Antimicrobial resistance (AMR) is one of the world’s most pressing and urgent global health threats—one that could erode the current progress against tuberculosis (TB), malaria, HIV/AIDS, and many other infectious diseases. AMR poses an enormous threat to the safety and feasibility of complex surgeries and procedures like organ transplantation and chemotherapy, but could also make childbirth, minor infections, and hospital stays more perilous. While AMR has emerged as a critical issue at the global level, current efforts to address AMR are insufficient to curb its spread. Immediate, cross-cutting, and multidisciplinary action is required to adequately address the multidimensional drivers of AMR. In the health sector, strengthening the systems through which health services and medicines are provided is a prerequisite to making progress against AMR.

GLOBAL CONTEXT

AMR can be found in every corner of the globe and in all populations—cutting across geographic divides, political boundaries, and socioeconomic groups. Although high-income countries are continuing to struggle to contain AMR, the problem is even more worrisome in low- and middle-income countries (LMICs) where resources, capacity, and political will are frequently insufficient to adequately address the issue.

Patients with drug-resistant infections typically require more difficult and expensive treatment options. Such infections increase morbidity and mortality in individual patients and leave them infectious for longer periods of time, putting others in the community at greater risk of becoming infected. The wide-ranging effects of AMR go far beyond individuals and the community. Left unchecked, AMR has the potential to derail global public health efforts, undermine sustainable trade and economic development, and block the achievement of global initiatives such as the Sustainable Development Goals.

In one scenario, the World Bank estimates that AMR could cost the global economy as much as $3.4 trillion by 2030. Microbes naturally develop resistance to antimicrobials over time; however, AMR is accelerated by the overuse and misuse of antimicrobial medicines, improper infection control or prevention practices, and non-adherence to treatment regimens.

To raise awareness of the potentially dire consequences...
Combating Antimicrobial Resistance with Stronger Health Systems

of AMR and catalyze global action, the World Health Organization (WHO) published the Global Strategy for Containment of Antimicrobial Resistance in 2001; devoted World Health Day in 2011 to AMR; and passed several World Health Assembly resolutions, most recently resolution WHA68.7 that endorsed the Global Action Plan on AMR. In September 2016, the United Nations General Assembly also elevated AMR as a major area of concern for global leaders at a high-level meeting on AMR; this is only the fourth time a health issue has been raised to that level.

STRATEGIC RESPONSE

SIAPS recognizes that AMR is a fundamental threat to expanding universal health coverage, creating an AIDS-free generation, ending preventable child and maternal deaths, and combating other infectious disease threats. Investing in strong and resilient health systems that are able to provide equitable access to safe and effective medicines and quality services and optimize medicine use is a critical component to WHO’s strategy against AMR. The SIAPS approach, rooted in the WHO health system building blocks model and the key principles of the Global Health Initiative, works to address AMR through health system-strengthening interventions at the global, regional, national, and local levels.

Building on the work of its predecessor projects, SIAPS supports counterparts in LMICs in building awareness of the threat of AMR, advocating for a coordinated response, and implementing interventions that support the goals of WHO’s Global Action Plan on AMR. SIAPS works across disease-specific programs with multiple professional disciplines and a wide spectrum of stakeholders in both the private and public sectors to build resilient health systems, increase local capacity, and advance tools and technologies that help contain AMR. SIAPS has implemented activities in nearly 20 countries (table 1) that directly or indirectly contribute to AMR containment.

SIAPS and its predecessor projects have published multiple resources, tools, and publications that support key aspects of AMR containment, including rational medicine use, advocacy and coalition building, standards and guidelines, infection prevention and control, preservice curriculum reform, pharmacovigilance, and medication adherence, among many others (box 2). These materials are rooted in each project’s experience in implementing rational medicine use and AMR containment activities in LMICs and are intended for program implementers and health care providers working in those settings. Each of the following sections describes examples of SIAPS implementation experiences in four key areas where our efforts have helped to directly or indirectly combat AMR.

IMPLEMENTATION EXPERIENCE: ADVOCATING FOR AWARENESS AND ACTION

As highlighted in WHO’s Global Action Plan, raising awareness and improving understanding of AMR are necessary first steps toward making long-term strides against this global threat. SIAPS collaborates at the global level with WHO and other partners and at the regional and national levels to help raise awareness, share knowledge, and advocate for greater investment in AMR containment.

