The Core Elements of
Human Antibiotic Stewardship Programs in Resource-Limited Settings:
National and Hospital Levels

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

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Centers for Disease Control and Prevention
Robert R. Redfield, MD, Director

National Center for Emerging and Zoonotic Infectious Diseases
Rima Khabbaz, MD, Director

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Acronyms

AMR	Antimicrobial resistance
ASP	Antibiotic Stewardship Program
AST	Antimicrobial Susceptibility Testing
CDC	Centers for Disease Control and Prevention
CRE	Carbapenem-resistant Enterobacteriaceae
EML	Essential Medicine List
EMR	Electronic Medical Record
GAP	Global Action Plan
ID	Infectious Disease
LMIC	Low- and middle- income countries
MOH	Ministry of Health
PPS	Point Prevalence Survey
WHO	World Health Organization

Introduction

Global, coordinated action to address the rising threat of antimicrobial resistance (AMR) is a public health priority. Rates of AMR have been increasing worldwide; limited available data also demonstrate high rates of AMR in low- and middle-income countries (LMIC) where resources to combat resistance may be insufficient [1–3]. The World Health Organization released its Global Action Plan (GAP) to combat AMR in 2015, a key component of which is the development and implementation of antibiotic stewardship programs (ASP)[4].

Antibiotic stewardship refers to coordinated efforts and activities that seek to measure and improve use of antibiotics. Implementation of ASPs has demonstrated positive public health and clinical impacts including reducing costs, lengths of hospital stays, and the burden of antibiotic resistance while maintaining or improving patient outcomes [5,6]. The U.S. Centers for Disease Control and Prevention (CDC) released the Core Elements of Hospital Antibiotic Stewardship Programs in 2014, which outlines essential components for ASPs in hospitals and provides practical guidance for implementing a robust ASP in an acute care facility [7]. Variations to the Core Elements have been developed to deal with the particular challenges in small, rural or critical access hospitals in the United States [8] and in outpatient facilities [9] and nursing homes.

However, to date, implementation strategies have all been aligned with expected resources in high-income countries, such as the United States, that have robust regulatory frameworks and well-functioning healthcare systems. Practical, high-yield strategies to implement the Core Elements concepts in international resource-limited settings with weak health systems are urgently needed to move ASPs forward in such settings. Such strategies must be feasible, sustainable, and tailored to the resources that are currently available in such countries while capacity is built in areas of need to ensure access and reduce the inappropriate use of antibiotic agents. Additionally ASPs must be aligned with other national and international public health programs, such as the global sepsis initiative, so that conflicting guidance on antibiotic use is avoided.

This document seeks to provide a framework for thinking about implementation of antibiotic stewardship programs in such settings and the approach outlined here is based on expert opinion and experiences in implementing ASPs in the United States and globally. The document includes both national and facility-level activities, as the former are a critical compliment to the activities that are undertaken in hospitals and other health care facilities. First, national level policies and programs will be discussed and grouped by capacity and resources needed to implement the activities. Next, facility-level activities at the acute care level will be discussed, also grouped by capacity and resource level. Stewardship is needed at multiple levels of care, including outpatient settings. This document includes national policies that can improve use across the spectrum of care. There is also a focus on ASP implementation at the acute care level as a starting place for facility-level implementation in countries; future documents will address implementation in outpatient and other settings. The focus of the ASPs described here are on the human health side, but linkage with the veterinary and agricultural sectors should be considered where appropriate.

Approaches for National-Level Implementation

Challenges for implementation of ASPs in resource-limited settings

Low- and middle-income countries have a number of challenges in implementing ASPs. These include gaps in the availability of appropriate policies and guidelines, few infectious diseases-specific and pharmacy-specific training programs, limited diagnostic and laboratory capacity, gaps in data on antibiotic use or antibiotic resistance patterns, weak data management systems, inexperience with data analysis and program implementation, and scarce human and material resources [10–13]. Additionally many low- and middle-income countries struggle with limited access to antibiotics, which can also drive inappropriate use. While these challenges may pose barriers to implementing all stewardship activities recommended by global or local public health agencies, meaningful steps toward implementing a national stewardship program are possible in any setting.

Tiered national-level antibiotic stewardship activities in resource-limited settings

We categorized core ASP activities by levels of capacity frequently seen in resource-limited settings (Table 1). We defined basic activities as those that typically do not require substantial resources except for personnel time and access to some technical expertise. Intermediate activities were defined as those that require some resources, planning, and dedicated staff to implement. Advanced activities were defined as those that require the establishment of a program with trained staff and allocation of dedicated resources.

