USAID MEDICINES, TECHNOLOGIES, AND PHARMACEUTICAL SERVICES (MTAPS) PROGRAM

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Strengthening Antimicrobial Stewardship (AMS) in Ethiopia

Technical Brief

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Overcoming barriers to building institutional capacity for AMS

Background

The World Health Organization (WHO) has declared AMR among the top 10 threats to human health. The US Agency for International Development (USAID) is working to address AMR in low- and middle-income countries supporting Global Health Security Agenda (GHSA), an international effort that brings together more than 70 countries and nongovernmental partners to collectively achieve the vision of a world safe and secure from global health threats posed by infectious diseases. The USAID Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program (2018–2024) is a key implementer supporting the GHSA vision to prevent and contain AMR in Ethiopia. MTaPS began its

work in Ethiopia in 2018, was temporarily paused in the country in 2020 due to COVID-19, and restarted activities in October 2021.

In Ethiopia, MTaPS has focused on providing support in developing a national strategy/action plan for AMR (NAP-AMR), establishing a platform for multistakeholder coordination of national efforts on AMR prevention and containment at the Ministry of Health (MOH), strengthening the National AMR Advisory Committee (NAMRAC), and building capacity for infection prevention and control (IPC) and antimicrobial stewardship (AMS).

Problem Statement

AMR represents a major threat to the Ethiopian healthcare system and to the health of the population, as evidenced by several studies referenced in the Ethiopian Public Health Institute's AMR surveillance plan.¹ For example, at Hawassa University Comprehensive Specialized Hospital, a high level of resistance to antibiotics (mainly penicillin G [81.8%] and co-trimoxazole [81.1%]) was documented for Grampositive bacteria. Gram-negative bacteria indicated high resistance to ampicillin (92.5%), tetracycline (85%), and co-trimoxazole (93.1%). The overall pooled prevalence of multidrug resistance in Ethiopia was 70.5%, higher than in many other countries, largely driven by hospitalacquired infections.² The COVID-19 pandemic increased the widespread and inappropriate use of antimicrobials. Such improper use of antimicrobials could aggravate the emergence and spread of AMR. A study conducted at four COVID-19 treatment centers in Ethiopia reported that 72.1% of COVID-19 patients received antibiotics, either before or during admission without evaluation of bacterial culture or inflammatory markers.³ Studies in other countries indicated very few (10%) COVID-19 patients had bacterial or fungal infections that would justify the use of antibiotics.⁴

For more than a decade, Ethiopia has taken steps to contain the spread of AMR. The Government of Ethiopia launched its first National Strategic Framework for the Prevention and Containment of AMR (NAP-AMR) in 2011, followed by a second five-year strategy in 2015.⁵ In a 2016 assessment using the WHO Joint External Evaluation (JEE) tool, Ethiopia demonstrated limited capacity (level 2 of 5) for AMS.

Ethiopia faces many challenges in strengthening AMS.

When MTaPS began work in the country in 2018, Ethiopia had a national AMR strategic plan in place, but enforcement of policies to prevent and contain AMR remained weak. Approximately two-thirds of all antibiotics in the country were sold without a prescription.⁶ Practical AMS guidelines existed, but most health facilities (HFs) had not implemented them. The country lacked an adequate monitoring mechanism for antibiotic consumption and use. The limited capacity of public and private health institutions—inadequate governance structures, institutional and human resource capacity, and systems and practices at the facility level—hampered the country's efforts to prevent and contain AMR.

Technical Approach

MTaPS' goal in Ethiopia was to strengthen the capacity of government and other stakeholders to contain AMR. MTaPS took a health system-strengthening approach to the design and implementation of interventions, which provides an opportunity to holistically address complex challenges by considering all health system components. MTaPS coordinated with and strengthened existing systems, when available, by aligning its interventions with MOH work plans. MTaPS supported the development of relevant workforce capacity for AMS, supported the MOH in instituting appropriate governance structures for AMS at the national, local, and facility levels, and helped to mobilize resources and generate information for evidence-based decisionmaking. By supporting AMS, MTaPS contributed to improved quality of care. MTaPS' activities have been guided by the WHO JEE tool (Version 2, from 2018) and the WHO Benchmarks for International Health Regulations (IHR) Capacities (2019).⁷ These tools are designed to help countries identify and implement recommended actions to make progress in key GHSA

¹ Ibrahim RA et al. Antimicrobial resistance surveillance in Ethiopia: Implementation experiences and lessons learned. Afr J Lab Med. 2019 Dec 6;8(1):1109. DOI: <u>10.4102/ajlm.v8i1.1109</u>.