AMR Advocacy

By leveraging strong partnerships with regional and national organizations, SIAPS supports local advocacy initiatives against the common threat of AMR and these efforts by
training advocates, journalists, and partners to ensure that accurate messages, effective interventions, and appropriate tools are disseminated across these networks.

On a regional scale, SIAPS supported the Ecumenical Pharmaceutical Network (EPN), a faith-based regional network with member organizations in multiple countries, to conduct a training of trainers workshop on AMR and appropriate antibiotic use; participants included EPN experts from Zimbabwe, Tanzania, and Zambia. Equipped with the necessary tools and resources to train others, participants developed action plans for carrying out AMR-related trainings and interventions tailored to their unique country context. SIAPS also partnered with EPN and ReAct to issue the Call to Action: Combat Antimicrobial Resistance and Preserve Antimicrobials for Future Generations, which was adopted during EPN’s 2016 Biennial Forum.

To help increase the public’s awareness of AMR and improve the quality of reporting on the topic, SIAPS assisted Ethiopia’s regulatory authority in training journalists from an array of media outlets on how to accurately report issues surrounding rational medicine use and AMR. As a result, between 2012 and 2014, 218 news pieces were published to inform and educate the public on these topics.

**National AMR Strategies and Action Plans**

WHO has recommended that all member states develop national action plans on AMR that align with the Global Action Plan to ensure a coordinated and widespread response. SIAPS supported country counterparts in finalizing and publishing the Strategy for the Prevention and Containment of AMR (2015–2020) in Ethiopia. In addition, in South Africa, SIAPS has supported both national- and provincial-level government entities in developing AMR plans and strategies.

**Multisectoral Coordinating Groups and Coalition Building**

AMR is an issue that cuts across many disease programs and sectors of society, including finance, agriculture, and trade. The potential for AMR to affect a wide range of stakeholders calls for a multisectoral approach so that different actors are working in coordination toward a common goal.

In Namibia, SIAPS helped build a multisectoral coalition against AMR by mobilizing policy makers, program managers, and health practitioners to issue a call for action to minimize the risk of AMR. An action framework and action plan were developed and agreed upon by stakeholders to guide the implementation of activities to enhance rational medicine use and contain AMR in the country. In Swaziland, SIAPS worked alongside the Ministry of Health to help establish a new National AMR Containment Committee, which was tasked with developing a national AMR strategy in collaboration with partners and stakeholders from a variety of disciplines and sectors.

**Partnering with Professional Associations to Raise Awareness**

In South Africa, SIAPS supported national and provincial efforts to promote the role of pharmacists and pharmacy services during National Pharmacy Week campaigns in 2013 and 2014. SIAPS partnered with the South African Pharmacy Council, the Pharmaceutical Society of South Africa, and the National Department of Health to develop and print communication material for the campaigns. The 2014 campaign focused on the responsible and rational use of antibiotics. In Namibia, SIAPS worked with the Pharmaceutical Society of Namibia (PSN) to execute their annual pharmacy week in 2013, which focused specifically on AMR. SIAPS, the Ministry of Health and Social Services, and PSN developed and customized material for an accredited continuing professional development seminar and supported the development and placement of AMR-related articles in local newspapers and the airing of a one-hour live television special on AMR.
IMPLEMENTATION EXPERIENCE: STRENGTHENING SYSTEMS FOR APPROPRIATE USE

Effective governance and transparent management of medicine supply chains and the pharmaceutical services through which they are provided are central to country-level interventions that help curb the spread of AMR. Strengthening national pharmaceutical systems helps to reduce the number of falsified medicines available, reduces inappropriate distribution and dispensing of antimicrobials, and helps to create an enabling environment that reduces the barriers patients face in seeking and staying on treatment.

SIAPS works with ministries of health, national regulatory authorities, and private-sector stakeholders to improve medicine use and address AMR through strengthened regulatory functions; the development and implementation of standard treatment guidelines (STGs), essential medicines lists (EMLs), and formularies; surveillance of medicine safety, effectiveness, and quality (pharmacovigilance); improved infection control practices; and human resource capacity building.

