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Multidisciplinary Strategies for Antimicrobial Stewardship and Combating Antimicrobial Resistance in Healthcare

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Abstract

Background: Antimicrobial resistance (AMR) has emerged as one of the most pressing global public health threats of the twenty-first century, with estimates suggesting 1.3 million deaths directly attributable to bacterial AMR in 2019 alone. The problem is disproportionately severe in low- and middle-income countries (LMICs) and conflict-affected settings, where healthcare infrastructure is limited and antimicrobial misuse is prevalent.

Aim: This review aims to synthesize current evidence on multidisciplinary strategies for antimicrobial stewardship (AMS) and combating AMR in healthcare settings, with particular emphasis on implementation challenges, successful interventions, and the evolving roles of various healthcare professionals.

Methods: A comprehensive narrative review was conducted synthesizing evidence from peer-reviewed literature, WHO guidelines, and proceedings of international patient safety summits published between 2020 and 2026. Key databases including PubMed, Scopus, and Cochrane Library were searched for studies addressing AMS implementation, multidisciplinary approaches, and AMR containment strategies.

Results: Antimicrobial stewardship programs consistently demonstrate significant reductions in antibiotic consumption and improve adherence to prescribing guidelines, with substantial cost savings. Key successful interventions include prospective audit and feedback, formulary restriction, education and training, and guideline implementation. However, implementation barriers remain substantial, particularly in resource-limited settings, including insufficient staffing, lack of microbiology laboratory support, limited leadership commitment, and cultural resistance to change. The WHO AWaRe classification has emerged as a critical tool for optimizing antibiotic selection, with studies demonstrating significant shifts from Watch to Access category antibiotics following stewardship interventions. Nurses play an indispensable role in AMS through patient assessment, specimen collection, medication management, and prompting antibiotic review—activities grounded in patient advocacy and nursing leadership.

Conclusion: Effective AMS requires a multidisciplinary approach integrating physicians, pharmacists, nurses, microbiologists, and infection prevention specialists. Tailored strategies addressing local barriers, sustained political commitment, and investment in healthcare infrastructure are essential for sustainable implementation. The expansion of AMS into primary care, humanitarian settings, and long-term care facilities represents a critical frontier for global AMR containment efforts.

Keywords: Antimicrobial stewardship, antimicrobial resistance, multidisciplinary strategies, implementation science, low- and middle-income countries, infection prevention and control.

Introduction

Antimicrobial resistance (AMR) constitutes one of the most significant threats to global public health in the modern era, jeopardizing decades of medical progress and threatening the effective treatment of infectious diseases worldwide. The discovery of antibiotics has been acknowledged as one of the most prominent developments in clinical medicine, with antibiotics radically changing the future of medicine by curing once-lethal infections [1]. However, it was established early on that bacteria, when exposed to antibiotics, develop survival strategies, raising an unprecedented concern for the imperative need for judicious prescription to

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preserve their unparalleled value and efficacy [1]. The acknowledgment that humanity is perilously approaching the "End of the Miracle Drugs" due to the unjustifiable overuse and misuse of antibiotics has prompted a critical reassessment of their usage [1]. The magnitude of this crisis cannot be overstated. According to the World Health Organization (WHO), AMR has emerged as one of the top ten global public health threats of the twenty-first century [2]. In 2019, approximately 1.3 million deaths were directly attributable to AMR, and if no measures are taken, it is projected that by 2050 AMR could lead to the deaths of 10 million people annually, with up to 90% of these fatalities occurring in low- and middle-income countries (LMICs) [2]. The global rise in AMR is claiming the lives of more than 1.2 million people each year, and this global health crisis is particularly acute in Africa, largely due to fragile and underfunded health systems [3†L7-L10]. Beyond mortality, AMR imposes a substantial economic burden on healthcare systems, with resistant infections necessitating the use of more expensive and often more toxic second-line or third-line treatments [2].