² Alemayehu T. Prevalence of multidrug-resistant bacteria in Ethiopia: a systematic review and meta-analysis [Internet]. J Glob Antimicrob Res. 2021;26:133–139. Available from: <u>https://doi.org/10.1016/j.jgar.2021.05.017</u>.

³ Seid G, Laurens L, Fentaw T, et al. Antibiotic Overuse for COVID-19: Are We Adding Insult to Injury? Am J Trop Med Hyg. 2021;105(6):1519–1520. <u>https://doi.org/10.4269/ajtmh.21-0603</u>.

⁴ Rawson TM et al. Bacterial and fungal coinfection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020 Dec 3;71(9):2459–2468. DOI:<u>10.1093/cid/ciaa530</u>.

⁵ The Government of Ethiopia, Strategy for the Prevention and Containment of Antimicrobial Resistance for Ethiopia, second edition, 2015–2020. October 2015, Addis Ababa. Available from: <u>https://www.who.int/publications/m/item/ethiopia</u>.

⁶ Belachew SA, Hall L, Selvey LA. Non-prescription dispensing of antibiotic agents among community drug retail outlets in Sub-Saharan African countries: a systematic review and meta-analysis. Antimicrob Resist Infect Control. 2021;10, Article 13. <u>https://doi.org/10.1186/s13756-020-00880-w</u>.

⁷ International Health Regulations (IHR) (2005), an instrument of international law that is legally binding in 196 countries, establishes rights and obligations for countries related to reporting, surveillance, and response to public health events, with the aim of protecting public health globally. IHR covers 19 technical areas, including AMR.

technical areas, including AMS. Like the JEE, the WHO benchmarks categorize country capacity on multisectoral coordination, IPC, and AMS on a scale ranging from 1 (no capacity) to 5 (sustainable capacity).⁸

Stakeholder Engagement

In strengthening AMS, MTaPS collaborated with the Federal MOH's Pharmaceuticals and Medical Equipment Directorate (PMED), the Ethiopian Public Health Institute (EPHI), the Ethiopian Food and Drug Administration (EFDA), the Ethiopian Agriculture Authority (EAA), the NAMRAC, regional health bureaus (RHBs), eight MTaPS-supported hospitals, the WHO, the Food and Agriculture Organization (FAO) and the USAID Infectious Disease Detection and Surveillance (IDDS) program.

Interventions

To slow the emergence of resistant bacteria and prevent the spread of resistant infections, MTaPS is supporting Ethiopia in optimizing the use of antimicrobial medicines by strengthening governance for AMS, strengthening institutional and human resource capacity to manage AMS, and improving AMS practices and services. Since beginning its work in Ethiopia, MTaPS has provided technical assistance and support to the MOH's PMED, as well as to the RHBs for facilitylevel interventions, to carry out the following activities:

Strengthen AMS governance

- Restructured the multisectoral NAMRAC and established an AMS technical working group (TWG) under NAMRAC with clear terms of reference (TOR) to oversee AMS implementation in hospitals.
- Facilitated inclusion of the AMS program as a core operational standard in the Ethiopia Hospital Services Transformation Guidelines and standard treatment guidelines (STGs), making AMS standards

a requirement for implementation at hospitals to improve quality of care.^{9,10}

- Updated the national essential medicines list (EML) and the STGs for general hospitals with antibiotics classified into Access, Watch, and Reserve (AWaRe) classes as per the 2019 and 2021 WHO recommendations, respectively, and prevailing country context. Facilitated the printing, popularization, and dissemination of the revised EML and STGs at various events, including trainings, symposia, and review meetings.
- Supported finalization and printing of an STG implementation manual to guide stakeholders in implementing the updated STGs.
- Supported the review, printing, and familiarization of the "A Practical Guide to Antimicrobial Stewardship in Ethiopian Hospitals," which was developed in 2018, to guide healthcare facilities in the design, establishment, implementation, and monitoring of AMS programs.¹¹ This guide also helps to standardize AMS practices across healthcare facilities.

Strengthen institutional and human resource capacity for AMS

- Selected eight hospitals in consultation with the MOH. Selection criteria include the following:
 - Willingness and commitment of hospital managers to work together on AMS improvement
 - A baseline assessment conducted at the facility by the MOH, Armauer Hansen Research Institute, and WHO in 2021
 - Presence of functional AMS, IPC, and Drug and therapeutics committees (DTCs). (The presence of a functioning microbiology laboratory was a plus.)
 - Number of professional staff and availability of professional mix in the hospital, including an internist, clinical pharmacist, microbiologist, and nurse trained on IPC. (The presence of an infectious disease physician was a plus.)

