquinolone resistance in *Salmonella* Typhi and increasing ciprofloxacin resistance in non-typhoidal *Salmonella* (32). Surveillance in the United Kingdom showed a steep increase in ciprofloxacin-resistant E. coli between 1993 and 2007. Similarly, a 6-month surveillance pilot program in Ghana in 2014 showed that resistance rates were higher than expected. For example, 80 percent of the isolates tested were resistant to older drugs such as ampicillin, tetracycline, chloramphenicol, and trimethoprim/sulfamethoxazole (co-trimoxazole) (23).

Surveillance data can help shape hypotheses to be tested in epidemiologic studies and provide data for mathematical models of AMR. Studies using surveillance data can focus on specific outbreaks, linking illnesses to sources and risk factors. Or they can combine data from multiple outbreaks to explore risk factors for the spread of resistance, mechanisms for the emergence of resistance, and the diversity of strains showing

TABLE 1: Benefits of Antimicrobial Resistance Surveillance

Benefits	Actions Taken
Monitor trends in antimicrobial resistance	• Ghana: 80% of isolates resistant to ampicillin, tetracycline, chloramphenicol, and trimethoprim-sulfamethoxazole • South Africa: Emerging fluoroquinolone resistance in *Salmonella Typhi* and increasing ciprofloxacin resistance in non-typhoidal *Salmonella*, 2011 • United Kingdom: Increase in ciprofloxacin-resistant *E. coli*, 1993-2007
Establish and evaluate targets for AMR reduction	• France, South Korea, and Turkey: Set reduction targets • United Kingdom: Set target of 50% reduction of MRSA, 2004-2008; 56% reduction achieved
Guide epidemiologic studies and mathematical modeling; set priorities for research and data collection	• United Kingdom: Increase in MRSA in 1990s attributed to 2 emerging strains; led to further study on related risk factors • United States: 500 deaths per year attributed to multidrug resistant *Acinetobacter* spp.
Develop evidence-based public health policy	• Denmark: Increased CRE in poultry and hogs contributed to growth promoter ban, 1990s; "yellow card" system implemented to force high users to reduce antibiotic use • India: Discovery of NDM-1 led to creation of a high-level AMR committee in the Ministry of Health • South Africa: Hospital VRE outbreaks in 2012 led to a national AMR strategy framework and early warning and notification system • United Kingdom: Increased carbapenem resistance in *E. coli* and *Klebsiella* spp. included in national action plan • United States: Cephalosporin resistance in *Salmonella* led to restrictions on use in food animals
Design and evaluate public health interventions	• India: High resistance rates led to implementation of laboratory-based AMR surveillance • Latin America: High carbapenem resistance led to establishment of AMR surveillance programs in Brazil, Argentina, and Colombia • United Kingdom: Created the TARGET tool for antimicrobial use in primary care; developed 5-year national action plan for AMR; created national alert system to inform clinicians about emerging types of resistance
Update treatment guidelines	• United Kingdom: Vancomycin added to treatment guidelines for staphylococcal endocarditis due to methicillin resistance; treatment guidelines for gonorrhea updated to address ciprofloxacin resistance
Create public health engagement campaigns and support training for professionals	• Europe: EARS-Net provides capacity building for laboratory technicians in participating facilities • South Africa: National AMR strategy established web-based and in-person AMR training for clinicians • United States: FoodNet epidemiologists train local public health officers to conduct outbreak investigations
Influence industry practices	• Canada: Link between multi-drug resistant *Salmonella* in humans and ceftiofur use in poultry led to voluntary ban on ceftiofur in Quebec chicken industry • Denmark: ESBL in *E. coli* led to voluntary withdrawal of cephalosporin and new management practices for disease control in the hog industry • Japan: Cephalosporin resistant *E. coli* in broilers led to voluntary withdrawal of ceftiofur in Japanese hatcheries
Improve data quality	• Europe: Regular data reporting for EARS-Net improved data quality and reporting and facilitated development of a standardized definition of resistance

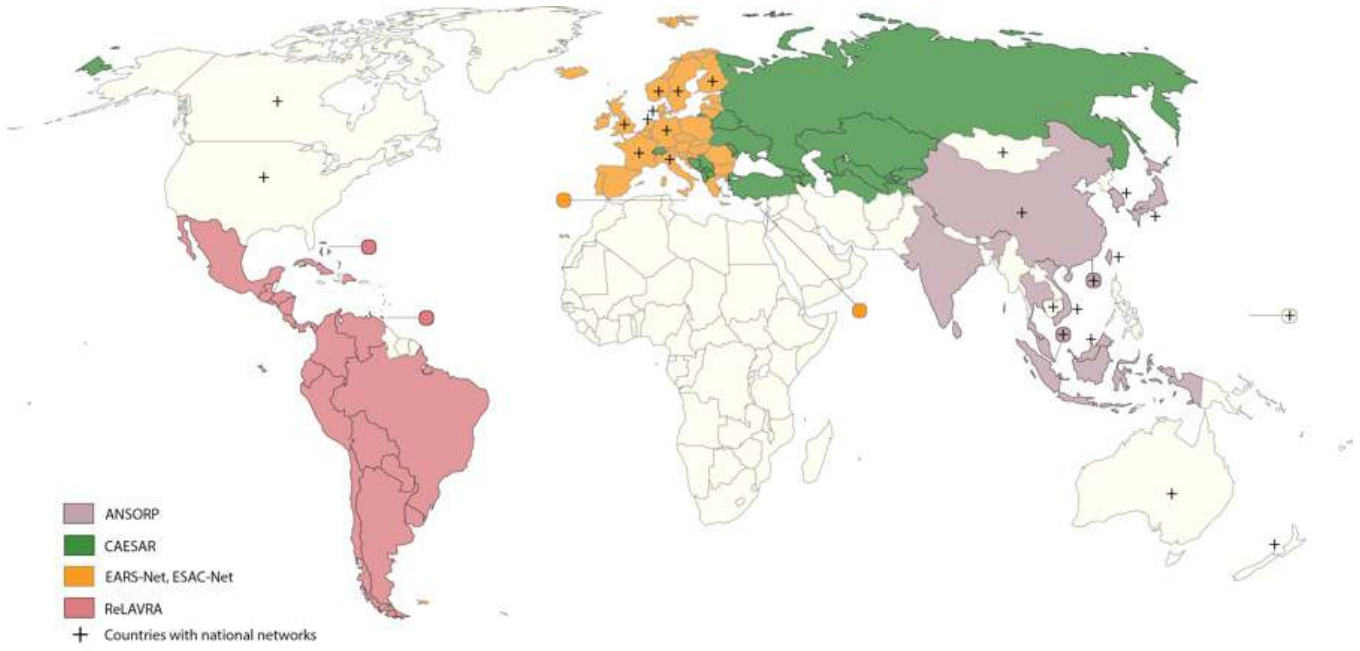


FIGURE 2: Countries and regions that currently support antimicrobial surveillance networks (Source: CDDEP) (1,22,24–30)

resistance (25,33). In the United Kingdom, surveillance data showed that the increase in MRSA prevalence in the 1990s was attributed mainly to two emerging strains, EMRSA-15 and EMRSA-16 (25). In the United States, a study using data from NARMS showed that 63 percent of *Acinetobacter* spp. infections in 2013 were multidrug resistant, resulting in an estimated additional 500 deaths in that year (34).

Further, these results can help to set priorities for future research and data collection (33). This type of evidence is needed to warn of emerging threats, change relevant clinical guidelines, and detect counterfeit or substandard drugs. In South Africa, tests of *Enterococcus faecium* bloodstream isolates in early 2012 revealed high levels of resistance to vancomycin, which led to large outbreaks of vancomycin-resistant enterococci (VRE) in hospitals that year (35). In 2015, South Africa released an antimicrobial resistance strategy framework that outlined an early warning and notification system for drug resistance patterns of concern (35). In the United Kingdom, surveillance data are already used to feed a similar national alert system that informs clinicians about emerging types of resistance and how to detect them. For example, the alert system highlighted the emergence of carbapenem-resistant Enterobacteriaceae (CRE) in 2005, which led to the creation of a toolkit for their detection, management, and control (25). In addition, treatment outcomes inconsistent with surveillance data can indicate counterfeit or substandard antimicrobials.

Public health officials can also set and evaluate progress toward AMR reduction targets if surveillance data are available. For example, the United Kingdom set a target of 50 percent reduction in MRSA between 2004 and 2008. Using surveillance data, they were able to document a 56 percent reduction by 2008 (25). France, South Korea, and Turkey are also currently implementing reduction targets based on international surveillance data (22).

Informing policies and interventions to reduce the burden of antimicrobial resistance

From epidemiological information, policymakers and interest groups can design and evaluate effective public health interventions to control resistance (36,37). Policies and interventions can target antimicrobial use and resistance in humans, animals, and the environment.

Policies and interventions in human medicine and public health

Many policies and interventions target antimicrobial use and resistance in humans. Surveillance data are particularly useful for creating policies that guide antimicrobial use at local and higher levels (33), such as updating treatment guidelines. In the United Kingdom, vancomycin was added to the treatment guidelines for staphylococcal endocarditis after surveillance showed increased resistance to methicillin (a narrow-spectrum penicillin) and documented increases in ciprofloxacin resistance led to changes in treatment guidelines for gonorrhea (25). Informed treatment guidelines help to improve patient care and safety and reduce treatment costs (18,38).

Other policies establish antimicrobial stewardship or surveillance programs. For instance, in the United Kingdom, policy-

makers used surveillance data to support creation of the TARGET tool for antimicrobial use in primary care and development of a five-year national action plan for controlling and reducing resistance (25). Global surveillance data from the SENTRY program in the late 1990s showed that Latin American countries had the highest levels of carbapenem resistance, which drove implementation of antimicrobial resistance surveillance programs in Brazil, Argentina, and Colombia (34). Similarly, research showing high resistance rates in India spurred the creation of the National Programme on Antimicrobial Resistance to perform laboratory-based AMR surveillance (39).

Surveillance systems also provide useful information for public engagement campaigns aimed at both the general public and professionals (36). For example, surveillance data are used to create training curricula for students and professionals (36), and to educate clinicians about relevant antimicrobial resistance trends in their communities (29). Surveillance networks provide an indirect link to expert training. In South Africa, increasing resistance led to the creation of a mandatory, web-based antibiotic prescribing course for clinicians and an in-person "train the trainer" course on AMR and informed prescribing for clinicians in underserved areas without antimicrobial stewardship programs (35). Epidemiologists who work with the Foodborne Diseases Active Surveillance Network (FoodNet) surveillance system of foodborne illness in the United States become experts in conducting multistate outbreak investigations and are then able to train local public health officers (40). The European Antimicrobial Resistance Surveillance Network (EARS-Net) system in Europe provides capacity building for laboratory technicians in facilities that participate in their surveys. For example, the European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) project within EARS-Net combined a survey about CRE epidemiology with a capacity building workshop training technicians to perform PCR to confirm carbapenemase production (41).