In response, numerous relevant medical societies have initiated a concerted effort to combat resistance by implementing antibiotic stewardship programs within healthcare institutions, grounded in evidence-based guidelines and designed to guide antibiotic utilization [1]. Antimicrobial stewardship (AMS) has emerged as a cornerstone strategy in the global fight against AMR. Defined as a coordinated set of actions designed to optimize antimicrobial use, reduce adverse effects, and address AMR, AMS programs aim to ensure that the right antibiotic is administered to the right patient at the right time, for the right duration, in a cost-effective manner [2]. Stewardship programs are essential in internal medicine wards, where patients often present with complex comorbidities and prolonged hospital stays, increasing the risk of MDRO infections and inappropriate antimicrobial use [2]. This review aims to synthesize current evidence on multidisciplinary strategies for antimicrobial stewardship and combating AMR in healthcare settings. It examines the scope of the AMR problem, the evidence base for AMS interventions, implementation challenges and facilitators across different settings, the evolving roles of various healthcare professionals, and future directions for strengthening the global response to AMR.

The Scope of the Antimicrobial Resistance Problem

The global burden of AMR has been systematically quantified, providing comprehensive estimates of AMR-attributable mortality across multiple countries. The findings are sobering: bacterial AMR was directly responsible for 1.27 million deaths in 2019 and was associated with an additional 4.95 million deaths [1]. The Global Burden of Disease study provided robust evidence on the toll of AMR on global mortality, demonstrating that this toll is disproportionately higher on low-income settings, particularly in Sub-Saharan Africa [3]. Studies cite that countries with lower social development status often have higher mortality rates related to AMR [4]. It has been estimated that the burden of deaths from AMR could rise to 10 million each year by 2050, along with substantial cost implications, if swift action is not taken to address this growing threat [5]. Healthcare-associated infections are the most frequent adverse event in healthcare, affecting 5-15% of patients in acute care hospitals, leading to high morbidity and mortality with incalculable economic costs [6]. AMR is an additional major menace, listed as one of the ten most urgent health threats in 2019 by the WHO [6]. The economic burden of AMR on healthcare systems is substantial, with resistant infections necessitating the use of more expensive and toxic treatments, significantly increasing treatment costs [2]. The annual global cost of AMR has been estimated to reach 100 trillion USD by 2050 if current trends continue [2].

LMICs face a disproportionate burden of AMR and encounter unique challenges in implementing effective stewardship programs. Developing countries risk AMR for its high consumption of antimicrobials; moreover, another major obstacle is their lack of structured ASPs [4]. The operation mode of ASPs often varies due to differences in available resources, workforce, technology, local medical culture, and insufficient support from hospital administration [4]. Data from the WHO Global Antimicrobial Resistance Surveillance System (GLASS) reveal concerns resistance rates in LMICs. For example, in Malawi, over 75% of Klebsiella pneumoniae and Escherichia coli isolates from blood cultures were resistant to ceftriaxone. In India, among Klebsiella pneumoniae isolates, over 75% were resistant to cefepime, with nearly 50% resistant to carbapenems. Similarly concerning patterns have been documented in Egypt, Nepal, Nigeria, Pakistan, and other countries [1]. For comparison, the United Kingdom reported less than 25% resistance to third generation cephalosporins for isolates of Klebsiella pneumoniae and Escherichia coli [1]. The underlying drivers of high AMR rates in LMICs are multifaceted. These include limited access to quality healthcare, over-the-counter availability of antibiotics, weak regulatory frameworks, inadequate laboratory infrastructure, and insufficient infection prevention and control measures [1]. Water sanitation remains a critical concern, as universal access to sanitized water could decrease antimicrobial prescribing for diarrheal illness by 60% [1]. Improved sanitation including hand hygiene have demonstrated benefit in decreasing transmission of

hospital acquired infections in LMICs [1]. Initiatives such as the Clean India Mission provide examples of government sponsored efforts to improve water sanitation [1].