⁸ The benchmark activities and levels for MSC, IPC, and AMS are detailed at <u>https://ihrbenchmark.who.int/document/3-antimicrobial-resistance</u>. See Benchmarks 3.1, 3.3, and 3.4.

⁹ Ministry of Health, Federal Democratic Republic of Ethiopia. 2016. Ethiopian Hospital Services Transformation Guidelines. Volume 1, Sept 2016. Available from:

http://repository.iifphc.org/bitstream/handle/123456789/219/Ethiopian%20Hospital%20Services%20Transformation%20Guideline%20Volume%201.p df?sequence=1&isAllowed=y.

¹⁰ Ministry of Health, Ethiopia. 2021. Standard treatment guidelines for General Hospitals. 4th edition, 2021. https://www.scribd.com/document/607423404/STG-Final-4th-Edtion-2021.

¹¹ EFDA, A Practical Guide to Antimicrobial Stewardship in Ethiopian Hospitals. May 2018. <u>https://www.ghsupplychain.org/sites/default/files/2019-03/Guide%20to%20Antimicrobial%20Stewardship%20Program%20in%20Hospitals.pdf</u>.

- Prepared an AMS training package consisting of a participant manual, trainers' guide, and PowerPoint presentations. Trained 24 trainers/champions on the package. Cascaded the AMS training to 154 healthcare workers at eight MTaPS-supported hospitals, including one private hospital (Worabe, Tibebe Ghion, Eka Kotebe, MCM Korea, Bishoftu, Debre Markos, Jimma Medical Center, and Tirunesh Bejing). The training package also served as a source document for the design and provision of integrated training (for 145 healthcare workers) and training of trainers (for 47 healthcare workers) on AMS, IPC, and Diagnostic Stewardship (DS).
- Developed an e-Learning course on AMS based on the MOH's approved continuing professional development (CPD) AMS training package and the MOH's requirements; the e-Learning course is available via the MOH's CPD portal.
- With FAO and the EAA, MTaPS trained 27 veterinary professionals on AMS, the first training of its kind for the animal health sector, resulting in plans for each participant to establish AMS programs in their respective veterinary practice areas.
- Supported the eight target hospitals in updating their facility-specific medicines lists in line with the WHO AWaRe classification of antibiotics and per national guidelines. Of these hospitals, five (62.5%) have completed the update of their facility-specific medicines list. In addition, MTaPS supported four of the hospitals in conducting an antimicrobial consumption survey.



Health professionals participate in AMS training at Eka Kotebe General Hospital, Addis Ababa, August 2022. Photo credit: Getachew Alemkere, MTaPS

Improve AMS practices and services

- Revitalized or established AMS committees at the eight selected hospitals and supported the development of facility action plans.
- Provided technical support to PMED to conduct a baseline AMS analysis at the national and HF levels

in 20 selected hospitals, including six MTaPSsupported hospitals (five public, one private), using the WHO periodic AMS national- and facility-level assessment tools.

- Trained health workers in the eight supported hospitals on AMS core components, followed by supportive supervision and mentoring.
- Assisted the eight hospitals in drafting and implementing action plans based on both the baseline analysis and the AMS training. Provided mentoring and supervision to support the facility AMS committees and health workers in the implementation of these plans.
- Contributed to the integration of indicators on the use of antimicrobial medicines into DHIS2, the country's national health information reporting system. Conducted a rapid assessment of AMS at five MTaPS-supported hospitals.
- Following the assessment, introduced audit and feedback practices on antimicrobial prescribing at all hospitals to improve future monitoring.

Results and Achievements

Ethiopia now has an established TWG serving as a governance body for AMS at the national level; updated core documents for AMS in place, including the EML and STGs based on the WHO AWaRe classification of antibiotics; a developed and tested AMS training package; and is implementing AMS quality improvement interventions in eight healthcare facilities.

The MTaPS rapid assessment conducted at five supported hospitals from July to August 2022 indicated that all hospitals had DTC and IPC committees, each with approved TOR and minutes of their meetings. At that time, only two (40%) of the five target hospitals had an AMS committee with an approved TOR and with documented meeting minutes. None of the hospitals were conducting regular audits and feedback services. As of December 2022, all five hospitals had a fully functional AMS committee with an approved TOR. Since MTaPS began work in Ethiopia, a total of 693 healthcare workers received training on AMS core components. MTaPS supported the MOH to conduct a baseline AMS survey and improved its understanding of AMS elements at 20 selected hospitals, including 6 MTaPS-supported facilities. Through supportive supervision and mentoring, eight target hospitals received technical

assistance in the development and implementation of AMS action plans, which were based on the gaps identified during the assessments.