Table 1 – National-level antibiotic stewardship program activities and policies, categorized into **Basic**, **Intermediate**, and **Advanced** categories

Capacity / resource level	Activity
Basic: *require only limited resources*	• Promote the creation of national committees and teams with clear terms of reference • Develop national and/or sub-national antibiotic stewardship action plans • Participate in antibiotic awareness campaigns • Adopt policies requiring prescriptions
Intermediate: *require some resources, planning, and dedicated staff*	• Develop and ensure access to recommended formularies • Create and promote adherence to evidence-based treatment guidelines for common clinical syndromes • Promote diagnostic stewardship • Support inclusion of antibiotic stewardship training in pre-service curriculums or stand-alone courses
Advanced: *require establishment of a formal program with trained staff and dedicated resources*	• Enforce policies requiring prescriptions • Track antibiotic dispensing using available data and set national targets for improvement • Measure antibiotic use and assess appropriateness • Describe resistance patterns to improve treatment guidelines and identify priority pathogens • Monitor antibiotic quality • Address drivers of inappropriate prescribing behavior

Basic level national activities: require only limited resources

Promote the creation of national committees and teams with clear terms of reference. One of the most important components, and one of the first activities a country should undertake, is the establishment of relevant national ASP committees and teams, which typically would include a coordination and leadership team and a technical working group [14]. An ASP coordination/leadership team may consist of at least one Ministry of Health (MOH) focal person with dedicated time to lead the ASP, additional Ministry stakeholders (e.g., agriculture), and important stakeholders and subject matter leaders (e.g., pharmacists, infectious disease specialists, and microbiologists). The responsibilities and terms of reference of a national ASP leadership group may include developing a national antibiotic stewardship action plan or policy; convening and liaising with stakeholders; and reviewing the progress of these programs.

An additional technical working group may also be formed, which could consist of technical level staff to oversee the implementation of the national action plan or policy. Terms of reference could include developing protocols or standard operating procedures, monitoring and evaluation, and reporting progress to policy makers and other interested national and global groups. Depending on the country, additional committees and teams might needed at the sub-national levels, if appropriate.

Develop a national and/or sub-national antibiotic stewardship action plan. National antibiotic stewardship action plans, or national action plans on AMR that cover stewardship, are vital tools for countries as they take the broad stewardship goals outlined in the WHO GAP and adapt them for their country context. National action plans are also important to outline country priorities and as a first step toward securing additional resources for implementation. A country may also choose to develop sub-national stewardship action plans instead or in addition to the national action plan. Publicly available resources to assist countries with development of such plans exist: several national action plans that specifically focus on stewardship are available from high resource settings [15–17] and a searchable database of national action plans on AR from a variety of resource settings are available online from the WHO [18], though not all of these address stewardship specifically. Additionally, the WHO has provided a sample template for countries who may need assistance with drafting a national action plan for AR, which includes specific objectives around antibiotic stewardship [19]. As with any action plans, there is a need to align the content of antibiotic stewardship action plans with other initiatives that provide guidance on use of antibiotics.

Participate in antibiotic awareness campaigns. Public health campaigns can be used to support behavior change [20–22] and can contribute to improvements in overall antibiotic use [23]. Examples of nationally supported antibiotic awareness campaigns include India's Red Line public awareness campaign [24], and Thailand's Antibiotic Smart Use (ASU) program [25]. While creating and implementing a customized awareness campaign might be resource intensive, countries can also access existing materials through the WHO website **http://www.who.int/campaigns/world-antibiotic-awareness-week/en/** [26] or CDC website **https://www.cdc.gov/antibiotic-use/week/index.html** [27]. Other awareness campaign resources include "How to improve the use of medicines by consumers [28]" "Promoting rational use of medicines: core components [29]" and CDC's "Be Antibiotics Aware Stakeholder Toolkit [30]."

Adopt policies requiring prescriptions for antibiotics. Widespread access to antibiotics without a prescription is prevalent in many low- and middle-income countries. Policies that require a prescription from a healthcare provider are a critical first step, although probably not sufficient, toward improved rational use of antibiotics. Experience from countries in Latin America has demonstrated that policies requiring prescriptions alone are not as effective as when such policies are paired with dedicated regulatory enforcement [31,32]. However, approving such policies may not require many resources and must be done before enforcement can be carried out. While such policies may themselves have some impact on antibiotic use, assessing and improving compliance will require resources (see Advanced category).