Fragile and conflict-affected settings bear an even more severe burden of AMR due to the compounding effects of weak health policies, disrupted medical supply chains, and lack of knowledge about antibiotic stewardship among both healthcare providers and health service users [3]. Several compounding factors can contribute to the emergence and spread of AMR in these settings, including constrained access to quality water as a key element for proper hygiene and sanitation in communities and health facilities, self-medication practices in countries with absence of law enforcement on sales of over-the-counter antibiotics, lack of awareness on the topic among health workers involved in service delivery, absence of laboratory infrastructure, and conflicting agendas in prioritization of programs when immediate life-saving priorities need to be addressed with limited resources [3]. In addition to these challenges, outpatient settings in high-income countries are known to be the level of care where most antibiotics are prescribed, and often inappropriately. A literature review on antibiotic prescription practices in LMICs and primary health care highlighted that antibiotics are highly prescribed also in these settings, often exceeding 50% of overall medical consultations, with a high proportion of inappropriate use [3]. The analysis performed did not take into consideration settings affected by acute conflicts or suffering from post-conflict situations, where the patterns of antibiotic prescriptions are not known and arguably as equal as, or worse than, the ones reported in the review [3]. The COVID-19 pandemic has contributed to a documented increase in inappropriate antibiotic prescriptions, which in turn can further aggravate the pre-existing burden of AMR [3]. Healthcare systems in fragile and conflict-affected settings often rely on external support, with a variety of humanitarian and development agents playing a complementary and at times partly substitutive role to that of local institutions in analyzing the health situations, designing, implementing, and monitoring health interventions, and generating evidence to inform health programming [3].

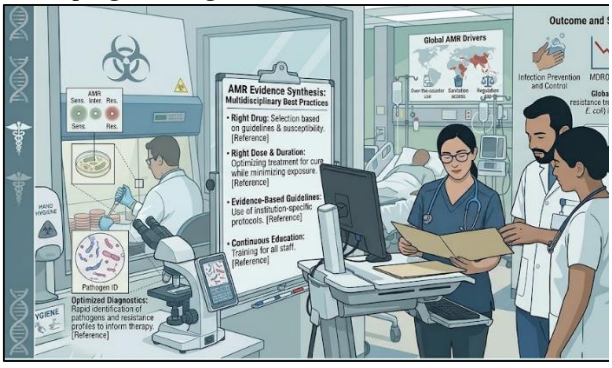

Fig. 1: Antimicrobial Stewardship.

Antimicrobial Stewardship Programs: Evidence and Effectiveness

The WHO has established eight core components for infection prevention and control programs, which provide a framework for AMS implementation at both national and healthcare facility levels. These components encompass: (1) IPC programs with dedicated trained teams, (2) evidence-based guidelines, (3) IPC education and training, (4) facility-based surveillance, (5) multimodal strategies, (6) monitoring and feedback of IPC practices, (7) appropriate workload, staffing, and bed occupancy, and (8) a clean and hygienic built environment with appropriate materials and equipment [6]. For AMS specifically, the CDC has defined core elements including leadership commitment, accountability, pharmacy expertise, action to improve antibiotic use, monitoring and reporting, and education [6The WHO AWaRe (Access, Watch, Reserve) classification provides a framework for categorizing antibiotics and guiding stewardship efforts. Access antibiotics are first- or second-line agents with lower resistance potential; Watch antibiotics are broader-spectrum agents with higher resistance potential; and Reserve antibiotics are last-resort treatments for multidrug-resistant infections [2]. The WHO has introduced since 2017 the Access, Watch and Reserve (AWaRe) classification for antibiotics in its essential medicine list, a tool to prioritize specific categories as targets of AMS intervention and monitoring [3]. More recently, the "WHO Essential Medicines List Antibiotic Book" initiative has suggested key implementation strategies to improve AMS at all levels of care, as a key component of quality of care [3].

The evidence base for AMS effectiveness has grown substantially over the past decade. Several studies have directly examined the role of ASP in LMICs. A 2019 scoping review of interventions to reduce antimicrobial prescribing in LMICs examined 102 studies across primary care, hospital, and pharmacy settings. Among a subset of 41 studies with the most complete study designs, 21 demonstrated a positive effect (decreased antimicrobial consumption) of various ASP interventions compared to only 4 demonstrating negative effects [1]. A 2017 systematic review and meta-analysis examined 46 studies primarily focused on upper-middle- or high-income countries, with 11 studies from LMICs. The study found a decrease in antimicrobial consumption and length of stay while demonstrating cost savings. There was no negative impact on mortality. The most examined ASP interventions were PAF (17 studies) and antimicrobial restriction (8 studies) [1]. A separate systematic review and meta-analysis published in 2018 examined 77 studies with 43 from LMICs. The most common ASP interventions were PAF (29), education/training (23), and institutional guidelines (18). Most of the studies demonstrated

decreased antimicrobial consumption with cost savings ranging from 12-73%. A non-significant reduction in mortality was observed [1]. Part of the role of ASPs is to ensure guideline-directed empiric therapy. A 2016 meta-analysis in Lancet Infectious Disease examined 145 studies and demonstrated a 35% relative risk reduction in mortality when guideline-directed empiric antimicrobials were prescribed. The same study demonstrated no statistically significant increase in mortality from intravenous to oral recommendation, narrowing of antimicrobial therapy, or restricting antimicrobials [1].