Both surveillance data and ad hoc laboratory findings can catalyze the development of broad public health policies. For instance, the discovery of New Delhi metallo-beta-lactamase (NDM-1), which confers broad antibiotic resistance on a range of Gram-negative bacteria, led the Indian Ministry of Health to designate a high-level committee to make recommendations on AMR policy (39).

Policies and interventions in food animal production

Surveillance data can lead to policies and interventions to influence antimicrobial use in food animal production systems. In Denmark, data showing increasing VRE in poultry and hogs contributed to the growth promoter ban in the 1990s (33). When therapeutic antimicrobial use continued to rise after the ban was implemented, the government instituted a new system, in which farmers and veterinarians with the highest levels of use are given "yellow cards" and required to adhere to stricter injunctions to reduce their antibiotic use (22). Similarly, in the United States, NARMS data showing increased resistance to third-generation cephalosporins in non-typhoidal *Salmonella* provided the basis for the Food and Drug Administration's (FDA's) 2012 restriction on cephalosporin use in food animals (22).

Surveillance networks can indirectly influence industry practices and help to set priorities for drug development (29). In Canada, a documented link between increased multidrug resistance in *Salmonella* Heidelberg in humans and use of ceftiofur in poultry production led to a voluntary ban on ceftiofur in the Quebec chicken industry (33). Similarly, the Japanese broiler industry voluntarily withdrew use of ceftiofur in hatcheries in 2012 after surveillance data showed cephalosporin-resistant E. coli in healthy broilers. Within a year, a follow-up study documented a significant decrease in cephalosporin-resistant *E. coli* in broilers (42). In Denmark, surveillance data showed increased ESBL prevalence in *E. coli*. Subsequent policy changes pushed the hog industry to voluntarily withdraw use of cephalosporin in pig production and develop new management practices to control illnesses such as post-weaning diarrhea (33).

Benefits of regional antimicrobial resistance surveillance networks

Coordinated regional surveillance networks have additional value, as they allow for comparisons of antimicrobial use and resistance among countries and regions (31). Often, inter-country comparisons can incentivize action (22). In addition, organisms and resistance genes move easily between countries (16). Thus, the emergence and spread of resistance is often better observed across multiple countries, especially when the pathogen is rare (43).

As is the case for AMR surveillance generally, regional surveillance systems are difficult to evaluate quantitatively. However, qualitative insights can help to elucidate their value. For instance, surveillance networks improve data quality. Regular reporting makes laboratories more conscious of quality and incentivizes improved performance (Grundmann, personal communication). Also, surveillance facilitates creation of standardized measures. When EARS-Net began collecting data, officials realized that definitions of antimicrobial susceptibility varied across countries. They used global data to calibrate standardized MICs that laboratories use to classify organisms as susceptible, intermediate, or resistant (44).

Estimating the cost of implementing antimicrobial resistance surveillance

The antimicrobial surveillance activities of the EAPHLN project will be built upon an existing network of laboratories. Currently, most EAPHLN laboratories have the equipment they need to perform antimicrobial susceptibility testing but not necessarily the trained personnel or consumables needed. In order to provide optimal patient care, these laboratories will require additional personnel, reagents, and supplies. These upgrades to routine laboratory operations are necessary to perform antimicrobial susceptibility testing regardless of whether the laboratories participate in an AMR surveillance net-

TABLE 2: Anticipated annual budget for AMR surveillance in Kenya at the NPHL and 8 satellite laboratories

Item*	Total Needed	Unit Cost (Ksh)	Total Cost (Ksh)
NPHL personnel (salary and benefits)			
Principal investigator/project manager (full-time)**	1	120,000	120,000
Clinical consultant (hourly)	108	8,000	864,000
Data analyst (per session)	5	200,000	1,000,000
Data manager (full-time)	1	600,000	600,000
Subtotal			2,584,000
Training and strategic planning			
Strategic planning session	1	2,000,000	2,000,000
Training for NPHL microbiologists	1	50,000	50,000
Training for satellite laboratory microbiologists	8	90,000	720,000
Sensitization of hospital sites	96	80,000	7,680,000
Subtotal			10,450,000
Equipment			
Printer/scanner	8	25,000	200,000
Desktop computer	24	100,000	2,400,000
Subtotal			2,600,000
Services			
Internet access***	0	0	0
Subtotal			0
Office supplies			
Printer toners	16	15,000	240,000
Printing paper (carton)	40	3,000	120,000
Printing	1	100,000	100,000
Subtotal			460,000
TOTAL (Ksh)			16,094,000
TOTAL (USD)			159,347

*See Appendix C for item descriptions.

**A principal investigator was already present in Kenya and thus not included in their national surveillance budget, but would otherwise be an essential budget item.

***Internet access is currently available in most EAPHLN laboratories, but would be an additional cost if needed.

work. We choose not to include these as surveillance costs, but others might decide differently. Where patients must bear the costs of tests—reducing demand for bacteriological testing—some financing from a surveillance budget could result in both better patient care and a greater information yield for AMR surveillance.

The cost of AMR surveillance should be a relatively modest add-on to existing laboratory costs, when built on well-functioning laboratories. The routine testing carried out by the laboratory forms the raw surveillance data. Apart from some additional quality control testing, no additional laboratory analyses are required to support a surveillance network.

Kenya is in the process of constructing a national AMR surveillance network and has provided its implementation plan and associated cost estimates as a reference for this report. Their network will initially include the National Public Health Laboratory and eight satellite laboratories. Table 2 outlines the additional costs – beyond the laboratories' general operating budgets – to start and operate an AMR surveillance network in Kenya. Expenses include additional personnel to manage and analyze data and consult on surveillance; planning and training related to data collection and management; internet access at laboratories; and additional equipment and supplies, at a one-time cost of about $2 million USD in the first year and some proportion of that in subsequent years.

Based on current expenses in Kenya, establishing and running an AMR surveillance network with eight well-functioning satellite (or county) laboratories will cost about $160,000 USD per year. Some costs scale to the size of the network (e.g., personnel and hardware at satellite sites) and some would increase in larger steps, depending upon how many laboratories could be supported centrally by core surveillance staff. We could find no data to establish the breakpoints at which increases would be needed.

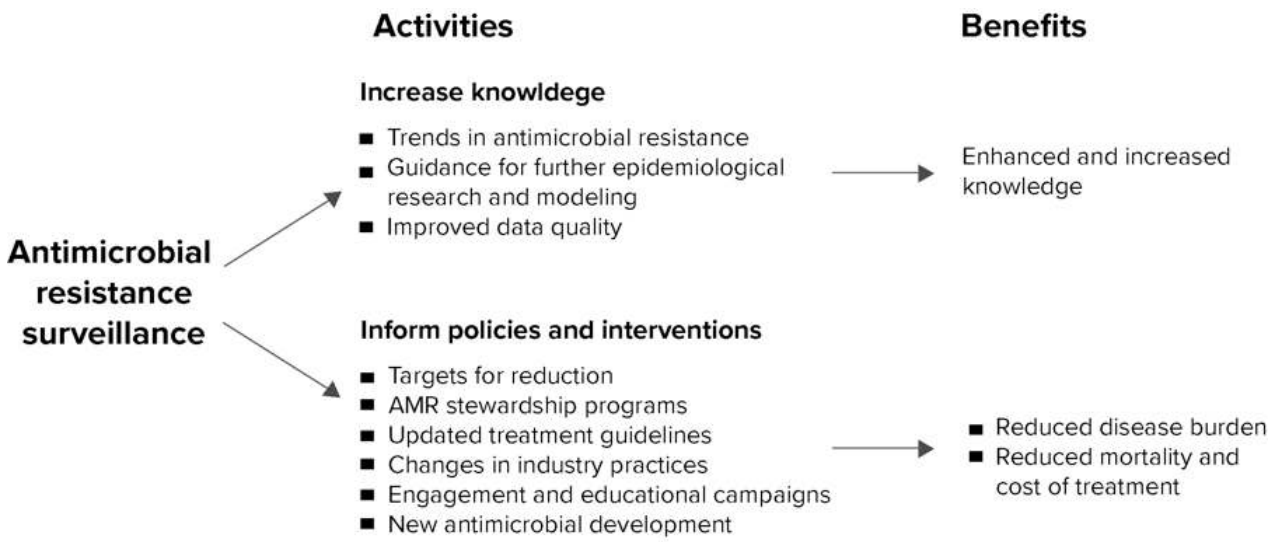


FIGURE 3: Benefit streams from antimicrobial networks (Based on Babo Martins et al. (45), Figure 2)

However, we believe that most LMICs would initially plan for a size similar to the proposed Kenya network. Estimates for other countries can be made by applying appropriate national unit costs to the volume of goods and services required.

Estimating the economic and health benefits of antimicrobial resistance surveillance

Surveillance data can be used to track trends in antimicrobial resistance rates over time, most usefully by specific pathogen-antibiotic combinations. However, implementing an antimicrobial resistance surveillance network, by itself, has no public health benefit unless the information it generates is acted on. It is the activities triggered by resistance surveillance, as described in table 1, that are beneficial. Figure 3 describes the mechanisms through which antimicrobial resistance surveillance can improve public health.

The economic benefits of AMR surveillance networks, as detailed above, are multifaceted and challenging to measure. Some benefits, such as increased knowledge of the trends in antimicrobial resistance and improved data quality, are not routinely quantified. As many of the other benefits of surveillance aim to reduce the prevalence of antimicrobial resistance, the economic benefit of the network can be estimated by assessing the impact of reduced disease burden. Reductions in antimicrobial resistance will reduce deaths from resistant infections, healthcare costs for treating those infections, and productivity losses. Even if changes are observed, attributing all or some of the changes to a surveillance system is difficult if not impossible. In fact, even if no changes are seen, the system may be keeping the rates from rising.

This is not to suggest that AMR surveillance is not effective, and in fact, all indications suggest that it is. The most likely (though not the only) chain of events through which AMR surveillance can lead to health benefits is the following:

1. High and/or increasing rates of resistance to first-line antibiotics by specific pathogens are confirmed (or susceptibility to cheaper antimicrobials is identified) and made known to policy makers.
2. Policy makers revise treatment guidelines, changing first-line recommendations to highly effective (i.e., low resistance) antibiotics.
3. Guidelines are disseminated and clinical practice changes.
4. Deaths are reduced by an amount equal to the excess caused by antibiotic-resistant infections (from epidemiologic studies).
5. Treatment costs are reduced by an amount corresponding to the decrease in the proportion of resistant infections (from hospital-based studies) or the decrease in antibiotic costs, if cheaper antibiotics are found effective or effective treatments are instituted promptly to avoid treatment failure.

Alternative mechanisms that could result in health improvement involve the types of actions described in table 1, including behavior change that is spurred by recognition of antibiotic resistance patterns on the part of clinicians, farmers, government, and the pharmaceutical industry. These are even more difficult to quantify and monetize.