However, if not implemented thoughtfully, prescription policies in some countries might have the unintended consequence of limiting access in areas where healthcare providers are not readily accessible. To address this, a country could adopt policies to require prescriptions in certain geographic areas where access to medical consultation are more prevalent (e.g., in cities), while in other areas a prescription from a community health worker or pharmacist/chemist may be accepted. Similarly, countries may require that only certain antibiotics (e.g., broad-spectrum antibiotics where resistance or overuse is a concern) may require a prescription but other antibiotics that would be frequently used for common illnesses could still be accessed over the counter.

Intermediate level national activities: require some resources

Develop and ensure access to recommended formularies. Recommended formularies are lists of antibiotics that are suggested for certain healthcare settings. In developing a recommended formulary, countries should consider the needs of patients and facilities where they receive care. For example, clinicians in rural or primary health centers may need wide access to first-line antibiotics (e.g., penicillin, ampicillin, TMP-SMX), but last resort antibiotics such as carbapenems or colistin might be limited to tertiary care hospitals. Efforts to create antibiotic formularies may be linked to efforts within countries to create or update essential medicine lists (EML). The WHO is developing a version of the EML that takes into account some of these considerations, including three categories of antibiotics, "ACCESS", "WATCH", and "RESERVE" [33]. The ACCESS category are antibiotics recommended to be available at all times for a wide range of common infections; WATCH are first or second-choice antibiotics, which should be used carefully to avoid further resistance; and RESERVE antibiotics are last-resort options that should only be used in severe or rare situations. The WHO document "How to Develop a National Formulary Based on the WHO Model Formulary - A Practical Guide" is available to help countries develop a recommended list of antibiotics [34]. Once recommended antibiotic formularies are established, it is critical to take steps to ensure that national procurement and supply systems are able to reliably support access to the recommended medications.

Create and promote evidence-based treatment guidelines for common clinical syndromes. One important activity for a national program is to support the use of evidence-based treatment for common clinical syndromes (e.g., sepsis, community acquired pneumonia). Ideally, evidence-based standard treatment guidelines should reflect the local epidemiology and susceptibility of causative organisms within the country. If country-level data are not available, the guidelines might be based on expert opinion or guidelines from countries where the epidemiology is likely to be similar. It is important to stress that even if local data are not available, the presence of standard treatment guidelines is still a critical and necessary initial step to improving antibiotic use.

Following the development of guidelines by designated experts, ministries of health can promote adherence to these guidelines through education and messaging campaigns aimed at providers, the public, relevant professional societies, or training programs aimed at healthcare providers. Most commonly, campaigns have focused on common clinical syndromes such as respiratory tract infections, urinary tract infections and sexually transmitted diseases, where antibiotics are frequently misused [22]. Recognizing that education alone is often insufficient to change practice, countries may also consider developing incentives and/or disincentives to promote adherence to the guidelines, possibly as part of a multimodal strategy.

Promote diagnostic stewardship. Diagnostic stewardship ensures that patients get the right test at the right time. It should ensure that tests happen when needed, that specimens are collected properly, and that results are given to providers in a timely manner to guide patient treatment. Guidelines developed for the treatment and management of infections should include criteria for the appropriate use of laboratory tests [35]. In areas where some reliable antimicrobial susceptibility testing (AST) capacity exists, countries may focus on improving the use of these labs by providers, which will ultimately improve the data available to clinicians for appropriate antibiotic use and improved patient care [36]. To improve and expand the availability of diagnostic capacity, countries may encourage and prioritize allocation of sufficient resources for diagnostic testing, including culture diagnostics, to guide antibiotic therapy. Countries can promote appropriate diagnostic testing by conducting on-the-job trainings, improving collaborative communication between laboratories and providers, and strengthening pre-service curricula to highlight the importance of prudent testing.

Support inclusion of antibiotic stewardship training in pre-service curriculums, in-service programs, continuing education programs or stand-alone courses. Studies have consistently identified gaps in the knowledge, attitudes, and practices of healthcare students and professionals in LMIC [37–39]; and stewardship has not been consistently included in undergraduate and graduate training programs [40–42]. Training programs can help to improve clinical practice, although the implementation of such courses will take resources to implement. Examples are available [43–45] although countries should consider their local context, including treatment guidelines and regulations, when considering developing training courses.