ASP activities can be cost-effective. A study in the South African Medical Journal examined the financial impact of an ASP over four years, demonstrating a 2.8 million ZAR (approximately 193,000 USD at 2020 exchange rates) net savings primarily driven by decreased intravenous antimicrobial consumption [1]. Another study in an internal medicine ward demonstrated a significant reduction in antimicrobial consumption and improved prescription quality with substantial cost savings without negatively impacting patient outcomes [2]. The economic utility of ASPs must be firmly established in LMICs and communicated to decision makers. One could intuitively assume that ASPs are cost-saving in certain circumstances, and some studies have conclusively concluded that ASPs are cost-effective or cost-saving [5†L45-L49]. Institutions have reported reductions in antimicrobial expenditures ranging from 10% to 35% following program implementation [2]. A meta-analysis demonstrated that ASPs reduce antimicrobial consumption by up to 36%, decrease the incidence of resistant infections, and improve patient outcomes without compromising quality of care [2].

Implementation Challenges and Facilitators

Despite the compelling evidence for AMS effectiveness, implementation remains a major challenge across all healthcare settings, particularly in resource-limited environments. In limited resource settings, non-clinical pharmacists or nurses may need to play a larger role in ASPs [1]. A global survey of 660 hospitals across 67 countries conducted by the European Society of Clinical Microbiology and Infectious Diseases revealed that only 12% of hospitals in Africa reported the existence of an antimicrobial stewardship committee. Staff on these committees were primarily drawn from infection control personnel in Africa. Respondents from Africa and South and Central America noted the least average resource hours per week from an infectious disease-trained pharmacist or infectious disease physician. Lack of personnel or funding was the most commonly cited barrier to ASP activities among all surveyed institutions at 29% [1]. Several factors contribute to implementation barriers in LMICs. Insufficient staffing and lack of microbiology laboratory support are significant obstacles [5†L48-L52]. Limited support by federal governments and local healthcare facility administrators to establish resources for ASP is another major barrier [6]. Studies from Latin American healthcare facilities show that ASPs currently face various problems, including limited leadership support, and dedicated, multi-disciplinary staff for an effective ASP including infectious disease trained pharmacists [6]. Cultural and behavioral determinants pose a risk to sustainable ASP implementation as power distance and hierarchical relationships limit integration of pharmacists and non-physician roles in AS activities [6].

Outpatient settings are known to be the level of care where most antibiotics are prescribed, and often inappropriately. There is a large, unmet need for promoting ASP in the ambulatory sector [6]. Broad approaches for implementation are known in this setting, ranging from education of individual patients and general practitioners to electronic decision support tools to facilitate appropriate treatment decisions, and general education of the public [6]. Promising interventions are the introduction of small quality circles among primary care physicians, and the strengthening of the patient-physician relationship by point-of-care-testing and improved communication skills [6]. In humanitarian settings, constraints are even more pronounced. There is limited focus on ensuring the implementation of adequate antimicrobial stewardship in primary health care, which is known to be the setting where the highest proportion of antibiotics are prescribed [3]. The available toolkits for implementing AMS in resource-limited settings do not provide guidance specific to primary care facilities, remaining focused on hospitals [3]. There is no specific consideration for inclusion of AMS-inclusive preparedness measures related to situations in which priorities are competing, and availability of diagnostics, human resources and medicines can be heavily affected, such as in acute humanitarian emergencies [3]. Prescribing physicians in such situations can often be confronted with ethical dilemmas on how to balance patient-centered care with a public health approach focused on the broader population, similarly to what is described in ICUs or remote areas [3†L98-L100]. Humanitarian agencies can also find themselves in the difficult position of having to decide between rapidly filling immediate gaps in supply chains or adopting stricter approaches when performing donations of medical materials, leading to potentially counterproductive long-term consequences in the absence of AMS-sensitive policies [3].