Taking the five-step chain as the main route for achieving benefit, the rates at which these steps occur and the extent of change that eventually ensues cannot be measured easily under the best of conditions and has, in fact, not been done, although some estimates can be made for each step. Various elements of cost can also be estimated.

To estimate the benefits of surveillance, it is necessary to predict how much resistance rates would have changed in the absence of surveillance, a complicated and difficult task that has not been

BOX 2: Structured Expert Judgment

To estimate the benefits of AMR surveillance, we must first determine how resistance rates would have changed in the absence of surveillance. One method to estimate this counterfactual scenario is through structured expert judgment. A recent CDDEP study used this method to examine return on investment of an environmental health tracking program in the United States (50). SEJ could be used as one input into determining the value of AMR surveillance. In this instance, a group of experts could be asked to predict the burden of resistance – through resistance rates or mortality – for specific antimicrobial-organism combinations without the surveillance network. Experts provide a range of percentile values to represent an uncertainty distribution for their prediction. Each expert's predictions are weighted according to their responses to similar questions for which the answers are known. Predictions from the group of experts are then combined and compared to observed surveillance data to estimate the change in resistance that could be attributed to the surveillance network.

satisfactorily carried out anywhere. Box 2 describes the structured expert judgement (SEJ) approach for quantifying this counterfactual scenario.

Once the change in resistance rates attributable to surveillance is identified, other methods can be used to estimate the health and economic benefits of this change. Various techniques are used to value lives lost, which include both direct and indirect costs. The value of a statistical life (VSL) represents the amount that a society is willing to pay to prevent one death. Estimates of this value vary widely; however, a global meta-analysis conducted by the Organisation for Economic Cooperation and Development (OECD) in 2012 provides VSL estimates for use in policy analysis based on a compilation of stated preference studies. The OECD estimates that the VSL in member countries is $1.5 to 2.5 million USD (46). The VSL for countries in East Africa can be estimated by adjusting this OECD-specific estimate by the country's GDP per capita, adjusted for purchasing power parity (46). The VSL is then multiplied by the number of deaths avoided to estimate the value of reduced mortality.

Aside from increasing mortality, antimicrobial resistance also increases the cost of treating disease. The cost of illness method can be used to estimate the direct and indirect costs of health care and lost productivity due to antimicrobial resistance. This method requires estimates of the total cost of treating resistant infections from previous studies. For example, a 2006 study (47) provides estimates of the cost of treating methicillin-resistant *S. aureus* (MRSA), VRE, and penicillin- and cephalosporin-resistant *Streptococcus pneumoniae* compared to non-resistant strains in the United States. A 2012 study (48) compared the cost of health care through hospital charges and length of stay for resistant and susceptible infections in New York hospitals. In order to reflect treatment costs in East African countries, estimates of the direct costs of treatment can be adjusted by health expenditure per capita and estimates of indirect costs can be adjusted by GDP per capita, adjusted for purchasing power parity (49).

Conceptual framework for a cost-effectiveness analysis of antimicrobial resistance surveillance

Cost-effectiveness is a tool often used guide public health decisions in countries at all resource levels (51). The public health and economic benefit of AMR surveillance derives from the actions triggered by the information gathered, so the cost of these actions must be taken into account when assessing the value of surveillance networks. A cost-effectiveness analysis of the surveillance network would have account for the cost of implementing the network, as outlined table 2; the cost of sharing surveillance data with the regional and global public health communities; and the cost of further actions triggered by surveillance data, as described in table 1 (Figure 3) (45). Further actions could include public health interventions or educational campaigns, targets for reduction in use, or changes in treatment guidelines or industry practices (Figure 4).

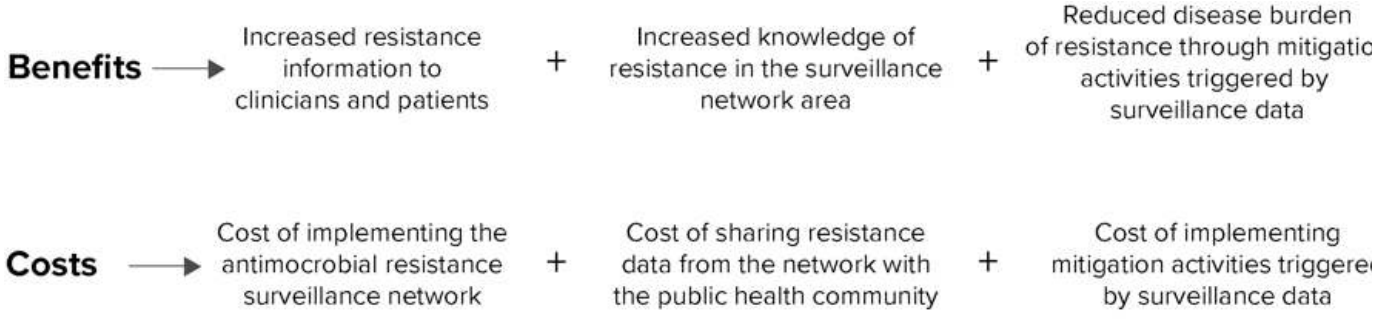


FIGURE 4: Theoretical framework for a cost-benefit analysis of antimicrobial resistance surveillance

AMR Surveillance Data Management

Once AST data are collected, efficient data management is essential to successfully contribute those data to an AMR surveillance system. Streamlined, electronic data management systems should be used to record, collate, and analyze data at the facility, national, and regional levels. Though some EAPHLN laboratories still record test results manually, keeping only paper records is not advisable because they are less consistent and more difficult to store, maintain, and analyze.

Each laboratory – including national reference and satellite – should use a laboratory information system (LIS) to record and collate data at the facility level from AST and other clinical tests. LISs are computer-based management systems that allow laboratory staff to store test results and patient information for one or more facilities. Some LISs can also be used to analyze data and identify trends. Laboratory technicians and managers should be trained in proper use of the LIS, and each facility should employ IT staff and/or data managers to provide technical support and oversight. For instance, laboratory technicians should be trained to record specific measurements from AST (e.g., zone diameters) along with test results. There are several proprietary and open source LISs available. For instance, EAPHLN laboratories in Kenya currently use LabWare LIMS™.

Laboratories should also utilize a program that can analyze AST results, especially if their LIS does not have his capability. WHONET is a free data management software developed by the WHO specifically for managing and analyzing AST results. WHONET can import data directly from a general LIS through its BacLink function or data can be entered manually. Facility-level analysis of AST results is essential for identifying local or hospital-based outbreaks.

Data collected at each participating laboratory should be aggregated at the national level. Each country should establish a database for aggregating surveillance data from participating laboratories and a system for analyzing data to identify trends and outbreaks. For example, CDDEP's ResistanceMap Surveillance Network (RSN) is an open-source software that can store and provide facility- and national-level analysis of resistance data. RSN currently operates only in the United States, but could be adapted for use in EAPHLN countries. Future versions of WHONET may also include an online platform and capability for aggregation between facilities. Data managers in each country should oversee the national AMR surveillance database and coordinate with epidemiologists for further analysis.

Capacity of EAPHLN for Antibiotic Susceptibility Testing

The East Africa Public Health Laboratory Networking Project is a regional World Bank funded project that is being implemented in five countries – Kenya, Rwanda, Tanzania, Uganda, and Burundi – in collaboration with the East, Central and Southern Africa Health Community (ECSA-HC), the East African Community (EAC), WHO, CDC, and others. The project aims to establish a network of efficient, high quality, accessible public health laboratories for the diagnosis and surveillance of tuberculosis and other communicable diseases. It provides support to enhance 1) access to diagnostic services for vulnerable groups to contain the spread of diseases in cross border areas; 2) capacity to provide specialized diagnostic services and conduct drug resistance monitoring at regional level; 3) capacity for disease surveillance and emergency preparedness efforts through the availability of timely laboratory data to provide early warning of public health events; and 4) evidence-based decision making through research.

The project was approved by the World Bank for Kenya, Rwanda, Tanzania, and Uganda in May 2010 and, in May 2012, Burundi was added. Additional financing was provided to scale up interventions in Burundi, Kenya, Tanzania, and Uganda in July 2015. The project has been supporting 32 laboratories in the participating countries in both capital cities and cross-border areas to become centers of excellence and increase access to laboratory services for poor and vulnerable populations in the areas (Figure 5). The laboratories are expected to provide specialized services to communities in these regions that are otherwise available only in the national reference facilities. (See Box 3 for a description of the general functions of district hospital laboratories.)

The project uses a "design regionally, implement nationally" approach. In other words, national institutions – including Ministries of Health and partners – execute and implement project interventions at the country level, and regional

institutions support the countries in executing activities such as knowlege sharing that cannot be performed efficiently by national agencies.

Regional working groups develop strategies for activities to be implemented at the national level and information is shared among the collaborating country representatives. Each country takes lead in a specific thematic area to guide the design, approval, and implementation of activities at national or regional levels, while ECSA-HC and EAC provide regional coordination and additional support to countries for project implementation.

Investments include improved infrastructure through renovation and construction of new laboratory facilities, equipment to expand testing capacity and scope, increased staffing level, hiring of mentors and other experts, and training for laboratory professionals. Some of the technical staff recruited by the project have been hired as government employees. Achievements of the project include:

- Financed construction and renovation of public health laboratories. These new facilities are complete and in use in some countries (five sites in Rwanda and five sites in Kenya). The Busia site in Kenya is about 85 percent complete.
- Procured laboratory equipment, including GeneXpert for tuberculosis diagnosis and rifampicin (Rif) resistance detection at the local level, incinerators, and new molecular technology for more rapid and accurate results.
- Strengthened training and capacity building to expand the pool of qualified personnel, including training of over 10,000 health personnel to date. The project expanded access to long-term courses (bachelor, masters, and PhD degree programs) and the gold standard Field Epidemiology and Laboratory Training Program (FELTP). In partnership with ECSA-HC, it supported a range of regional personnel training programs using a Training of Trainer (TOT) approach. A certificate course in laboratory management has been accredited and an inaugural course was offered at Muhimbili University of Health and Allied Sciences (MUHAS) in Dar es Salaam, Tanzania.
- Established an e-learning platform to increase access to laboratory and health training, especially in remote areas.
- Attained substantial quality improvements as documented by progress in Stepwise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) composite scores. SLIPTA is a WHO system to measure and evaluate the progress of laboratories toward international accreditation and identify areas for improvement. Facilities are awarded a rating of up to five stars based on an on-site audit of laboratory operating procedures, practices, and performance. During fiscal year 2015-16, 90 percent of project-supported laboratories achieved the project goal of two stars, compared to 20 percent at baseline, and 60 percent reached three stars and above. The Uganda National Tuberculosis Reference Laboratory achieved the gold standard ISO15189 accreditation and completed all requirements to become a WHO Supranational Reference Laboratory – the second of its kind in Africa. The Mnazi Mmoja Laboratory (Zanzibar, Tanzania) and National Microbiology Reference Laboratory (Nairobi, Kenya) were also recommended for ISO15189 accreditation by the South African National Accreditation (SANAS) and the Kenya National Accreditation Services (KENAS), respectively.
- Established a framework for outbreak investigations and created cross-border committees to conduct joint investigations and simulation exercises at various border zones, and provide training in integrated disease surveillance and response (IDSR). These activities have enabled countries to respond swiftly to several Ebola and Marburg outbreaks, containing potential epidemics and minimizing the number of confirmed cases.
- Facilitated knowledge exchange between individuals and teams to improve service delivery.