Standard Treatment Guidelines and Essential Medicines Lists

STGs and EMLs guide the selection of medicines and outline appropriate treatment regimens. Combined with a national formulary, these documents are the cornerstones of rational medicine use and reduce excessive, unnecessary, and inappropriate prescribing practices that can be major contributors to the spread of AMR.

SIAPS has supported 15 countries in developing or revising STGs. In South Africa, SIAPS provided technical assistance to South Africa’s National Essential Drug List Committee to develop the 2012 hospital-level STGs and EML as well as to complete, publish, and implement the primary health care STGs and EML.

**SIAPS has supported the development or revision of national EMLs in Angola, DRC, Dominican Republic, Guinea, Lesotho, Mozambique, and Namibia.**

Strengthening Regulatory Systems

More than 70% of countries in sub-Saharan Africa have minimal or no regulatory capacity, which severely limits their ability to manage and provide access to safe, effective, and quality medicines. This lack of regulation increases the availability of falsified or substandard medicines on the market, which can endanger patients and accelerate the spread of AMR. By strengthening the management of key national regulatory functions and pharmacovigilance activities, SIAPS is working to improve in-country processes that can help slow the spread of AMR.

SIAPS has worked to strengthen regulatory capacity and improving processes for medicines registration in Angola, Bangladesh, DRC, Ethiopia, Mozambique, and Namibia. Bangladesh, Mozambique, and Namibia have adopted and/or implemented the internationally endorsed Common Technical Document format and specifications to standardize the medicines registration application process and, along with Ethiopia, are implementing the medicines registration module of SIAPS’ web-based regulatory information system (Pharmadex) to make their processes more efficient and transparent.

In Ethiopia, SIAPS is working with the Food, Medicine and Health Care Administration and Control Authority to improve medicine quality through systematic and frequent inspections. SIAPS is also supporting national efforts to monitor adverse drug reactions by strengthening a centralized pharmacovigilance center within the regulatory authority. In Swaziland, SIAPS partnered with the National Pharmacovigilance Center, the National Tuberculosis Program, and the National AIDS Program to develop and strengthen the pharmacovigilance system for TB and HIV programs. Specifically, SIAPS helped develop an active surveillance and reporting system to collect data on adverse drug events associated with antiretroviral (ARV) and anti-TB medicines. These data are collected, analyzed, and disseminated at the national and regional levels through Medicine Safety Watch, a quarterly newsletter. This new reporting mechanism enables stakeholders in Swaziland to effectively monitor the safety and effectiveness of medicines and identify potential contributors to AMR early.

To ensure patient safety for new multidrug-resistant TB (MDR-TB) medicines and novel regimens, SIAPS collaborated with the Food and Drug Administration of the Philippines and other agencies to establish implementation guidelines for active pharmacovigilance surveillance of a new nine-month MDR-TB regimen and for the introduction of bedaquiline, a new TB medicine. SIAPS also helped to support the introduction of a new dispersible tablet for pediatric bedaquiline, which is expected to significantly reduce medication administration issues.

Engaging the Private Sector

Working across the public and private sectors is critical to ensuring comprehensive coverage of quality services for patients regardless of whether they visit a government-run or privately run health facility or pharmacy. However, engagement of the private sector remains largely untapped in many countries. Involving the private sector
in TB care and treatment has the potential to improve the referral, diagnosis, and treatment systems.

With support from SIAPS, the Tanzania National Tuberculosis and Leprosy Program piloted an intervention designed to increase early TB case detection by engaging private-sector medicine dispensers to identify and refer persons with presumptive TB. The results of the pilot intervention demonstrated that the private pharmaceutical retail sector has the potential to contribute to early TB case detection. A similar program is being initiated with medicine dispensers in Pakistan, where the initiative has gained support from national stakeholders and the program is being scaled up.

**IMPLEMENTATION EXPERIENCE: BUILDING LOCAL CAPACITY**

- **Drug Resistant Infections: A Threat to Our Economic Future, World Bank Group**

  Appropriately managing the use of medicines in hospitals, health facilities, and community settings is integral to slowing the spread of AMR. SIAPS supports antimicrobial stewardship by strengthening drug and therapeutics committees (DTCs), revising preservice curricula, improving infection control and case management practices, and evaluating medicine use and prescribing practices.