Strong organizational support and multidisciplinary collaboration have emerged as key facilitators of successful AMS implementation. The availability of antibiotic guidelines, ASP protocols, and dedicated personnel are important enabling

factors [5]. The WHO has developed practical resources to support AMS implementation, including the "Antimicrobial Stewardship Programmes in Health-Care Facilities in Low- and Middle-Income Countries: A WHO Practical Toolkit" [1]. This toolkit emphasizes a stepwise approach, building existing structures and reporting, maximizing teamwork, and encouraging champions and clinical staff to participate [1]. Free resources are also available through non-government agencies such as ReAct, a web-based open access toolkit funded by the Swedish International Development Cooperation Agency and Uppsala University. Their current strategic focus is in low resource settings and includes helping to develop national action plans. Their website also includes educational resources on AMR and discusses potential stewardship interventions in LMICs [1]. Country-level support and data are highly valuable in creating hospital-level efforts. If resources are available, a gap analysis can be performed to help determine regional needs [1]. The basis for the successful implementation of IPC programs and ASP is the support of political and healthcare leaders through legislation and processes that facilitate creation of the necessary resources for these programs [6]. Coordination of implementation within a country, but also within a healthcare institution, are key to efficiently use the available human and financial resources [6]. Dedicated healthcare personnel with different skill sets are essential for effective IPC programs and ASP [6].

Multidisciplinary Approaches to Antimicrobial Stewardship

Effective AMS requires a multidisciplinary approach integrating diverse healthcare professionals. The AMS committee ideally includes an infectious disease physician, clinical pharmacist, clinical microbiologist or technologist, and nurses with infection control training [1]. An expert panel from Asia also recommended the addition of an information technology expert [1†L201-L202]. In settings where specialist personnel are not available, institutions may need to rely on antimicrobial stewardship champions—physicians, pharmacists, or nurses with a special interest in AMS [1]. The importance of multidisciplinary collaboration cannot be overstated. As noted in the proceedings of the 5th Global Ministerial Summit on Patient Safety, dedicated healthcare personnel with different skill sets are essential for effective IPC programs and ASP [6]. Pharmacists bring unique expertise in pharmacology and medication management that complements the diagnostic and clinical skills of physicians. The committee may also be established as a subcommittee of a pre-existing committee such as an Infection Prevention committee. In the latter instance, it is important that Antimicrobial Stewardship be a standing agenda item for reporting and discussion [1].

Physicians, particularly infectious disease specialists, play a central leadership role in AMS programs. They are typically responsible for developing treatment guidelines, leading prospective audit and feedback activities, and making formulary decisions [1]. The role of the ASP committee is to optimize antimicrobial use along with promoting behavioral change in antimicrobial prescribing and dispensing. The aims of the committee should be to improve quality of care, reduce unnecessary antimicrobial exposure (with the goal of reducing the emergence of AMR) while also decreasing unnecessary health-care costs [1]. However, physician engagement and behavior change remain significant challenges. Prescribers in LMICs agree that AMR is a growing problem, although few acknowledge that their own practice contributes to this issue [1]. Among 78 medical doctors and 106 medical students in Kisangani, Democratic Republic of Congo, more than 70% answered on a questionnaire they would prescribe antibiotics for an upper respiratory tract infection [1]. Similarly, Donkor and colleagues found that just under half of the students at tertiary level facilities in Ghana had poor knowledge about the suboptimal use of antibiotics [1]. Addressing these knowledge gaps requires targeted education during medical school and through continuing professional development. The WHO Department of Health Workforce has produced reports on e-learning that could be utilized for this purpose [1]. A key target for closing knowledge gaps is in medical school education, with evidence that medical students would prefer additional education on appropriate antimicrobial prescribing while in medical school [1]. Direct education in the context of active patient interventions from ASPs to providers have proven to be some of the most effective education strategies (these include prospective audit and feedback along with antimicrobial restriction) [1].