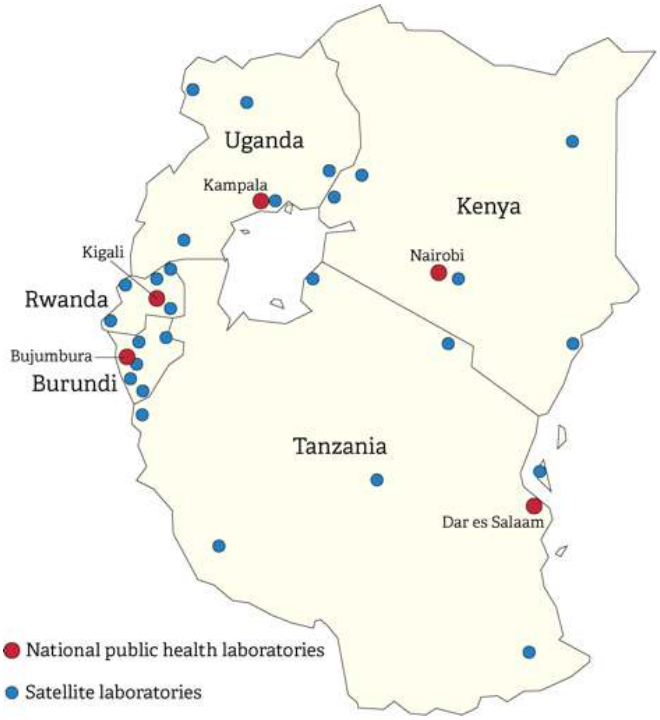


FIGURE 5: EAPHLN laboratories (See Appendix D for laboratory names; Source: CDDEP)

BOX 3: District Hospital Laboratory Functions

- Clinical: Laboratory input toward disease diagnosis and management for individual patients. This includes determining a patient's biochemical, cellular/ histopathological, and hematological parameters; genotyping; and identifying and performing susceptibility testing of the etiologic agents of infection.
- Epidemiological: Support for infection prevention and control, surveillance of hospital-acquired infections, microorganism alerts, and outbreak management
- Education: Consultations and training for laboratory and point-of-care testing staff and trainees in test execution as well as clinical and epidemiological staff in test interpretation and infection control. Consultation includes representation on hospital infection control, drugs and therapeutics, and antimicrobial stewardship committees.
- An optimally operating laboratory will:
- Provide an appropriate, comprehensive test menu that is responsive to physician needs. Tests will include those in the areas of hematology, clinical chemistry, histopathology, and microbiology. Microbiology testing should include microscopy for parasites, damaged/ displaced human cells, and bacteria; culture, identification, subtyping, and susceptibility testing for bacteria; and molecular and immunological testing for viruses.
- Establish a relationship with an external laboratory for performance of infrequent, expensive, or sophisticated testing that cannot be performed on site. This will include tests for infrequently encountered pathogens.
- Provide cut-off times for processing test requests and turnaround times for reporting results.
- Provide guidelines for specimen collection and transport.
- Maintain an effective computerized system for acknowledging receipt of specimens, tracking testing that is in progress, and reporting results. Immediate notification to the physician of critical results should be a component of an overall communication system.
- Periodically publish antimicrobial susceptibility patterns for the most commonly isolated bacteria in the institution and disseminate those data to institutional stakeholders.
- Maintain a program of quality control that ensures the accuracy of all offered tests.
- Establish a laboratory that conforms to regulatory standards.
- Maintain a system for short-term storage of all specimens and long-term storage of important isolates to facilitate additional testing if required. (60–62)

Laboratory infrastructure, equipment and supplies

We assessed the capacity for EAPHLN laboratories to perform antimicrobial susceptibility testing and contribute to AMR surveillance through structured questionnaires, interviews of select staff members and consultants who administered those questionnaires, and two site visits in Kenya, which did not include any of the border-area laboratories. Twenty-four district laboratories in Uganda, Burundi, Kenya, Rwanda, and Tanzania were evaluated for this purpose, as were the national reference laboratories in each country, for a total of 29 laboratories.

Laboratory infrastructure and capacity

GLASS (17) lists (at the minimum) stool, urine, urethral/ cervical swabs, and blood as priority specimen types. These specimen types can be processed at a basic bacteriology laboratory similar to many in the EAPHLN network. All of the laboratories assessed are performing below capacity, though a sufficient number of stool, urinary, cerebrospinal fluid, and other specimens are cultured to begin to contribute to a national surveillance program. However, the laboratories process few or no blood cultures. Only one of the five national reference laboratories and four of the 24 satellite laboratories processed more than one blood culture per week on average in 2015. Thirteen of the satellite laboratories did not process any blood cultures in 2015 (Table 3). Blood culture captures data from severe and invasive systemic bacterial infections and is therefore crucial for a surveillance network in Africa. Ultimately, not all the laboratories would have to perform blood culture to greatly enrich a surveillance system with those data. Still, many of the laboratories process a wide

variety of specimens and some even use VITEK® rapid automated systems for identification and susceptibility testing. At least some of these laboratories have the potential to develop blood culture capacity. Many of the laboratories also underperformed in antimicrobial susceptibility testing. All of the national reference laboratories carried out ASTs, and two of the five processed over 15 per week on average. However, 15 of the 24 satellite laboratories did not process any ASTs during 2015, and only three of the satellite laboratories processed more than one to two ASTs on average per week (Table 3).

Laboratory equipment

In contrast to some other resource-poor settings, equipment is not presently the capacity-limiting feature of the EAPHLN laboratories. Most of the EAPHLN facilities have resources for basic aerobic bacterial culture and are therefore equipped to provide basic data for priority organisms for global surveillance, including *Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Staphylococcus aureus, Streptococcus pneumoniae, Salmonella* spp., *Shigella* spp., and *Neisseria gonorrhoeae* (17). Surveillance in this network should also include organisms of regional importance that can be captured by the same facilities, such as toxigenic Vibrio cholerae. In practice, however, not all of the laboratories will be able to deliver data on isolates belonging to all of these species and some of them may currently be unable to contribute data at all. However, these shortfalls do not arise from lack of equipment.

Underutilized capacity: Seven of the 19 laboratories evaluated are equipped to perform bacterial culture, identification, and susceptibility testing but do not offer these services. Ten laboratories also have CO2 incubators, which could allow them to culture microaerophiles such as *Campylobacter* and *Helicobacter* species (the latter if gastric biopsies are collected). These are not standard organisms in most surveillance programs but could be useful within the region. However, only one of the EAPHLN facilities that reported having one or more CO2 incubators also had a CO2 tank. Therefore, they would not be able to use this piece of equipment even if CO2 can be procured locally. (CO2 can typically be procured within African countries; where there are no suppliers of hospital gases, CO2 can be obtained from carbonated drink plants.) Similarly, some of the laboratories are equipped to provide reference laboratory level surveillance information on resistance genotypes or resistant bacterial clones. Some capacity exists at the reference laboratories, though staff training is needed to use the requisite molecular biology equipment in district hospitals.

Laboratory reagents and supplies

All of the laboratories assessed are equipped to perform susceptibility testing by disc diffusion. In addition to some basic equipment, diffusion testing requires media certified for clinical susceptibility testing (such as Mueller Hinton or Iso-sensitest agars), appropriate (sufficiently flat and wide) and sterile Petri dishes, inoculum standards, swabs for surface application of cultures, standardized susceptibility testing discs, and control strains of known susceptibility patterns. For those that do provide the service, the absence of one or more of these requisite supplies will compromise data quality even if it does not prevent testing entirely.

Many of the laboratories assessed lack adequate control organisms for culture, identification, and susceptibility testing quality assurance. There are also reports of stock outs, meaning that bacterial culture and susceptibility testing might be available only intermittently, or is only intermittently quality assured.

In addition to disc diffusion testing, some laboratories have functional VITEK machines, which can be used for both bacterial identification and susceptibility testing and are easy to quality assure. In addition, laboratory staff tend to enjoy using automated clinical equipment. In fact, automated chemistry and haematology tasks draw laboratory staff away from microbiology and bacteriology, the specialties that perform bacterial culture and susceptibility testing. Thus, VITEK machines are valued by these laboratories and probably would be used extensively if demand for cultures were increased and supplies for the machines were available. Unfortunately, the laboratories with VITEK machines are unable to procure cards – the specialized consumables required to use the machine. Card stock outs ranged from six months to two years and were much worse than stock outs for bacteriology media and regents. VITEK machines appear to be what E-test® MIC strips were two decades ago (52): expensive tests that are easy to quality assure. They are cost effective – even in resource limited settings – yet require specialized consumables that can be procured only from a single, unassured source.

Microbiology-related stock outs extend beyond VITEK cards, however. Qualitative assessments revealed that stock outs are the most commonly proffered reason for absent, reduced, or intermittent blood culture and antimicrobial susceptibility testing capacity. Microbiology is particularly vulnerable to stock outs. Routine culture and susceptibility testing of a blood culture specimen using basic bench methods requires 25 to 48 different components (depending on the disease etiology) and unavailability of any of 14 key "bottlenecking" consumables will make it impossible to perform any testing at all on a collected blood specimen.

Stock outs shut down select laboratory services, and their implications for surveillance are considerable. They can cause temporal biases in surveillance, excluding times of the year when specific pathogens may be more common. Therefore, procurement assistance is needed to build the surveillance network. This assistance could include selecting protocols that rely on supplies available from multiple sources, pooling

procurement between laboratories and/or countries, and warehousing important consumables for the network. Stock outs are attributed to low demand, resulting in low incentive for suppliers to maintain a continuous supply. Ordering from one or a few suppliers could improve demand and potentially reduce stock outs.

Staffing capacity and training

In a 2004 Ghana study, less than 25 percent of laboratory staff were professionally qualified (53). By contrast, all but three of the EAPHLN laboratories evaluated possess at least one staff member holding a bachelor's degree or higher, which bodes well for increasing the activities and responsibilities in their workplaces. Educational background is important but continuing education is just as essential for diagnostic functions and surveillance. Technicians performing routine antimicrobial susceptibility testing can often become sloppy without refresher courses, and training is essential to stay up-to-date on new resistance profiles protocols, standards, and reporting. Availability and frequency of training programs appears to vary across the network. Importantly, for some facilities, no bacteriology training has been conducted since inception. A surveillance program should include initial training and continuing education for laboratory staff, which would also improve the quality of routine services offered by each laboratory.