Advanced: require a formal program with dedicated resources

Enforce policies requiring prescriptions. Policies requiring a prescription for antibiotics do not always result in adherence to the policy. To improve compliance with policies, Ministries may consider various approaches, ranging from enforcement with penalties for non-compliance; to incentivizing improved compliance; or even public education campaigns to inform the general public about the requirements and importance of getting a prescription prior to obtaining antibiotics.

Track antibiotic dispensing using available data and set national targets for improvement. Countries have an interest in understanding the types of, quantities of, and locations where antibiotics are being used. This is the objective basis for identifying which antibiotics may be targeted for improved use, or which areas or locations could benefit from stewardship activities. Furthermore, these data can be used, depending on collection methodology, to compare use within a country and track trends. Antibiotic use can consist of prescribing, dispensing, and consumption data. Availability of these data will certainly vary by country, but a wide variety of prescribing or dispensing data sources may already be available such as importation/production data, national purchasing data, sales data, claims, or proprietary data (e.g., IQVIA) and can be leveraged for this activity. This is distinct from antibiotic consumption data (see below), which often require access to medical records or the novel collection of data.

Using antibiotic dispensing data for action will require the ability to analyze what may be a complex dataset. Additionally, countries should consider which actions they are prepared to take since the use of these data should be tied to some kind of policy or program action to improve stewardship. For example, the data can be used to establish national targets for dispensing so that all stakeholders can work collaboratively toward a common goal.

Measure antibiotic consumption and assess appropriateness. Antibiotic consumption data differs from dispensing data in that the former actually measures patient-level use, and may also approximate the appropriateness of that use. A common way to measure antibiotic use is through a point prevalence survey (PPS). Protocols for PPS that include antibiotic use have been well developed and such studies have been conducted in a number of countries [46–48]. In a PPS, a population is surveyed (e.g., hospital or outpatient populations) to describe the prevalence of antibiotic use, which antibiotics are being used, and the indications for use; data can also be collected to assess the appropriateness of the use. Typically, hospital-based PPS require access to medical records, including pharmacy records. Outpatient PPS may require patient records, patient interviews, and pharmacy data. Assessing the appropriateness of use can benefit from robust, locally-

informed clinical guidelines, where available. Because of the volume of data collection needed for a PPS, resources involved with such an effort are usually substantial, but time-limited, as conducting a PPS is done periodically, not continuously. Alternatively, a PPS on antibiotic use may be simplified or targeted at high-risk medications, such as carbapenems, if resources do not allow for a comprehensive survey. Other options for measuring antibiotic use include studies, longitudinal surveillance, and EMR-based "data dumps" [49].

Describe resistance patterns to improve treatment guidelines and identify priority pathogens. Assuming treatment guidelines for common clinical syndromes and quality assured AST are available, countries can review and analyze available AST data to improve treatment guidelines. Ideally, representative AST data are available, undergo regular data analysis, and summary information is widely available in reports, publications, or on the internet. Countries should review their AST data to determine priority pathogens or syndromes for targeting interventions. For example, if review of AST data demonstrated high frequency or prevalence of multi-drug resistant Gram-negative bacteria, such as carbapenem-resistant Enterobacteriaceae (CRE), countries could target facilities to improve their CRE infection prevention and control programs. Additionally, countries may identify syndromes, populations, drugs or provider types to target stewardship activities.

Monitor antibiotic quality. Reports in the literature have demonstrated that in some instances, the quality of the antibiotics available for use in some countries may be of varying quality [50, 51]. In these reports, antibiotics may have reduced dosage of antibiotic, which can result in unknowingly sub-therapeutic treatment and the development of resistance. While the testing, monitoring, and actions needed to address this issue are beyond the scope of this document, it is nonetheless important to highlight this important issue, as governments should consider this topic when developing national action plans.

Address drivers of inappropriate prescribing behavior. In some countries, antibiotic recommendations by clinicians and pharmacists can be subject to incentives and other drivers, which are separate from accepted guidelines or norms of practice. For example, in some countries, health care providers earn a large portion of their income by selling prescription drugs, leading to inappropriate or irrational antibiotic prescribing sometimes up to twice the WHO standard [52]. Where clinical practice deviates substantially from guidelines, Ministries can take action to better understand these drivers, and consider policies to address these drivers.