**Drug and Therapeutics Committees**

DTCs help health facilities and hospitals select and manage medicines for the formulary, evaluate medicine use, and implement strategies to improve medicine use. Many facilities in resource-limited settings, however, either do not have DTCs or lack the capacity to manage them efficiently. SIAPS helps to strengthen the functionality and management of DTCs by providing trainings; supporting studies evaluating medicine use; and assisting with the planning, management, and monitoring processes.

SIAPS has enhanced the capacity of DTCs in DRC, Ethiopia, Jordan, Mozambique, South Africa, and Swaziland. In collaboration with in-country stakeholders, SIAPS has worked in these six countries to strengthening the functioning and effectiveness of DTCs. As of April 2015, 51 trainings that included 1,411 participants had been held, and ongoing support, such as onsite technical assistance and supportive supervision, had been provided. With SIAPS support, 447 DTCs were created and 49 were revitalized. DTCs helped conduct 36 medicine use studies or evaluations and 68 ABC/VEN analyses; develop or implement five treatment/prophylaxis guidelines and two formularies; develop five DTC- or rational medicine use-related policies; conduct 15 in-service trainings on rational medicine use or DTC topics; and revise two preservice curricula to include DTC-related topics.

To address the variations in the operations and effectiveness of DTCs in South Africa’s Gauteng province, SIAPS collaborated with national counterparts to develop guidance that outlines governance structures, operating procedures, accountability systems, roles and responsibilities, and communication strategies. SIAPS also collaborated with committees in three provinces, including Gauteng, to analyze pharmaceutical data and design corrective interventions to address medicine use problems.

**Infection Prevention and Control**

Infection prevention and control programs in health facilities help minimize the risk of hospital-acquired infections, including those that are drug resistant. Using an infection control self-assessment tool (ICAT), combined with a continuous quality improvement (CQI) methodology, SIAPS helps to develop, implement, and monitor infection control practices. SIAPS developed a version of the ICAT specifically for use in primary health care settings.

In South Africa, the ICAT tool was adopted nationwide as the official standardized infection prevention and control approach. It was adapted to align with the levels of care described in South Africa’s National Core Standards for Health Establishment and has been identified as a key tool to contain AMR. This checklist-style tool provides the necessary governance, support, and guidance needed by health care professionals to provide quality care and strengthen the effectiveness of the health system. ICAT and the CQI methodology were also adopted nationally in Namibia. A pool of 40 health professionals was trained to help disseminate and roll out the infection prevention and control guidelines and tools, which have since been implemented at all 35 district-level hospitals.

SIAPS supports countries to implement infection control practices through the development and use of guidelines, tools, and job aids like the one at left from South Africa on proper hand hygiene.
Medicine Use Reviews/Evaluations and Operational Research

Reviewing and evaluating how medicines are prescribed, dispensed, and used is vital to optimizing their use. SIAPS has supported reviews and evaluations of medicines used in TB and HIV/AIDS treatment settings in Bangladesh, Ethiopia, Ukraine, and Uzbekistan. In Jordan, SIAPS facilitated an MUE and established a CQI system in three hospitals to improve the use of antibiotic prophylaxis during cesarean sections. Reviewing the use of antibiotics led to standardized antibiotic prophylaxis protocols and procedures, improvements in the correct administration of antibiotics, and overall cost savings for each facility. Since the first MUE for cesarean sections, this same approach has been adopted by other hospitals and for other surgical procedures.

Operational research can also shed light on how patients, pharmacists, and physicians influence and affect antimicrobial use. SIAPS worked to build the capacity of its regional partner, EPN, to administer and oversee AMR and antimicrobial stewardship-related research projects conducted by its member organizations. The projects were implemented by the Christian Health Association of Malawi, the Zimbabwe Association of Church-related Hospitals, and Gertrude’s Children’s Hospital in Kenya. Activities completed by the projects team include trainings on proper hand hygiene guidelines, the publication of 16 articles on AMR following a training for journalists, and an assessment of adherence to STGs. In addition, SIAPS is helping national counterparts conduct operational research using data from SIAPS-supported tools to determine the rates of treatment enrollment, regimen switches, and drug resistance among pediatric HIV/AIDS patients in Swaziland and Namibia. In South Africa, SIAPS is helping to conduct a study to assess the feasibility of using SIAPS’ RxSolution for monitoring outpatient antibiotic prescribing practices and consumption levels at district- and provincial-level hospitals.