The laboratories are currently performing below capacity in bacteriology. Relatively few patient specimens are cultured and only a portion of those specimens are tested for antibiotic susceptibility. Most of the laboratories did no blood cultures in 2015, which represent the most serious infections for which test results could have the greatest benefit to patients. Low microbiology laboratory utilization is a common phenomenon in settings where laboratory testing has been historically unavailable or of sub-optimal quality (54–56). Staff training should include building capacity for interfacing with clinicians about the availability and value of microbiology assays. Providing surveillance data to clinicians or involving medical pathologists may also increase utilization of laboratory services.

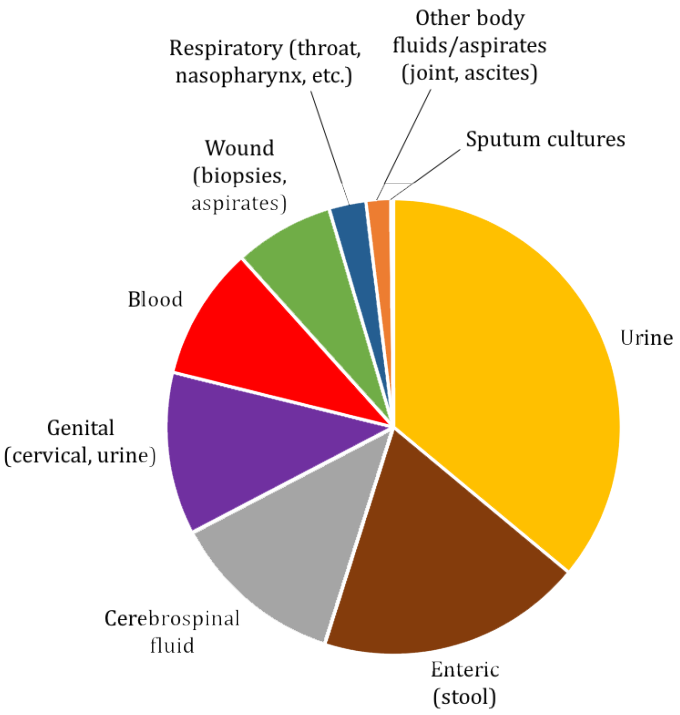


FIGURE 6: Specimen types processed in 24 EAPHLN district laboratories in 2015

Antimicrobial susceptibility testing practices

Culture media preparation and specimen processing

Reagent and media quality is critical to precision. Most of the laboratories use brands of media that are certified for diagnostic testing. However, blood to produce blood and chocolate agars are not available. Blood agar prepared with human blood from blood banks is inferior for bacteriology because human blood contains components that may inhibit bacterial growth. Only three satellite laboratories and at least two national reference laboratories can procure sheep blood. (Blood procurement information was not available for the other national reference laboratories.) Ten of the 19 satellite laboratories evaluated specifically listed animal blood procurement as a barrier to service delivery.

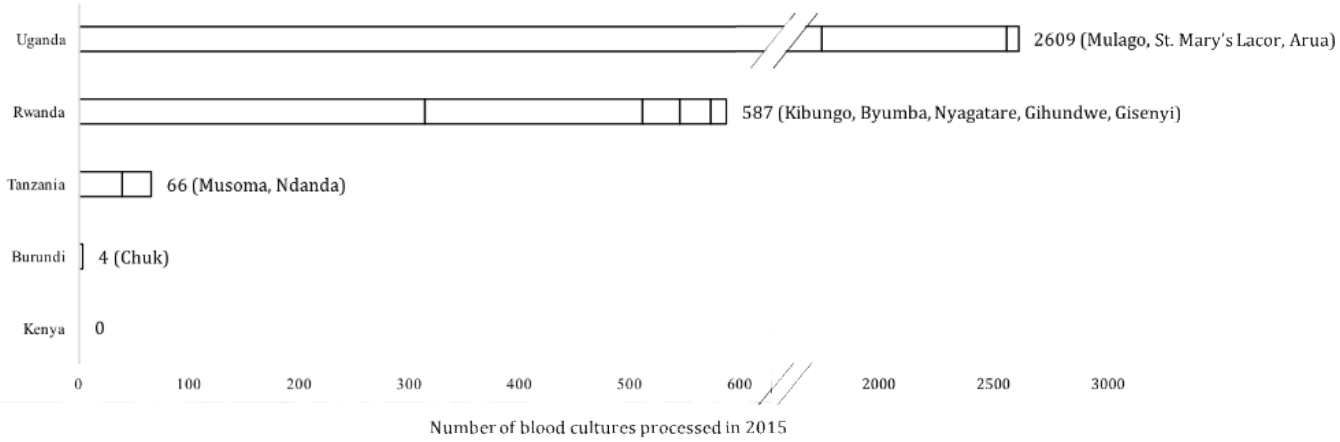
Twelve of the laboratories performing bacteriological culture are using human blood all or most of the time and none of them reported a single *S. pneumoniae* isolate – an important pathogen that often cannot be cultured using human blood. A reliable and quality assured supply of sheep or horse blood is essential to improve bacterial isolation and identification. It may be most sustainable to support sites in obtaining a regular supply of blood from in-country veterinary farms or national reference laboratories rather than shipping in commercial sheep blood, horse blood, or ready-made blood agar plates.

Bacterial identification

Most EAPHLN laboratories identify bacterial isolates biochemically, which is standard for diagnostic laboratories. Biochemical test kits (e.g., API®, Microbact®) or automated systems (e.g., VITEK®) are easier to perform and quality assure but typically cost more than manual processing and use proprietary consumables that may be challenging to procure. The precision of identification using traditional biochemical tests depends on the specific tests available and schema used. There are standard manuals for most schema;

TABLE 3: EAPHLN Laboratory Performance on Selected Bacteriology Measures

Country	Laboratory	Bacteriology samples processed	Blood cultures processed	Antimicrobial susceptibility tests (ASTs)	Annual frequency of participation in external quality assurance (EQA)
Burundi	National Institute of Public Health (INSP)	650	0	324	2
	District Laboratory	4340	4	2055	3
	District Laboratory	0	0	0	0
	District Laboratory	0	0	0	0
	District Laboratory	0	0	0	0
	District Laboratory	0	0	0	0
	TOTAL	**4990**	**4**	**2379**	**5**
Kenya	National Microbiology Reference Laboratory (NMRL)	1600	0	804	4
	District Laboratory	40	0	0	3
	District Laboratory	400	0	0	3
	District Laboratory	800	0	0	3
	District Laboratory	36	0	0	0
	District Laboratory	300	0	0	0
	TOTAL	**3176**	**0**	**804**	**13**
Rwanda	National Reference Laboratory	761	254	211	1
	District Laboratory	296	196	53	1
	District Laboratory	205	29	38	1
	District Laboratory	53	13	9	0
	District Laboratory	673	315	270	2
	District Laboratory	172	34	33	1
	TOTAL	**2160**	**841**	**614**	**6**
Tanzania	National Health Laboratory Quality Assurance and Training Centre (NHL-QATC)	650	0	468	3
	District Laboratory	80	0	0	3
	District Laboratory	884	0	62	1
	District Laboratory	525	0	0	0
	District Laboratory	767	39	0	3
	District Laboratory	162	27	0	0
	TOTAL	**3068**	**66**	**530**	**10**
Uganda	Central Public Health Laboratory (CPHL)	759	32	800	1
	District Laboratory	150	49	51	0
	District Laboratory	2905	804	0	3
	District Laboratory	0	0	0	0
	District Laboratory	11910	1756	1498	1
	TOTAL	**15724**	**2641**	**2349**	**5**



*This figure includes data from the 11 satellite laboratories – out of 24 total (five each in Burundi, Kenya, Rwanda, and Tanzania, and four in Uganda) – that processed blood cultures in 2015. Laboratory names are listed in parentheses.

FIGURE 7: Blood cultures processed at EAPHLN district laboratories by country in 2015

however, we note that most laboratories procure "standard" operating procedures (SOPs) from unspecified sites on the internet therefore the precision of identification could vary between laboratories. Additionally, stock outs of one or two biochemical reagents or media can lead to intermittent errors in identification without shutting down bacteriological services.

Blood culture

Blood culture is one of the most rewarding and challenging bacteriology services to set up and maintain. Even in optimal situations, blood culture will not always recover a culturable invasive pathogen when one is present and it is more prone to contamination than other forms of culture. Not all of the problems associated with the technique come from the laboratory. Patient treatment history, available sample volume, and sample collection and transport methods can compromise blood culture results just as often as laboratory factors (57).

Physicians value blood culture services, which provide life-saving information for some of their most challenging cases. Thus, provision of high quality blood culture service builds clientele. Clinicians also distrust blood culture if the service they use frequently turns up common contaminants associated with the skin surface or the environment, or no useful information. Therefore, when blood culture is offered, it must perform at a high standard. Clues that a blood culture service is functioning well include 1) recovery of fastidious but common bacteremia isolates such as *Streptococcus pneumoniae*; 2) infrequent recovery of common contaminants such as *Bacillus* and *Lactobacillus* spp.; and 3) low level of "mixed" infections (57).

As shown in Figure 6, though febrile illness is a principal cause of illness and death within the region, the vast majority of cultures processed by the district laboratories in the EAPHLN are for urinary tract and enteric infections. Almost all blood cultures were processed in Ugandan laboratories (Figure 7), with very little capacity for this service elsewhere. As mentioned above, blood culture is crucial for a surveillance network in Africa because it captures data from severe and invasive systemic bacterial infections. Four EAPHLN reference laboratories can already perform blood culture, and ongoing capacity building efforts are adding blood culture capability to select district laboratories. Still, automated blood culture – which would be desirable at district laboratories and essential for reference laboratories – was available only at the Kenya National Microbiology Reference laboratory at the time of assessment.

The EAPHLN laboratories appear to have prioritized stool, urine, and other easier-to-culture specimens (Figures 6 and 7). However, when resources are scarce, available evidence suggests that focusing on invasive infections (specifically blood and cerebrospinal fluid cultures) is the most cost-effective approach (54). In tropical African countries, and in particular those in the EAPHLN region, systemic infection for which blood culture could improve care and/or conserve antimicrobials is a principal cause of disease and death. Aboderin et al. (58) used a Nigerian case study to show that blood culture and susceptibility testing of patient

isolates can dramatically reduce the cost of inpatient care in resistant infections. More broadly, Penno et al. (59) recently computed that surveillance data that informs antimicrobial therapy for bloodstream infections could save over $25 USD per patient in the management of these infections. Thus, an antimicrobial surveillance network that includes data from bloodstream isolates is one of the most important potential offerings from EAPHLN. So far, we find that very few of the health institutions served have access to blood cultures via these laboratories. Overall, not enough blood cultures are performed across the network to inform surveillance and few of the laboratories have blood culture capacity at all.