Furthermore, the facilities introduced audit and feedback practices on the prescription and use of antimicrobials in the surgical wards of the eight hospitals. Under the leadership of the AMS and IPC committees, the hospitals have begun implementing a quality improvement project focusing on the use of antimicrobials for surgical site infection prophylaxis and hand hygiene practices in surgical wards. Data have been collected from five of the eight sites implementing this quality improvement project. The intermediate results are promising, though much remains to be done to bring about sustained change in practices. At Tibebe Ghion hospital, the intervention helped to enforce the use of cefazolin (a first-generation cephalosporin antibiotic) for surgical prophylaxis, recommended as a first-line choice in the country's clinical guidelines: cefazolin use increased from 7% to 39% in surgical prophylaxis cases while the use of ceftriaxone, a thirdgeneration cephalosporin antibiotic, which country clinical guidelines recommend for life-threatening infections, decreased by 14 percentage points, from 62.8% to 48.8%. This change also reduced the waste of cefazolin already procured, as 400 vials were administered to patients as per clinical guidelines before their expiry dates. This translates to a saving of 14,664 birrs.

Aggregate data from the five hospitals indicates that the percentage of prophylactic antibiotic doses within the recommended range increased from an average of 11.2% to 61% (figure 1).





Improvement was also recorded in the timing of presurgery initial dose administration (an increase from 68% administered at the correct time to 82.6%), despite challenges related to recording and documentation. The hospitals showed some improvement in the appropriate duration of prophylactic antibiotic use (from 35% to 44.6%), with the biggest change recorded at Korea Hospital (53.5% to 79.6%) followed by Debre Markos Hospital (30.6% to 46.0%); however, this increase was much lower than anticipated, with change in practice hampered by surgeon resistance to early discontinuation due to fear of infection. The use of oral antibiotics upon discharge of patients has completely stopped at all hospitals compared to the baseline where about 14 discharged patients received antibiotics.

Lessons Learned

- Adapt governance structures to country realities. Originally, the MOH and partners sought to identify an infectious disease specialist or senior clinician with infectious disease experience to lead the hospitals' AMS program, supported by a multidisciplinary AMS team consisting of a microbiologist and clinical pharmacist. However, given human resource constraints in Ethiopia where infectious disease specialists are few—the country has taken up a more flexible staffing approach. In low-resource settings, general practitioners and pharmacists may be tapped for lead AMS roles.
- Identify and address root causes of provider concerns. When MTaPS began AMS work at the facility level, some physicians were reluctant to share patient charts because they feared being reprimanded for their antibiotic prescribing practices. By explaining the purpose of the AMS program in supporting rationalization of antibiotic use—and underlining that the program will not be used to punish healthcare workers—the healthcare providers gradually came to support AMS and champion AMS interventions.
- Foster co-creation to build ownership and ensure locally appropriate approaches. In the revision of AMS documents, the engagement of a mix of healthcare professionals, stakeholders, and expert specialists in the development, consultation, review, and validation process has proven successful in building ownership and understanding of AMS. At the facility level, the establishment of individualized, facility-specific AMS action plans ensures both ownership and appropriateness of interventions.
- Disseminate local evidence and showcase best practices. By disseminating information such as monitoring results and facility-level best practices, including patient outcomes and savings in cost and time, MTaPS increased the support of hospital managers and regional and national counterparts. Sharing information about AMS interventions can encourage other facilities to mirror and integrate best practices, driving improved AMS implementation across the country. Information about AMS successes can be shared through conferences, publications, and fostering collaboration on specific AMR points.