Approaches for Facility-Level Implementation

Challenges for implementing ASPs in hospitals in resource limited settings

Hospitals in resource-limited settings face a complex series of challenges to implementing ASPs. Resources are needed to support stewardship activities, including persons who can dedicate time to such activities. Even when money, staff, and time are available, there is often a lack of expertise or experience among clinical staff. Implementing stewardship activities may also be limited by gaps in laboratory capacity, since reliable lab data play a crucial role in guiding appropriate therapy. Gaps are also present in the ability to track and report relevant data on antibiotic use to clinicians and hospital administrators. Obtaining support and buy in for stewardship activities might also be challenging due to existing hierarchies within hospitals.

The goal of this section is to give a practical, stepwise framework for hospitals in resource-limited settings to develop ASPs. It is also to illustrate how such facilities can and should establish some form of sustainable ASP, given current resources and abilities, even if it is limited in scope and reach, with an eye toward more complete implementation of Core Elements once additional resources and capacities are available. We emphasize the foundational structures and the processes needed to identify and act upon target priorities in facilities. We also briefly discuss the specific activities that can help achieve the target priorities, in addition to the laboratory and pharmacy data that are typically required to conduct these activities. As with the national-level antibiotic stewardship plans, ASPs at facilities should ensure that content is aligned with other initiatives that concern antibiotic use that are ongoing at the facility to avoid conflicting guidance on appropriate antibiotic use.

Foundational structures of ASPs in an acute care facility

The foundations of any ASP are: 1) a single point of contact responsible for the program and 2) support from hospital leadership. These map to the Core Elements of Accountability/Expertise and Leadership Commitment, respectively.

Single focal point with responsibility for the program

Identifying an ASP focal point for the facility is critical. Stewardship guidance from high-income countries often stress the value of an infectious disease (ID) trained physician as the most effective leader of an ASP with a pharmacy co-lead who also ideally has ID training. Such personnel are often not available in resource-limited settings, even if a pharmacy is on site. Data from stewardship work in South Africa demonstrated that pharmacists without formal ID training can effectively oversee an ASP when stewardship-specific training was provided to supplement existing knowledge [53]. Physicians without formal ID training have long been ASP leaders or co-leaders in the United States and could

serve in this capacity in resource limited settings as well. In the hierarchy of the hospital, having a senior physician involved and committed to the ASP, even if not leading it, can often be of great value in obtaining agreement from other hospital stakeholders. In resource-limited settings, non-traditional staff types, such as infection control nurses or clinical microbiologists, may be tasked with stewardship activities, though the efficacy of such staff categories in running an ASP has not been studied [54]. Whatever the background of the ASP focal point, leadership and communication skills are essential characteristics of an effective leader.

Given the wide range of staff categories that may be involved in stewardship in LMIC, formal or on-the-job training on antibiotics and stewardship is essential for the stewardship lead to ensure they are prepared to manage an ASP. This may be done in person if available, or via off-site support through tele-stewardship. Both of these methods have been used in small remote hospitals in the United States that face similar personnel challenges [55]. Massive open online courses on antibiotic stewardship are also now globally available in several languages, though they require reliable internet connectivity. Professional societies can also play an important role in the mentorship (either formal or informal) of stewardship leaders with national or international support as has been described in a South Africa mentoring program supported by Ohio State University [56].

Support from hospital leadership

A committed focal point for overseeing the ASP is not a sufficient foundation for initiating an ASP until it is paired with support from hospital leadership. This includes, at a minimum, the commitment of time and other resources for the stewardship leader to receive training as well as plan and conduct the activities that are included in the ASP. In addition, hospital leadership/administration buy-in is critical to dedicate the time and other resources required for sustainable implementation. If governance structures, such as a Medicines and Therapeutic Committee, exist within the hospital, they can be asked to oversee stewardship efforts. However, such committees often are not initially designed with such responsibilities in mind and thus may need to be refocused to accommodate and support ASP activities. Hospital leadership can also leverage their influence to promote ASPs via facility circulars, policy statements and other public communications from hospital administration to employees, all of which have negligible associated cost. Further agreement from other stakeholders in the facility are likely necessary and should be guided by the focus of the ASP, but leadership support is required regardless.