Susceptibility testing

There are a number of methodological options for susceptibility testing, and surveillance systems typically collect and amalgamate data from laboratories irrespective of the methods they use. Manual MIC testing methods (technically known as broth- and agar-dilution tests) can be the most difficult to quality assure. None of the laboratories evaluated use MIC tests, which bodes well for surveillance. Disc diffusion methods work well for routine testing and surveillance in resource-limited settings and are relatively easy to quality assure. Currently, all of the evaluated laboratories in the network performing susceptibility testing use this method and a few use VITEK® testing, which provides automated MICs that are easy to quality assure when cards can be procured. Use of disc testing throughout the network is advantageous for training, procurement, and quality assurance.

There are multiple standards for disc testing. Currently, all of the laboratories use Clinical Laboratory Standards Institute (CLSI). However, not all of the laboratories have CLSI documentation, which includes guidelines as well as interpretation breakpoints. European Committee on Antimicrobial Susceptibility Testing (EUCAST) represents a viable alternative for the network since documentation is free. However, EUCAST and CLSI protocols are not identical and many of the laboratories receive capacity development assistance from North America, where CLSI is used. Use of CLSI standards will permit comparisons with laboratories elsewhere in Africa where CLSI predominates. WHONET software includes interpretation standards for CLSI, EUCAST, and other systems. Introducing this software to the laboratories will, in addition to making them surveillance ready, improve the chances that interpretations are made correctly. Documentation will still be required as it includes guidelines for test selection and performance.

For susceptibility testing by disc diffusion, most laboratories are testing isolated organisms against just two sets of antibiotics, one for Gram-positive organisms and the other for Gram-negative organisms. Sometimes this approach is used because a certain set can be easily procured and proficiency tested. More commonly, single panels for Gram negative and Gram positive organisms are used because the lab uses multidiscs – a single application disc product that includes discs pre-selected by the manufacturer. Whatever the reason, using single antibiotic panels for broad groups of organisms is less useful for clinicians than using appropriate single discs for specific organism types. For example, Pseudomonads, *Acinetobacter* and Enterobacteriaceae are all Gram-negative organisms but should be evaluated against different sets of antibiotics since treatment preferences will vary for these different organism subtypes. Most of the laboratories use or approximate CLSI standards, so they should also select individual antibiotics following CLSI guidelines.

To facilitate quality assurance, easy reinterpretations upon revision of breakpoints, and detection of new resistance mechanisms – even if laboratories report only resistance information for immediate clinical use – raw data in the form of zone diameters or MICs should be recorded and archived in a retrievable format. Recording raw data allows data managers or others to update surveillance data when breakpoints change.

Paper records can be kept but are rarely retrievable or analyzable. Networks that use them must invest considerable human resource in error-prone data handling; therefore, electronic records, databases, and analytics are unquestionably the preferred method. Data capture, analysis, and dissemination is currently not carried out in most EAPHLN labs. In some cases, laboratories keep only logbook records and most of the laboratories with electronic data management systems have no staff trained in data analysis or retrieval. In contrast to some commercial systems, WHONET is user-friendly and tech-supported, so less training is required.

Other than returning test results, there is insufficient communication between clinicians and laboratories. Also, there is no evidence of meetings, data-sharing, or antimicrobial stewardship committees. Such activities could increase both the demand for testing and the local value of surveillance data when these become available. Laboratory staff and infection control committees could initiate these discourses but would be greatly enabled by pathologists with microbiology specialization. Pathologists are few in sub-Saharan Africa, but evidence suggests that they could be instrumental in fostering communication between laboratories and clinicians. The Aga Khan University Hospital in Nairobi has a pathologist training program; such programs may be able close the clinical microbiology gap if appropriate conditions are created to recruit and retain consultant microbiologists.

Quality assurance

Internal and external quality assurance will have to be boosted across the network in order to create a robust surveillance system. Presently, all or some of the SOPs used by laboratories are from indeterminate sources on the internet. Very few laboratories have known control organisms for media and identity test verification. Also, some laboratories assessed indicated that they lacked freezers to store quality control strains. Only two reference laboratories reported that they had appropriately stored strains. The six district laboratories that had frozen stocks of quality assurance strains were all in Tanzania (3) and Uganda (3). Machakos-Kenya once had stocks of control strains but had lost them. Kitale-Kenya has stocks but their identity is unclear. The dearth of quality assurance strains is compounded by the fact that cheap and easy to disseminate options (such as Oxoid's Cultiloops®) are no longer available to many African countries. National reference laboratories could help by maintaining stocks of control strains and disseminating them periodically to the laboratories. Alternatively, the EAPHLN could designate, equip, and train one or a few of its own facilities to perform this task for the network. In addition, the EAPHLN could provide freezers so that laboratories can properly store quality control strains.

In order to competently provide a clinical service and contribute surveillance data, laboratories need internal quality assurance procedures and should be using protocols consistent with the standards they use (e.g. CLSI, EUCAST, etc.). Additionally, they should be enrolled in an external quality assurance program and undergo regular proficiency training.

Major Findings and Recommendations

These findings and recommendations were developed based on the EAPHLN laboratories and the national systems in place in their host countries, and therefore apply directly to this group of laboratories and countries. Based on our collective experience and from the global literature, however, they are also generalizable to many or most other LMICs.

Surveillance

1. Laboratory-based AMR surveillance is the second consumer of antibiotic susceptibility test results, after the patient and treating clinician.

The added value of surveillance is not free, but comes at a relatively low cost, assuming well-functioning laboratories that produce reliable results, which are needed for the primary, patient-level use. Additional costs are largely for information technology, data analysis capacity, personnel time and training, and software at the facility and national levels. Beyond that, epidemiologic and general public health expertise is essential for interpreting the data for public policy use. Kenya is in the process of establishing a national AMR surveillance system, with an estimated annual budget of about $160,000 USD.

2. AMR surveillance creates value at the facility, national, and global levels. Aggregated at each level, these include:

- Facility (local) level: information to guide antimicrobial teatment when laboratory results are analyzed regularly (e.g., monthly) and communicated to clinical staff; early detection of outbreaks of particular AMR strains and hospital-acquired infections generally
- National level: information to update standard treatment guidelines and track trends in AMR, including geographic variations
- Global level: promote understanding of AMR in each country compared to global patterns; helps complete the global picture

3. None of the five EAPHLN countries has an operational national AMR surveillance system, but all have plans to develop them, some more advanced than others.

RECOMMENDATION: All five countries should enroll in WHO's Global Antimicrobial Surveillance System (GLASS), which has promised assistance for capacity building, training, and implementation.

RECOMMENDATION: Countries should also consider contributing eligible susceptibility data (from invasive isolates) to CDDEP's ResistanceMap, which is currently the largest global repository of susceptibility test data. Currently, few laboratories produce qualifying data.

4. Computers are available in about half the laboratories, but capacity specifically for AST recording is unclear. One laboratory in Kenya, one in Burundi, and two in Tanzania report having software to record AST results.

RECOMMENDATION: Each laboratory should have a computer with appropriate software and sufficient storage for input of AST results and hospital-level analysis. If computer(s) are shared with other laboratory functions, sufficient use time should be allocated to AST results. WHONET should be installed on the designated computer in every laboratory for this purpose, and a minimum of two microbiology staff members should be trained in its use. WHONET is free and training can be arranged through WHO.

Microbiology laboratory capacity

5. Upgrading bacteriology capacity has lagged behind some other laboratory services (e.g., hematology) in the EAPHLN laboratories, even with significant infrastructure and equipment investments.

A similar pattern is likely in many laboratories throughout the region, and possibly in LMICs generally. We identified the following probable causes, which may vary by facility:

- Lack of demand from clinicians, related to length of time to get results (at least 2 days); lack of trust in results; lack of laboratory capacity for blood cultures, which are needed for many of the most serious, life-threatening infections
- Low priority given to diagnostic supplies by hospitals and other decision makers who control purchasing
- The multi-component nature of bacterial culture and antimicrobial susceptibility testing, which makes it especially vulnerable to weak supply chains and frequent stock outs; results cannot be obtained if essential components are unavailable when testing is needed
- Lack of recognition that microbiology requires dedicated, trained personnel, leading some facilities and ministries of health to rotate staff in and out of microbiology
- Few options for automated testing relative to haematology, chemical pathology or HIV testing, which may be more satisfying to staff, leading to low morale
- Requirement for patients to pay out of pocket for diagnostic tests in many countries

6. Consumable stock outs are a major roadblock to routine antimicrobial susceptibility testing in laboratories and decrease prescriber confidence in laboratory services.

Stock outs would cripple and potentially invalidate a surveillance program. The laboratories generally obtain supplies from country ministry of health central stores, which prioritize medicines over diagnostics. Of particular note, the single-source consumables required by some analytical equipment (such as the VITEK machines in the EAPHLN laboratories) increases vulnerability to stock outs.

RECOMMENDATION: Ministries of health should consolidate and prioritize inventories for infectious disease management so that antimicrobials are procured along with diagnostic media and reagents required for the optimal use of the antimicrobials, some of which are very expensive. This strategy would prevent diagnostics stock outs, optimize use, conserve expensive reserve drugs such as later-generation cephalosporins, and work toward the global goal of containing antimicrobial resistance.

RECOMMENDATION: The need for single-source consumables should be avoided when possible, or long-term agreements for a continuous source of these supplies should be included in equipment purchase agreements.

7. The laboratories are operating below capacity in microbiology culture and isolation and antibiotic susceptibility testing, and there is limited demand for the services they could provide.

RECOMMENDATION: Capacity building energies should focus on the services that clinicians value most strongly - blood and cerebrospinal fluid cultures – as well as other cultures for critically ill patients and collation and dissemination of local antibiogram information from those cultures to support empiric prescribing at the facility level. This falls into the general category of diagnostic stewardship.

RECOMMENDATION: Consultant clinical microbiologist(s) should be appointed to the network, which will enhance communication between laboratories and clinicians. We understand that qualified clinical microbiology pathologists are in short supply in the region and suggest that visiting consultants work with a handful of laboratories until more pathologists can be trained. We recommend recruiting clinicians in training to microbiology residencies, such as that at the Aga Khan University Hospital in Kenya.

RECOMMENDATION: At the periodic meetings of the network, countries or laboratories involved in surveillance should present summary reports on AMR surveillance, including specimen type and pathogen-antimicrobial combinations.

8. Laboratory testing involves a number of specialized tasks, which vary depending on the test to be performed, the scale of testing, and the types of equipment and consumables used.

Therefore, laboratory scientists must be fully trained for each task they will execute. Quality assurance for the entire laboratory depends on maintaining acquired expertise through staff training and retention. Depending on protocols used in different laboratories, repeated staff transfers – even when they do not reduce overall staff level – undermine capacity and quality.