- Leverage resources across facilities. Access to microbiology laboratories for drug resistance monitoring is a key success factor in rationalizing antibiotic use. By increasing opportunities for crossfacility networking and resource sharing, facilities can use limited microbiology laboratory resources to their best advantage.
- Strategically engage facility management. Familiarizing hospital administrators with facilitylevel interventions and successes, as well as with national AMS programs, requirements, and frameworks, can motivate them to adopt core AMS elements in their hospitals. Building a business case for an AMS program by demonstrating cost savings, presenting real-world evidence to demonstrate the role of the AMS program as a patient safety initiative, and engaging facility-level champions for AMS play a crucial role in garnering management support for AMS.
- Integrate to leverage resources. When feasible, AMS activities should be integrated within existing country initiatives, structures, and programs. The effect of this is twofold: it lowers AMS program costs through cost-sharing and reduces the strain on human resources and laboratory capacities. Similarly, maximizing the opportunity for cascaded training can reduce costs, with the AMS training conducted on an as-needed basis. Within facilities, integration of AMS and IPC committees or embedding an AMS committee within a DTC or clinical management team can leverage resources and further AMS implementation.
- Engage multiple stakeholders to build ownership. Because the MOH and the EFDA collaborated on the most recent EML revision, with the MOH engaging hospitals, universities, and RHBs, as well as the Ethiopian Health Insurance Agency and the EPHI, the current EML has been accepted and followed in a way that earlier versions were not.
- Employ a systems approach. It is necessary to identify AMS system structures and policies that must be put in place/revitalized/updated, to allow for successful facility-level interventions toward the rationalization of antimicrobial medicines and take appropriate action. These may include AMR strategy, guidelines, national- and facility-level AMS committees, human resource capacity, and IT tools.
- Develop and disseminate implementation tools such as the STG implementation manual, to

support the implementation of new policies or guidelines.

Empower facilities with information for datadriven decision-making to achieve improvements in practices. A data-driven AMS action in the surgical wards helped target investment and identify feasible interventions to improve surgical antibiotic indication, choice, dosing, pre-surgery initial dose timing, and duration. Using data to shape its decisions, the facility introduced basic interventions including education and non-regular audits and feedback, and achieved improvement in choice, dosing, initial dose timing, and duration of antibiotic use.

Pathway to Sustainability

"We [included] the antimicrobial stewardship program as one of the operational standards in the Ethiopia Hospital Service transformation guideline as well as in Health Center guidelines, so that [AMS] is one of the mandatory components that each and every hospital should require. . . to renew its license. . . that this is one of the biggest achievements we made so far."

---Mr. Yidnekachew Degefaw, AMR Team Coordinator, PMED/MOH, Secretary of NAMRAC

By supporting the formation and operation of AMS governance bodies at the national and facility levels and building the capacity of the MOH/PMED and the RHBs to implement AMS interventions, MTaPS has established embedded structures for AMS implementation. With the inclusion of the AMS program in the Ethiopia Hospital Service Transformation Guideline and the STGs, meeting basic AMS standards has become a requirement for HFs. An AMS indicator (percentage of antimicrobials prescribed) is institutionalized in the national DHIS2, and it serves as a proxy for the national level to monitor AMS in facilities. More than 600 health professionals are trained in antimicrobial stewardship. AMS resources are now readily available to healthcare workers, including the revised AMS practical guide and an e-Learning course on the newly developed AMS training packages.

As MTaPS phases out its activities, the MOH will continue to train and engage in joint activities with partners to further bolster local capacity to continue AMS activities in the country.

Conclusions

With technical and financial support from MTaPS, Ethiopia has strengthened governance and implementation of antimicrobial stewardship in the country, at the national, regional, and facility levels. Healthcare workers at participating facilities have recognized the benefits of the AMS interventions—in terms of patient outcomes and savings in time (fewer injections to administer) and money. Evidence from facility-level implementation has demonstrated the success of AMS in the Ethiopian context, helping to build overall national support for AMS; however, many challenges remain.

To help move AMS forward, Ethiopia will need to address the challenge of limited access to first-line antibiotics to enable facilities to change their prescribing practices in line with the country's clinical guidelines. Ethiopia's MOH has voiced its strong commitment to AMS and is well-positioned to further demonstrate this commitment through the engagement of high-level government partners to champion the cause and rally financial resources. This will allow for scale-up of AMS to additional HFs, contribute to enforcement of AMS policies such as selling antimicrobials only with a prescription, and enable it to carry out central-level monitoring of AMS interventions to generate further country evidence on the benefits of AMS.

"With strong managerial support, antimicrobial stewardship (AMS) is possible in low-income countries. Because health care settings are critical stakeholders for AMR containment, we need to expand [AMS] on a large scale as soon as possible."

—Dr. Workeabeba Abebe MD, MPH, Associate Professor, College of Health Science, Addis Ababa University; and Consultant Pediatrician and Specialist in Infectious Diseases, Tikur Anbessa Specialized Hospital

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About USAID MTaPS:

The USAID Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program (2018–2024) enables low- and middle-income countries to strengthen their pharmaceutical systems, which is pivotal to better health outcomes and higher-performing health systems. The program is implemented by a consortium of global and local partners, led by Management Sciences for Health (MSH), a global health nonprofit.