Beyond the foundation: a stepwise approach to building a stewardship program

Guidance produced in high-income countries often provides a general discussion of ASP activities, without a discussion of building the ASP program. We propose the following stepwise approach to building an ASP that relies on the foundation outlined above and emphasizes beginning where a facility has resources and interest, and building toward a larger stewardship program. These map to the CDC Core Elements of Hospital Antibiotic Stewardship, with some modifications [7].

1. **Form an antibiotic stewardship committee:** The stewardship committee should aim to bring together the relevant hospital stakeholders, including any personnel with infectious disease or pharmacy background /expertise, to keep them engaged in and updated on stewardship activities, in addition to successes and challenges. The committee is also important to obtain agreement and buy-in from various departments to enhance the likelihood of a successful program. The designated focal point for stewardship activities should sit within this committee, ideally as the chair or lead.

   Representation on this committee can be fundamental to the success of the ASP. In one pilot of a stewardship program in Egypt, senior surgeons were identified in facilities to participate in the ASP by auditing antibiotic prescriptions for surgical prophylaxis and providing feedback. This led to significant increases in the optimal use of such antibiotics [57]. Nurses and infection control personnel are also important to include since their involvement in stewardship activities is needed and they can provide valuable linkages to other related initiatives in a facility, such as multi-drug resistant organism or healthcare-associated infection surveillance, if they exist.

2. **Start with a single priority area of the ASP:** In most hospitals, there are many areas in which antibiotic use can be optimized, but attempting to introduce change in many areas simultaneously can be difficult – especially with substantial resource constraints. We recommend starting with a single priority or focus for the program. The priority area would ideally be identified by reviewing existing data on antibiotic use, if available, or via conducting a focused needs assessment or situational analysis of antibiotic use at the facility. However, it is important to note that a lack of facility-level data on antibiotic use or prescribing practices, while consistently mentioned as a barrier to beginning an ASP in surveys of resource-limited facilities [54], should not be viewed as a requirement for choosing a priority. In the absence of data, expert opinion, for instance that of the stewardship committee, can and should be used to identify the priority.

Identifying the priority should take into account existing hospital resources, such as laboratory and pharmacy capacity, which may limit addressing some priority items despite known issues. Priorities may also be focused within a specific unit or area where antibiotic use is known to be high (e.g., an intensive care unit or operating room where perioperative prophylaxis is given) and do not need to be hospital-wide to be meaningful. Initial priorities might also be hospital-wide but narrowly defined in terms of their scope - such as reviewing the need for antibiotics after 48 hours, especially when cultures are negative. Examples of priorities could be:

- Reducing inappropriate use of colistin, carbapenem, or 3rd generation cephalosporin antibiotics
- Improving adherence to guidelines for empiric treatment for community acquired pneumonia or sepsis
- Ensuring appropriate use of antibiotics during surgical prophylaxis

3. **Ensure appropriate policies or guidelines are in place, especially for the priority area:** in order to improve antibiotic use, there should be some clinical guidance, or standard, to strive toward. Indeed, issuing of guidelines was identified as one of the most effective ASP interventions in a survey of hospital staff across 58 LMIC [58]. In the absence of such guidance, it becomes difficult to hold prescribers accountable to ideal use and encourage changes in practice. Facilities may use or adapt national, regional or local guidance if available, modifying as needed for realities in their facility (e.g., drug availability, acuity of patients). It should be noted that the guidance does not need to be overly exhaustive, or even based on rigorous, locally-produced evidence. Facilities may choose to start with a short, targeted document for the priority area, based on a simple adaptation of national guidelines to fit the local context.

4. **Educate staff and publicize stewardship campaign:** Once a priority area is chosen and policies and guidelines are in place, frontline staff may require additional education around these guidelines. Even if guidelines are already in place, refresher training via in-service training or other educational opportunities (e.g., grand rounds) may be helpful. Educating staff should not be viewed as a single endeavor but rather as an ongoing process with training repetition, as is feasible for the facility to support, in order to ensure that new staff, rotating staff (e.g., interns and junior doctors), and students receive education as well as reinforcement of previously trained personnel. Education of staff may be general or targeted depending on the priority area chosen, for instance if the priority area is around surgical prophylaxis, focusing on training relevant staff categories, such as surgeons, anesthesiologists and nurses on surgical floors would be the priority. Such a targeted training has been successful in an ASP pilot in Egypt [57].