Preservice Curriculum Development and Training

Ensuring that the current and future cadres of health care workers have the required skills to effectively manage medicines, implement infection control practices, and support surveillance activities is a key strategy to curb AMR. Using the guidance document, Revising Preservice Curriculum to Incorporate Rational Medicine Use Topics, SIAPS helps national stakeholders carry out preservice trainings and establish rational use and AMR-related competencies for health care workers.

In Namibia, SIAPS collaborated with the School of Pharmacy at the University of Namibia to integrate case-based and self-directed learning on AMR and rational medicine use into the preservice training of undergraduate pharmacy students to equip them to fight AMR in their future careers. SIAPS also helped design and develop courses on rational medicine use at the University of Western Cape in South Africa and at the Universidad Central del Este in the Dominican Republic.

Community Case Management

Planning, coordinating, delivering, and reviewing health services provided to an individual within a health facility or community setting is referred to as community case management. Through proactive, supportive, and patient-centered care, effective community case management can help maintain the therapeutic efficacy of medicines, improve health outcomes, and minimize the risk of drug resistance.

Working with the ministry of health and community health workers (CHWs) in Burundi, SIAPS has developed job aids, checklists, and consistent reporting mechanisms to improve outreach, response, and referral times for treating sick children. With the help of these interventions, 86% of children under the age of five that presented with a fever were seen by CHWs within 24 hours. Of these, 98% were tested with rapid diagnostic kits, and 97% of those who tested positive for malaria were treated with artemisinin-based combination therapies. By helping CHWs to identify and treat malaria symptoms at the outset, SIAPS is accelerating access to appropriate treatment regimens while also putting into place mechanisms that help to ensure the completion of treatment and adequate follow-up with patients.

IMPLEMENTATION EXPERIENCE: TECHNOLOGY AND TOOLS

While not feasible in all situations, technology and tools are increasingly making it easier for program managers, providers, and patients to access the information they need when they need it, which helps improve decision making by providers and encourages healthy behaviors by patients. For providers, these types of tools can provide access to the latest treatment guidelines and medicines lists and can also improve health services through improved record and appointment keeping systems. Improving access to information can help providers ensure that they prescribe medicines in a way that minimizes the risk of AMR. Through these types of tools, patients can also receive additional information about their diagnosis, treatment regimen,
and potential side effects and can be reminded to take medications or refill prescriptions.

Online and mHealth Tools

After South Africa’s National Essential Drug List Committee published the 2012 hospital-level STGs and EML with SIAPS support, the committee recognized that even when these documents are available, it is not always easy for providers to reference them during patient consultations because some prescribers have reservations about using them in front of their patients. To help encourage widespread use of the hospital-level STGs and EML, SIAPS worked with government partners to make the documents available through a smart phone application and to optimize the online, digital versions of both. By leveraging online and mobile technology, SIAPS is making these documents easier for prescribers to use and access, which in turn can help avoid prescribing unnecessary or inappropriate medicines.

In Namibia, SIAPS is piloting an SMS-based adherence reminder system that sends text message reminders to patients to remind them to stay on ARV treatment. The adherence reminder system integrates directly with information from SIAPS’ electronic dispensing tool (EDT) and has already been implemented at 10 health facilities.

Informing and educating a wide range of stakeholders—including clinicians, program managers, government officials, public health practitioners, and the general public—is critical in the fight against AMR and has been called out as a key action by WHO and others. Working toward this goal, SIAPS has developed, and partnered with K4Health to publish two free e-learning courses on AMR on USAID’s Global Health eLearning Center. These courses feature updated content, infographics, quizzes, and a completion certificate and can be used as an AMR primer for a wide variety of public- and private-sector stakeholders.

In addition, SIAPS supports a variety of online tools to support more effective supply chains and pharmaceutical services. For example, SIAPS’ e-TB Manager was developed to address the difficulty in managing the medicine regimens of patients diagnosed with drug-resistant TB (DR-TB). The web-based tool integrates data across all aspects of TB and DR-TB control, including information on patients, medicines, laboratory testing, diagnosis, treatment, and outcomes. In Ukraine, which has the second highest burden of TB in the WHO European region, e-TB Manager is being used to manage nearly 120,000 cases of TB/DR-TB and has helped to increase adherence to STGs by monitoring the use of non-standard TB treatment regimens.