Pharmacists are essential members of the AMS team, contributing expertise in antimicrobial pharmacology, dosing, drug interactions, and medication safety. In many settings, particularly in LMICs, pharmacists drive prospective audit and feedback strategies and formulary management [6]. A study in South Africa demonstrated significant cost savings from a pharmacist-driven ASP, with net savings of 2.8 million ZAR primarily driven by decreased intravenous antimicrobial consumption [1]. There is a clear need to expand the clinical pharmacy workforce in the inpatient setting, as pharmacists have unique skill sets that are complementary to physician expertise for optimal management of infectious diseases [6]. In resource-limited settings, non-clinical pharmacists or pharmacy technicians may need to play a larger role in AMS activities [1]. Other countries such as Oman have had success pooling limited resources into a single national antimicrobial stewardship team [1].

The nursing contribution to AMS has received increasing recognition in recent years. A comprehensive systematic review of nursing activities regarding antibiotic use found that nurses, in daily practice, already perform the majority of the proposed activities throughout the entire antimicrobial pathway [7]. These activities include assessment of clinical status, collection of specimens, management of antimicrobial medication, prompting review, and patient education [7]. Nurses' activities are grounded in three overarching intrinsic elements. First, patient advocacy—"striving for the best possible care for their patient"is a strong motivator for nursing participation in AMS [7]. Second, nurses take the lead in many parts of the antibiotic treatment process, including initiating culture sampling and participating in AMS rounds [7]. Third, communication is an essential element of nursing contribution, with nurses serving as a "central hub" in the AMS communication web [7]. Nurses may take the lead in clinical processes and are communicators in all aspects of the antimicrobial pathway. Patient advocacy appears to be a strong driver of bedside nurses' activities [7]. Nurses' activities are already integrated in the day-to-day nursing practice and are grounded in the essence of nursing, being a patient advocate and showing nursing leadership in safeguarding the antimicrobial treatment process [7]. Educating, engaging and empowering nurses in this already integrated role, could lead to a solid, impactful nursing contribution to AMS [7]. Several healthcare organizations such as American Nurses Association (ANA), CDC, Australian Commission on Safety and Quality in Health Care (ACSQHC), European Federation of Nurses (EFN) and WHO have acknowledged nurses for the important role they can play in protecting the 'power of antibiotic medication' [7]. These position papers suggest that nurses may contribute by assessing and monitoring patients' clinical status, participating in diagnostic culture and antimicrobial treatment management, and educate patients and families [7].

Microbiologists and laboratory personnel are critical for AMS success, providing the diagnostic data that guide antimicrobial prescribing. Lack of microbiological laboratory support is a significant barrier in LMICs, and lack of laboratory diagnostic ability has been associated with increased mortality [1]. A study of 251 children in Ghana demonstrated that approximately 40% of patients presumed to have severe malaria by symptoms actually had bacteremia [1]. Short-term solutions may include partnering with larger institutions with microbiology laboratory capabilities, while long-term solutions include prioritizing expanding microbiology laboratory infrastructure via a national action plan with dedicated funding [1]. Global programs such as Strengthening Laboratory Medicine Toward Accreditation (SLMTA) and Stepwise Laboratory Improvement Process Towards Accreditation are working to increase access to microbiology laboratories in LMICs [1]. Other resources are available to aid in developing microbiology labs in LMICs [1]. The role of the ASP committee should be to develop a plan for data collection. Electronic collection is optimal but paper-based collection can also be utilized based on local resources [1]. Data collection infrastructure is also essential to infection prevention and control programs and collaborative efforts could be considered in limited resource settings [1]. Sources of data collection can include pharmacy dispensing data or hospital antimicrobial purchasing data [1]. Data can also be utilized to generate an antibiogram through coordination with microbiology [1].

6. The WHO AWaRe Classification and Its Role in Stewardship

The WHO AWaRe (Access, Watch, Reserve) classification of antibiotics has emerged as a critical tool for monitoring and guiding antibiotic use. This classification groups antibiotics into three categories: access (first- or second-line antibiotics with lower resistance potential), watch (broader-spectrum agents with higher resistance potential), and reserve (last-resort treatments for multi-resistant infections) [2]. Within this framework, RESERVE category antimicrobials are a key target for ASPs [1]. The WHO introduced since 2017 the Access, Watch and Reserve (AWaRe) classification for antibiotics in its essential medicine list, a tool to prioritize specific categories as targets of AMS intervention and monitoring [3]. More recently, the "WHO Essential Medicines List Antibiotic Book" initiative has suggested key implementation strategies to improve AMS at all levels of care, as a key component of quality of care [3].