   Additionally, publicizing the stewardship campaign and alerting staff to the coming stewardship activities around the priority topic will be critical in order to raise awareness of the ASP and to gain buy in from prescribers and other healthcare personnel. Programs can engage champions, such as senior surgeons, physicians, or administrators within targeted groups to lead education and publicity efforts. This might include posters, text messages, posts on social media or other modalities already in use in a facility to promote hospital messaging. Some of these modalities have been used in high-income settings with success, especially those around using social media to promote ASP goals [59, 60].

5. **Implement stewardship activities targeted at the priority:** The designated stewardship leader with the buy-in of the committee should choose 1–3 activities targeted at the priority area, which will comprise the core of the ASP. As a general rule, starting with fewer activities and doing them well is preferable to implementing more activities which can be difficult to execute simultaneously.

   Given that there are many types of stewardship activities with a range of complexity and resource requirements, thought should be given to what is realistic to achieve in a facility given existing strengths and resource limitations, and which activities will most likely have the desired impact on the priority area. Table 2 provides a short description of ASP activities, and outlines which generally will require a functional bacteriology laboratory, or an on-site pharmacy/centralized antibiotics list. Of note, many of these activities, particularly the ones that require on-site pharmacy/centralized antibiotic lists are greatly assisted by the presence of an EMR from which data on prescriptions can be gathered. However, an EMR is not required for any activities.

Table 2. Selected stewardship activities and requirements for implementation at a hospital.

Activity	Description	Requires a functional bacteriology laboratory?	Requires participation from a dedicated pharmacy[1]	Requires a centralized[2] antibiotic list, paper or electronic
Training on guidelines	Pre-service, in-service, or even informal trainings or workshops to educate healthcare workers on guidelines or guidance; also serves to sensitize healthcare workers about the stewardship program	No	No	No
Antibiotic rounds	Rounds held on a regular basis to review and discuss antibiotic choices and ensure accordance with best practice guidelines	No	No	No
Prescription alerts	Alerts to clinicians where prescriptions may be overlapping or duplicative (e.g., overlapping anaerobic activity)	No	Yes[3]	No
Audit/ feedback	A review of prescribing practices that typically requires accessing a medical record to link clinical picture and antibiotic prescriptions with a goal of evaluating the appropriateness of prescribing in order to generate regular feedback to clinicians with a goal of modifying prescribing practices	No	No	No
Prior authorization	A requirement that clinicians must get approval before select antibiotics will be dispensed for patient use	No	Yes	No
Antibiotic restriction	A blanket rule that clinicians are unable to prescribe certain antibiotics in certain classes of patients	No	Yes	No

Activity	Description	Requires a functional bacteriology laboratory?	Requires participation from a dedicated pharmacy[1]	Requires a centralized[2] antibiotic list, paper or electronic
Automatic stop order	Antibiotics are stopped automatically after a predefined time period according to indication (e.g., 24 hours for surgical prophylaxis or 5 days for community acquired pneumonia) regardless of physician order	No	Yes	Yes
Automatic changes	An aspect of the original prescription is routinely changed usually without requiring a new clinician order (e.g., IV →PO fluoroquinolones)	No	Yes	No
Selective lab reporting	Labs report a limited number of antibiotics for susceptibility results as opposed to all antibiotics tested	Yes	No	No
Cascade lab reporting	Lab reports susceptibility testing to second line/ expensive antibiotics are only if an organism susceptibility testing meets certain criteria (e.g. resistant to first line antibiotics)	Yes	No	No
Antibiotic timeout	Defined, regular prompts to the clinician to re-evaluate antibiotic choices (e.g., at 48 hours a clinician is prompted to review any empiric IV antibiotic therapy)	No	No[4]	Yes
Antibiotic reminder	Prompts to the clinician that are tied to a particular prescription in real time (e.g., when a clinician chooses to order an IV quinolones, the clinician is asked if patient can take PO)	No	Yes	No
Facility-level antibiogram	Creation of an antibiogram based on results of facility susceptibility testing[5]	Yes	No	No

Table 2. - References

[1] Dedicated pharmacy mean a pharmacy that is required by the facility to participate in ASP activities. This could include a single onsite pharmacy, an off-site but participating pharmacy or a pharmacy network which is participating in the facility ASP. This does not include situations where patients or clinicians go off site to purchase medications in an unaffiliated pharmacy that is not participating in ASP activities.

[2] Centralized antibiotic list may be facility-wide list or a list of antibiotics received by all patients in a geographic area (e.g., ward) where antibiotic stewardship activities are taking place.