RECOMMENDATION: Ministries of health should be advised of this issue and discouraged from rotating laboratory staff between facilities and specialties when possible.

9. For susceptibility testing, laboratories must operate using up-to-date standards.

CLSI and EUCAST are the two main options. All of the laboratories have opted to use CLSI standards, but few have these standards at the bench.

RECOMMENDATION: EAPHLN should approach CLSI for discounted regular access to standard documentation. EAPHLN should then support annual CLSI subscriptions. National reference laboratories should be responsible for updating CLSI standards for all in-country laboratories. Although EUCAST is freely accessible on the internet, we do not recommend that the laboratories switch to EUCAST at this time. This change could result in mixed standards being used in-country and challenges working with partners in laboratory capacity building (such as the CDC and the American Society for Microbiology), all of whom currently use CLSI standards. In the event that CLSI is unable to offer free or heavily subsidized access to their standards for African countries, we recommend a medium-term plan to switch to EUCAST, which would require considerable staff training.

10. External quality assurance, including proficiency testing, is essential for ensuring that laboratory tests are performed to required standards.

All of the EAPHLN laboratories and other laboratories in their countries have difficulty procuring proficiency testing.

RECOMMENDATION: Where the WHO does not offer proficiency testing, arrangements should be made to procure in-continent proficiency testing for antimicrobial susceptibility testing for surveillance. (South Africa and Kenya present potential options.) In the long term, the network should develop capacity to perform within-region proficiency testing at affordable rates.

11. Internal quality control is equally important to validate the accuracy and reliability of the laboratory test results for patient management and surveillance purposes.

RECOMMENDATION: The National Reference Laboratories should facilitate provision of standard microorganisms (ATCC) for internal quality control of media and facilitate participation in external quality assurance to all the sites in order to improve the accuracy of the AST data generated by the laboratories.

12. In order to reliably culture and sensitivity test certain pathogens from clinical specimens, whole blood must be added to culture media.

Sheep or horse blood are typically employed for this purpose. When human blood is used (e.g., time-expired blood from blood banks), fastidious organisms like Streptococcus pneumoniae and Haemophilus influenzae may be inhibited. All of the satellite laboratories in the network have difficulty acquiring whole blood of suitable quality.

RECOMMENDATION: Countries should source animal blood or prepare blood agar plates centrally or regionally and then supply to laboratories.

13. Stepwise progress towards accreditation builds quality awareness, improves laboratory performance, builds confidence among clients, provides some external assurance for laboratories, and boosts professionalism, skills, and morale among laboratory staff.

RECOMMENDATION: The EAPHLN labs should be encouraged to continue their progress through the WHO Africa scheme for Stepwise Laboratory Improvement Process Towards Accreditation and towards international accreditation, motivating countries to maintain accreditation after the expiration of World Bank support.

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Abbreviations and Acronyms

AGAR	Australian Group on Antimicrobial Resistance
AMR	Antimicrobial resistance
ANSORP	Asian Network for Surveillance of Resistant Pathogens
ATCC	American Type Culture Collection
API	Active pharmaceutical ingredient
ASP	Antibiotic stewardship program
ARSP	Philippines Antimicrobial Resistance Surveillance Program
AST	Antimicrobial susceptibility testing
CAESAR	Central Asian and Eastern European Surveillance of Antimicrobial Resistance
CAIPARS	Canada Integrated Program on Antimicrobial Resistance Surveillance
CDC	United States Centers for Disease Control and Prevention
CDDEP	Center for Disease Dynamics, Economics & Policy
CHINET	China Antimicrobial Resistance Surveillance Study
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem-resistant Enterobacteriaceae
CSF	Cerebrospinal fluid
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Program
EAC	East African Community
EAPHLN	East Africa Public Health Laboratory Network
EAPHLNP	East Africa Public Health Laboratory Networking Project
EARS-Net	European Antimicrobial Resistance Surveillance Network
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ECDC	European Centre for Disease Prevention and Control
ECSA-HC	East, Central and Southern Africa Health Community
EIP	Emerging Infections Program
EMRSA	Epidemic methicillin-resistant *Staphylococcus aureus*
EQA	External quality assurance
ESBL	Extended-spectrum beta-lactamase
ESR	New Zealand Institute of Environmental Science and Research
E-test	Epsilometer test
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EuSCAPE	European Survey on Carbapenemase-Producing Enterobacteriaceae
FDA	United States Food and Drug Administration
FELTP	Field Epidemiology and Laboratory Training Program
FINRES-VET	Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents
FoodNet	Foodborne Diseases Active Surveillance Network
GARP	Global Antibiotic Resistance Partnership
GDP	Gross domestic product
GERM-VET	German National Veterinary Antibiotic Resistance Monitoring
GHSA	Global Health Security Agenda
GISP	Gonococcal Isolate Surveillance Program
GLASS	Global Antimicrobial Resistance Surveillance System
HIV/AIDS	Human immunodeficiency virus/acquired immune deficiency syndrome
IDSR	Integrated Disease Surveillance and Response
IT	Information technology
ITAVARM	Italian Veterinary Antimicrobial Resistance Monitoring
JANIS	Japan Nosocomial Infections Surveillance
JVARM	*J*apanese Veterinary Antimicrobial Resistance Monitoring System
KARMS	Korea Antimicrobial Resistance Surveillance Program
KENAS	Kenya National Accreditation Service
KES	Kenyan shilling
KONSAR	Korean Nationwide Surveillance of Antimicrobial Resistance
Ksh	Kenyan shilling
LIMS	Laboratory information management system
LIS	Laboratory information system
LMIC	Low- or middle-income country

MIC	Minimum inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
MUHAS	Muhimbili University of Health and Allied Sciences
NAMRU-2 PP	United States Naval Medical Research Unit 2 Phnom Penh
NARMS	National Antimicrobial Resistance Monitoring System
NARS-Singapore	Singapore Network for Antimicrobial Resistance Surveillance
NDM-1	New Delhi Metallo-beta-lactamase 1
NETHMAP/MARAN	Consumption of Antimicrobial Agents and Antimicrobial Resistance among Medically Important Bacteria in the Netherlands/ Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands
NHSN	National Healthcare Safety Network
NPHL	National Public Health Laboratory
NSAR	Malaysia National Surveillance of Antimicrobial Resistance Program
OECD	Organisation for Economic Co-operation and Development
ONERBA	l'Observatoire National de l'Epidemiologie de la Resistance Bacterienne aux Antibiotiques
NORM/NORMVET	Norwegian Surveillance System for Antimicrobial Drug Resistance
PCR	Polymerase chain reaction
ReLAVRA	Latin American Surveillance Network of Antimicrobial Resistance
Rif	Rifampicin
RSN	ResistanceMap Surveillance Network
SANAS	South African National Accreditation System
SEJ	Structured expert judgement
SENTRY	JMI Laboratory's SENTRY Antimicrobial Surveillance Program
SLIPTA	Stepwise Laboratory Improvement Process Towards Accreditation
SOP	Standard operating procedure
SWEDRES/SVARM	Swedish Veterinary Antimicrobial Resistance Monitoring
TARGET	Treat Antibiotics Responsibly, Guidance, Education, Tools
TB	Tuberculosis
TOT	Training of trainers
WHO	World Health Organization
USD	United States dollar
VINARES	Viet Nam Resistance Project
VRE	Vancomycin-resistant enterococci
VSL	Value of a statistical life

APPENDIX A

National, regional, and international antimicrobial resistance surveillance networks

Country or Region	Program(s)
European Union	European Antimicrobial Resistance Surveillance System (EARS-Net) European Antimicrobial Consumption Network (ESAC-Net)
Latin America	Latin American Surveillance Network of Antimicrobial Resistance (ReLAVRA)
Asia	Asian Network for Surveillance of Resistant Pathogens (ANSORP)
Central Asia and Eastern Europe	Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR)
Global	Global Antimicrobial Resistance Surveillance System (GLASS)
Australia	Australian Group on Antimicrobial Resistance (AGAR)
Cambodia	United States Naval Medical Research Unit 2 Phnom Penh (NAMRU-2)
Canada	Canada Integrated Program on Antimicrobial Resistance Surveillance (CAIPARS)
China	China Antimicrobial Resistance Surveillance Study (CHINET)
China, Hong Kong	Hong Kong Antibiotic Stewardship Program (ASP)
Denmark	Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP)
Federated States of Micronesia	Federated States of Micronesia Surveillance Network
Finland	Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents (FINRES-VET)
France	l'Observatoire National de l'Epidemiologie de la Resistance Bacterienne aux Antibiotiques (ONERBA)
Germany	German National Veterinary Antibiotic Resistance Monitoring (GERM-VET)
Italy	Italian Veterinary Antimicrobial Resistance Monitoring (ITAVARM)
Japan	Japan Nosocomial Infections Surveillance (JANIS) Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)
Malaysia	National Surveillance of Antimicrobial Resistance Program (NSAR)
Mongolia	National Laboratory Network
Netherlands	Consumption of Antimicrobial Agents and Antimicrobial Resistance among Medically Important Bacteria in the Netherlands/Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands (NETHMAP/MARAN)
New Zealand	New Zealand Institute of Environmental Science and Research (ESR) Antibiotic Reference Laboratory
Norway	Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM/NORM-VET)
Philippines	Antimicrobial Resistance Surveillance Program (ARSP)
Republic of Korea	Korea Antimicrobial Resistance Surveillance Program (KARMS) Korean Nationwide Surveillance of Antimicrobial Resistance (KONSAR)
Singapore	The Network for Antimicrobial Resistance Surveillance (NARS-Singapore)
Sweden	Swedish Veterinary Antimicrobial Resistance Monitoring (SWEDRES/SVARM)
Taiwan	Taiwan Surveillance of Antimicrobial Resistance
United Kingdom	English Surveillance Programme for Antimicrobial Utilization and Resistance
United States	National Antimicrobial Resistance Monitoring System (NARMS) Emerging Infections Program (EIP) National Healthcare Safety Network (NHSN) Gonococcal Isolate Surveillance Program (GISP) National Tuberculosis Surveillance System
Vietnam	Viet Nam Resistance Project (VINARES)

APPENDIX B

Annual laboratory improvement budget to perform AST at the Kenya National Public Health Laboratory and eight satellite laboratories