Studies have demonstrated that AWaRe-guided stewardship interventions can significantly shift prescribing patterns towards more appropriate antibiotic use. A study implementing a ward-specific ASP demonstrated a significant increase in the use of drugs in the ACCESS class, with the proportion rising from 17.8% at baseline to 26.5% during the intervention period. This suggests a positive shift towards prescribing drugs with a more favorable safety and efficacy profile. In contrast, an important reduction in the use of medications in the WATCH class was observed, from 72.5% in the control group to 63.5% in the intervention group [2]. The study also recorded a significant reduction in both carbapenem (-44.6%) and fluoroquinolone (-43.6%) use. These findings indicate that the ASP significantly reduced the use of broad-spectrum antibiotics such as carbapenems and fluoroquinolones, thereby improving the quality of antimicrobial prescribing and potentially enhancing patient safety without adversely affecting clinical outcomes [2].

Encouraging optimal use of antimicrobials through antimicrobial stewardship can help best utilize these limited resources. However, a disproportionate availability of WATCH or RESERVE antimicrobials compared to ACCESS antimicrobials may pose a barrier to effective stewardship in many countries [1]. One goal of the WHO is to increase utilization of ACCESS group antibiotics from the AWaRe classification to greater than 60% of all antimicrobials [1]. Essential to this goal is ensuring these ACCESS group antibiotics are available. Currently, lack of access to antimicrobials may cause more deaths than antimicrobial resistant pathogens in LMICs. A 2016 report in the Lancet extrapolated data from 101 LMICs and estimated 445,000 deaths per year from pneumonia in children under 5 compared to 214,500 deaths per year from neonatal sepsis related to antibiotic resistant organisms [1]. Essential to ASP activity is having access to appropriate antimicrobial therapy as defined in WHO essential medicines [1].

Infection Prevention and Control as a Complement to Antimicrobial Stewardship

Infection prevention and control strategies and antimicrobial stewardship programs are of increasing importance due to the substantial burden of healthcare-associated infections and antimicrobial resistance threatening patient safety [6]. IPC strategies and ASP are of high importance due to the substantial burden of HAI and AMR threatening patient safety [6]. Full implementation of effective programs remains a major challenge in all settings due to limited support by political and healthcare leaders, and human and financial constraints [6]. The implementation of the WHO IPC core components and ASP has been recognized as an essential step to battle the emerging burden of HAI and AMR. Experts from different countries and regions with different income levels gave their insights into their successes and problems in the implementation of national IPC programs [6]. Even though their conditions differ significantly, most of them face problems in the continued implementation process [6].

In Senegal, a national IPC program has been progressively implemented since 2004. The main achievements of the program have been to train healthcare workers in a specialized training facility, the establishment of IPC committees in all hospitals, the completion of three national HAI prevalence surveys, a dedicated program to improve hand hygiene and basic hygiene measures, as well as the regulation of the healthcare waste management. Unfortunately, the activities were not sustainable after the withdrawal of funding provided by external partners due to lack of human, material, and operational resources [6]. In Mexico, there is no overarching national IPC strategy, but 15 IPC initiatives are currently promoted including 6 regulatory frameworks and 9 manuals or guidelines. Examples for these IPC initiatives are the national standard for epidemiological surveillance and a manual of standardized procedures for hospital surveillance. The biggest challenges in patient safety experienced in Mexico are the development and implementation of collaborative strategies and the overall reduction of HAI, whose attributable case-fatality rate is estimated to be around 5% [6]. In Chile, already in 1983, Chile implemented a comprehensive national IPC program involving all public and private sectors. The IPC program became mandatory for all healthcare facilities in 1986. During the COVID-19 pandemic, Chile's healthcare system was heavily challenged by an increased number of outbreaks of HAI including outbreaks caused by multidrug-resistant bacteria, leading to a higher AMR incidence [6]. Despite these challenges, Chile managed to train an eight-fold higher number of healthcare workers in IPC during 2020 compared to previous years [6].