[3] Prescription alerts could be done by medical record review in absence of a dedicated pharmacy, however this would be extremely time and labor intensive and ideally should implemented at the pharmacy level.

[4] In the absence of a dedicated pharmacy, review of a facility or ward level antibiotic list could be reviewed by an ASP point person who would then prompt physicians via text or in person to re-evaluate antibiotic choices.

[5] Creation of a facility-level antibiogram is not sufficient to meet criteria for an ASP activity as ensuring the information provided in an anitibiogram is applied to antibiotic use in a facility requires dissemination and training of clinicians and prescribers as well.

While we have presented a stepwise approach, it will likely be necessary to regularly review and revise the approach while setting up an ASP. For instance, a stewardship committee may be initially set up but if surgical prophylaxis is identified as the facility priority, relevant stakeholders from the surgery department need to be recruited to the committee if they are not already present.

Monitoring and evaluation of ASP

ASP activities around tracking and reporting program activities can be added as a facility builds capacity. The CDC Core Elements for U.S. hospitals describes monitoring antibiotic use and outcome measures as fundamental ASP activities. However, this type of monitoring often requires longitudinal collection of additional data, which is resource intensive and logistically difficult in resource-limited settings given the absence of electronic health records and/or centralized prescription databases. Facility level stewardship activities outlined in this document can be done in the absence of any monitoring and evaluation schema. However, when implemented, monitoring and evaluation of an ASP can provide important information about the successes and challenges of the program and show the value it adds to hospital administration and other stakeholders.

Monitoring and evaluating processes. When a facility in a resource-limited setting embarks on developing a monitoring and evaluation plan for an ASP, a reasonable place to start is with tracking process measures. For instance, if a facility seeks to improve appropriate 3rd generation cephalosporin usage in an ICU through chart audits and feedback to providers, they may want to track measures such as 'number of charts reviewed' or 'providers contacted' at some frequency (e.g., weekly). This would enable them to monitor program

implementation and catch challenges or issues early on in the process. While process measurements can seem relatively simple to collect, gathering the necessary data on a regular basis can be complex and time consuming depending on data collection methods and human resource requirements. Therefore, we do not include monitoring, even of process measures, as a core ASP activities for resource-limited settings. However, when it can be done, it can provide valuable information and should be pursued.

Monitoring and evaluating impact. While process measures describe the implementation of a program, they are not able to reveal anything about the downstream impact of ASP activities. Moving beyond process measures, monitoring the impact of an ASP can be extremely useful in demonstrating effectiveness and value of a stewardship program, and are considered core elements of stewardship in high resource settings. A first step in facilities that are interested in pursuing this type of advanced monitoring and evaluation would be to set priority targets for an ASP and monitor progress towards meeting them. Tracking particular antibiotic use or consumption in hopes of reaching a pre-identified target (e.g., 50% reduction in carbapenem use) is a commonly used impact indicator in high-income settings. Often such antibiotic use indicators are easier to implement and more likely to demonstrate successes in the short term as opposed to clinical outcomes (e.g., 50% reduction in carbapenem-resistent Enterobacteriaceae infections). Measuring impact and outcome measures will generally require more time and effort than process measures and often requires the ability to collect real-time data on activities for feedback and action. Therefore, we suggest that this type of monitoring should be viewed as an advanced activity within an ASP, implemented when resources allow and paired with specific activities and targets rather than ongoing longitudinal collection of consumption data, for instance. Stewardship activities can and should still be implemented in the absence of a formal impact or outcome monitoring and evaluation schema. Some common ways to measure impact include:

- Total antibiotic use (measured as days of therapy or defined daily dose) [61,62]
- Appropriateness of antibiotic selection, dose and duration (e.g. % prescriptions that adhere to local guidelines for a given condition)
- Cost (e.g. a cost-effectiveness analysis of the program)
- Resistance
- Clinical outcomes (e.g. rates of *Clostridioides difficile* or methicillin-resistant *Staphylococcus aureus* infections)

Conclusions

This approach to building national and facility-level ASPs in resource-limited settings outlined here it is not an exhaustive list of approaches to ASP, it may serve as a starting point for stakeholders in resource-limited settings. Currently, there may be fewer ASPs in resource-limited settings, but almost certainly there will be more countries and facilities that will be designing and starting their own programs. Further experience with developing functional and impactful ASPs can help to improve documents such as these, and lessons learned will be invaluable assets toward improving the quality of antibiotic use globally.

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