Item	Total Needed	Unit cost (Ksh)	Total cost (Ksh)
NPHL personnel (salary and benefits)			
Laboratory supervisor (1)	0	0	0
Laboratory technicians (16)	0	0	0
ICT staff (3)	0	0	0
Data manager/statistician (1)	1	50,000	50,000
Procurement officer (1)	0	0	0
Subtotal			**50,000**
Satellite laboratory personnel			0
Laboratory microbiology technicians (2 per lab.; 45,000 Ksh/mo.)	2	45,000	90,000
Additional hospital staff (nurses, technicians; 10,000 Ksh/mo.)	64	120,000	7,680,000
Subtotal			**7,770,000**
Equipment			
Autoclave (2 per lab.)	0	0	0
Water distiller (1 per lab.)	0	0	0
Refrigerators/freezers (2 per lab.)	0	0	0
Incubators (2 per lab.)	0	0	0
Slide dryer (1 per lab.)	8	40,000	320,000
Carbon dioxide gas cylinder (2 per lab.)	16	20,000	320,000
Temperature data loggers (2 per lab.)	16	2,500,000	40,000,000
Cool boxes (4 per hospital, 20 per lab.)	288	2,500	720,000
Thermometers (8 per lab.)	64	5,000	320,000
Ultra low freezers (3 for NPHL)	1	2,500,000	2,500,000
Bacticinerator (3 per lab.)	24	400	9,600
Freezer management system and barcoding licensing (1 per lab.)	8	300,000	2,400,000
Freezer management system and barcoding installation (1 per lab.)	8	300,000	2,400,000
Subtotal			**48,989,600**
Services			
Courier (G4S)			
External quality assurance for NPHL	3	200,000	600,000
External quality assurance for satellite laboratories	1	2,000,000	2,000,000
Subtotal			**2,600,000**
Equipment service			
VITEK	8	400,000	3,200,000
BACTEC	1	50,000	50,000
PCR machine	2	100,000	200,000
Other basic equipment, including biosafety cabinets	8	300,000	2,400,000
Subtotal			**5,850,000**

Reagents			
API-10 (pack of 20 strips)	80	8,000	640,000
API-20E (pack of 20 strips)	80	8,000	640,000
API-20NE (pack of 20 strips)	80	8,000	640,000
MacConkey agar (bottle of 500g)	5	10,000	50,000
MacConkey agar with sorbitol (bottle of 500g)	5	10,000	50,000
Mueller Hinton agar (bottle of 500g)	5	10,000	50,000
Nutrient agar (bottle of 500g)	5	10,000	50,000
Sheep blood, defibrinated (bottle of 500g)	60	1,000	60,000
Triple sugar iron agar (TSI) (bottle of 500g)	5	10,000	50,000
Tryptone soya agar (TSA) (bottle of 500g)	5	10,000	50,000
Urea agar base (Christensen's agar base) (bottle of 500g)	5	10,000	50,000
Urea solution, sterile 40% (5mL)	50	10,000	500,000
Xylose lysine desoxycholate agar (XLD) (bottle of 500g)	5	10,000	50,000
Colombia blood agar base (bottle of 500g)	5	10,000	50,000
Cary blair medium (bottle of 500g)	5	10,000	50,000
Amies transport medium (pack of 50 packs)	80	8,000	640,000
Subtotal			**3,620,000**
Antibiotics			
Ampicillin, 10µg (5 cartridges per lab)	40	2,500	100,000
Cefotaxime, 30µg (5 cartridges per lab)	40	2,500	100,000
Ciprofloxacin, 5µg (5 cartridges per lab)	40	2,500	100,000
Erythromycin, 15µg (5 cartridges per lab)	40	2,500	100,000
Gentamicin, 10µg (5 cartridges per lab)	40	2,500	100,000
Tobramycin, 10µg (5 cartridges per lab)	40	2,500	100,000
Azithromycin (5 cartridges per lab)	40	2,500	100,000
Clindamycin (5 cartridges per lab)	40	2,500	100,000
Penicillin, 10 units (5 cartridges per lab)	40	2,500	100,000
Cefuroxime, 30µg (5 cartridges per lab)	40	2,500	100,000
Tetracycline, 30µg (5 cartridges per lab)	40	2,500	100,000
Rifampin, 5µg (5 cartridges per lab)	40	2,500	100,000
Norfloxacin, 10µg (5 cartridges per lab)	40	2,500	100,000
Nitrofurantoin, 300µg (5 cartridges per lab)	40	2,500	100,000
Sulfamethoxazole/trimethoprim (5 cartridges per lab)	40	2,500	100,000
Ertapenem (5 cartridges per lab)	40	2,500	100,000
Colistin (5 cartridges per lab)	40	2,500	100,000
Tigecycline (5 cartridges per lab)	40	2,500	100,000
Cefoxitin (5 cartridges per lab)	40	2,500	100,000
Mac Farland standard (2 per lab)	16	5,000	80,000
Sodium chloride (NaCl) (2 per site)	16	7,000	112,000
Glycerol (2 per site)	16	8,000	128,000
Gram stain kits large (12 kits per lab)	96	2,000	192,000
Subtotal			**2,412,000**

VITEK reagents			
Saline 0.45% (20 per lab)	160	7,500	1,200,000
VITEK 2 GN bacilli identification (21341) (200 per lab)	1,600	15,400	24,640,000
VITEK 2 GP cocci identification (21342) (200 per lab)	1,600	15,400	24,640,000
VITEK 2 AST GN (200 per lab)	1,600	15,400	24,640,000
VITEK 2 BCL GP bacilli identification (21345) (200 per lab)	1,600	15,400	24,640,000
VITEK 2 AST GP (200 per lab)	1,600	15,400	24,640,000
Subtotal			**124,400,000**
Consumables			
Blue pipette tips, non-sterile, 100-1000µl (5 packs per lab)	40	1,000	40,000
Yellow pipette tips, non sterile, 1-200µl (5 packs per lab)	40	800	32,000
BACTEC blood culture bottles (100 per lab)	800	1,000	800,000
Petri dishes, 100x15mm polysterene (10 cartons per lab)	80	9,000	720,000
Test tubes, beakers, flasks (1 set per lab)	8	80,000	640,000
Cryo vials (20 packs for NHPL)	20	3,000	60,000
Cryovial boxes (50 per lab)	400	1,000	400,000
Aluminium plate holders (10 per lab)	80	8,000	640,000
Graduated wire loops with handle (2 per lab)	16	3,000	48,000
Graduated wire loop replacements (20 per lab)	160	1,000	160,000
Inoculating loops and needles, disposable (100 packs per lab)	8,000	100	800,000
Petri dishes, 9cm (10 box per lab)	80	7,000	560,000
Urine collection containers, sterile (2000 per lab)	16,000	25	400,000
Slides (10 boxes per lab)	80	70	5,600
Slide boxes (20 per lab)	1,600	1,000	1,600,000
Polysterene tubes, 75mm (1 carton per lab)	8	12,000	96,000
Subtotal			**7,001,600**
Safety and waste management supplies			
Lab coats (2 per person, 15 people/lab)	240	1,000	240,000
Gloves (1 box/day/lab)	2,920	100	292,000
Biohazard autoclave bags, polyethylene (pack of 100;10 per lab)	80	1,000	80,000
Hand wash liquid soap (4 per lab)	32	500	16,000
Ethanol (5L bottle, 12 per lab)	96	3,000	288,000
Paper towels (1 cartons per lab)	8	4,000	32,000
Bleach (1 bottle per lab)	40	1,000	40,000
Subtotal			**988,000**
Office supplies			
Permanent markers (2 packs per lab)	16	2,000	32,000
Stationery (paper punches, staplers, staples, scissors, etc.)	8	10,000	80,000
Pens (2 packs per lab)	16	500	8,000
Pencils (2 packs per lab)	16	600	9,600
Folders (10 per lab)	80	400	32,000
CLSI guidelines for AST (500 USD)	1	50,500	50,500
Subtotal			**212,100**
TOTAL (Ksh)			203,893,300
TOTAL (USD)			2,018,746

APPENDIX C

Item descriptions for annual budget for AMR surveillance in Kenya (Table 2)

Item	Description
NPHL personnel (salary and benefits)	
Principle investigator/project manager	Full-time, existing
Clinical consultant	Part-time (8000 Ksh/hr)
Data analyst	Five sessions/year (200,000 Ksh/session)
Data manager	Full-time (50,000Ksh/month)
Training and strategic planning	
Strategic planning session	One-week external session to develop standard operating procedures, documents, forms, and training materials
Training for NPHL microbiologists	One-week training; meals, training, and materials for 20 people (500 Ksh/person/day)
Training for satellite laboratory microbiologists	One-week training; compensation for trainers and meals, training, and materials for 15 microbiologists (500 Ksh/person/day)
Sensitization of hospital sites	Transportation, food, and housing for three two-day trips per year per hospital (80,000 Ksh/trip); assuming 4 hospitals per laboratory
Equipment	
Printer/scanner	
Desktop computer	
Services	
Internet access	Existing
Office supplies	
Printer toners	
Printing paper (carton)	
Printing	Print standard operating procedures, request forms, and manuals for all laboratories and hospitals

APPENDIX D

EAPHLN Laboratories

Country	Facility	Facility Type
Burundi	Bujumbura	National Public Health Laboratory
	Chuk	Laboratory
	Kayanza	District Hospital
	Makamba	District Hospital
	Muyinga	District Hospital
	Rumonge	District Hospital
Kenya	Nairobi	National Public Health Laboratory (National Microbiology Laboratory; National TB Reference Laboratory)
	Busia	County Referral Hospital
	Kitale	County Referral Hospital
	Machakos	County Referral Hospital
	Malindi	Sub-County Hospital
	Wajir	County Referral Hospital
Rwanda	Kigali	National Reference Laboratory
	Byumba	District Hospital
	Gihundwe	District Hospital
	Gisenyi	District Hospital
	Kibungo	District Hospital
	Nyagatare	District Hospital Laboratory
Tanzania	Dar es Salaam	National Reference and Public Health Laboratory
	Kibong'oto	Hospital
	Kigoma	Hospital
	Mnazi Mmoja Zanzibar	Regional Hospital
	Musoma	Hospital
	St. Benedict's Ndanda	Referral Hospital
	Subawanga	Referral Hospital
Uganda	Kampala	Central Public Health Laboratory; National TB Reference Laboratory
	Arua	Regional Referral Hospital
	Mbale	Regional Referral Hospital
	Mbarara	Regional Referral Hospital
	Mulago	National Referral Hospital
	St. Mary's Lacor	Regional Referral Hospital

ABOUT THE CENTER FOR DISEASE DYNAMICS, ECONOMICS & POLICY

The Center for Disease Dynamics, Economics & Policy (CDDEP) was founded with the objective of using research to support better decision-making in health policy. CDDEP researchers employ a range of expertise—including economics, epidemiology, disease modeling, risk analysis, and statistics—to conduct actionable, policy-oriented research on malaria, antibiotic resistance, disease control priorities, environmental health, alcohol and tobacco, and other global health priorities.

CDDEP projects are global in scope, spanning Africa, Asia, and North America and include scientific studies and policy engagement. The CDDEP team is experienced in addressing country-specific and regional issues, as well as the local and global aspects of global challenges, such as antibiotic resistance and pandemic influenza. CDDEP research is notable for innovative approaches to design and analysis, which are shared widely through publications, presentations and web-based programs.

CDDEP has offices in Washington, D.C. and New Delhi and relies on a distinguished team of scientists, public health experts and economists around the world.