Early Warning Indicators

The number of people presenting with resistance to primary and secondary lines of ARV medicines is expected to grow as the number of people receiving therapy increases. To preserve the future effectiveness of ARVs, WHO recommends using early warning indicators to detect and minimize the risk of AMR.

SIAPS is assisting partners in Namibia to use the EDT to monitor early warning indicators for HIV drug resistance and treatment adherence in public hospitals and HIV/AIDS treatment facilities. Monitoring early warning indicators through platforms such as the EDT improves the accuracy of data, helps standardize dispensing practices, and enhances collaboration between antiretroviral therapy sites on improving service delivery.

Diagnostic Services

Too often, antimicrobial medicines are prescribed and dispensed unnecessarily or inappropriately for conditions that may not be effectively treated with antimicrobials. For example, in many low-resource settings, patients presenting with a fever may be presumptively treated with antimalarial medicines even though malaria may not be the cause of the fever. In many cases, diagnostic tests exist that can confirm a patient’s diagnosis and can help ensure that the appropriate medicine is prescribed.

A SIAPS-supported study showed that in Suriname, 45% of miners (a key population at risk for malaria) treat themselves presumptively with over-the-counter medications without first being tested to see whether they actually have malaria. The results of this study helped to establish mobile diagnostic and treatment centers to reach “hot spot” areas. In addition, SIAPS has worked with National TB Programs in Rwanda and Uganda to assess the potential to scale up the GeneXpert diagnostic tool, which can diagnose TB and some types of drug resistance in two hours. These efforts have yielded plans in both countries to mobilize additional funding to scale up the use of this important diagnostic tool.

In Swaziland, to advocate and act for AMR containment, the Raleigh Fitkin Memorial Hospital DTC implemented a quality improvement program that included performing culture and sensitivity tests on inpatients who were prescribed antibiotics. The results showed high levels of pathogen resistance to several antibiotics, including ceftriaxone and vancomycin. In response, the DTC led the development and implementation of hospital guidelines on prescribing antibiotics and switching from intravenous to oral antibiotic therapy. The Laboratory Department provides monthly culture and sensitivity test reports to the DTC to monitor drug sensitivity patterns for appropriate antibiotic prescribing.
To improve case management of malaria in Liberia, SIAPS conducted a study to determine feasibility of offering rapid diagnostic tests (RDTs) in private-sector pharmacies and medicine shops. The study showed that all owners of medicines stores were willing to use RDTs (n=26) and that 80% would accept a regulation stating that antimalarial medicines could only be given following a positive RDT test. In pharmacies, while three out of four pharmacists were willing to conduct RDTs, only one would accept a regulation requiring a positive RDT before dispensing an antimalarial. These results help to advance programmatic priorities that aim to reduce excess medicine use.

**Job Aids and Adherence Support**

Globally, only 50% of patients are able to adhere to treatment, and adherence tends to decrease over time. Ensuring that patients know when to take antimicrobial medicines, in what quantities, and for how long is crucial to curbing AMR.

Building on previous work carried out by the Strengthening Pharmaceutical Systems (SPS) Program on HIV treatment adherence, SIAPS has adapted a medication adherence tool to train adherence officers and treatment supporters in Swaziland to assess adherence to TB treatment regimens. Through the use of this tool, the National Tuberculosis Control Program can help patients who are struggling to adhere to treatment regimens through follow up with regional TB coordinators and adherence officers.

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Table 1. SIAPS-supported capacity building efforts that directly or indirectly contribute to AMR prevention and containment
THE WAY FORWARD

To ensure that people in every part of the world have access to safe and effective medicines, SIAPS is committed to continuing to build on our work, increase local capacity and ownership, engage with the global health community to share best practices, and collaborate with stakeholders at all levels of the health system to help accelerate the response to AMR.

SIAPS understands that the multifaceted and multidimensional drivers of AMR require systems-level approaches to truly make progress against its continuing spread. Through the strategic implementation of proven interventions, SIAPS is working to build stronger health systems that are better equipped to respond to the challenges of preventing and containing AMR.

Endnotes