Prevention policies must be the top priority in resource-limited settings. Too often, preventive actions are unforgivingly omitted. The leading causes of medical consultation in the great majority of resource-limited countries are preventable infectious diseases (especially, of respiratory and gastrointestinal origin). Evidence indicates that simple and low-cost preventive interventions, such as hand hygiene, have a big impact on the health of communities [5]. A community intervention that focused on hand hygiene promotion in a resource-limited country halved the incidence of both respiratory and gastrointestinal diseases in children under 5 years of age [5]. Initiatives such as vaccination (notably, against the leading viral agents that cause severe pneumonia) could avert use of antibiotics in a great number of patients [5]. Antimicrobial stewardship programs must be complemented by infection prevention and control initiatives at both the institutional and national levels [1].

Special Considerations in Antimicrobial Stewardship

Agriculture provides an additional target for ASP activities at the national level. In the United States up to 70% of antimicrobials are utilized in agriculture [1]. There is some evidence correlating antimicrobial resistant infections in humans to use in agriculture [1]. There are limited data on agricultural antimicrobial use in LMICs. The European Union has banned use of antimicrobials for growth promotion in animals and studies from Denmark demonstrate no adverse effects on livestock [1]. Many countries have taken action. China banned colistin for growth promotion in animal use in 2016, Malaysia followed in January 2019 and also plan to ban additional antibiotics as growth promoters in animal food. In South America, Argentina, Chile, and Columbia have banned various antimicrobials for growth promotion. Thailand and Vietnam have bans on antimicrobials

for growth promotion although exceptions exist for disease prevention. Many other countries have proposed legislation or have developed national action plans to address this growing threat [1].

LMICs, including sub-Saharan Africa, have higher infectious disease rates than other developed countries. Additionally, there is extensive self-purchasing of antibiotics in LMICs and much of the global increase in antibiotic consumption in recent years has been in LMICs [1]. The general public may come to expect the availability of non-prescription antibiotics, but these can pose a barrier to antimicrobial stewardship. AMR has been associated with non-prescription availability of antimicrobials [1]. Cost-effective measures LMICs can employ to combat AMR include public health campaigns designed to inform of the dangers of AMR and decrease unnecessary over the counter (OTC) antimicrobial use [1]. Improved labeling for OTC medications may lead to decreased antimicrobial utilization, especially for countries in Africa where nearly all antimicrobials are obtained over the counter [1].

On January 30th 2020, the WHO declared Coronavirus Disease 2019 (COVID-19) a public health emergency of international concern [1]. Although infection prevention programs have a defined role in outbreak management, to date ASPs have not been involved in outbreak response efforts. There is emerging literature on the role of ASPs in pandemic response efforts, specifically in the context of COVID-19 [1]. ASPs can help identify patients with COVID-19, develop treatment protocols utilizing novel or repurposed medications and help manage limited medication supplies through existing structures such as prospective audit and feedback or antimicrobial restriction. ASPs are likely to have a key role in future outbreak response efforts [1]. The COVID-19 pandemic challenged already well-established programs and highlighted the need for AMS integration into emergency preparedness planning [6].

Future Directions and Research Priorities

Implementation science is still a young and developing field. Nevertheless, recent studies have shown that with the help of implementation specialists, evidence-based measures can be successfully introduced with increased sustainability [6†L195-L196]. However, implementation is not a "one size fits all" model, as specific needs and expectations of involved healthcare personnel as well as setting specific characteristics need to be taken into account [6]. More investment in qualitative and health system level research is needed, to appreciate the complexity of the multidisciplinary approach needed in AMS interventions. Such approach would allow to better document the root causes of inappropriate antibiotic prescription and consumption in humanitarian settings, in order to design AMS strategies tailored to the specificities of these contexts [3].

Clinical decision support electronic algorithms have the potential of offering a powerful tool to improve prescription practices, particularly in situations in which there is critical lack of skilled health care workforce [3]. Their use could be promoted and scaled up in humanitarian interventions, and they could be customized on the local culture and epidemiology, which entails the need to secure funding for their maintenance and regular updates [3]. Mobile phone-based applications can be a valuable tool for information dissemination if local information technology support is available. According to the International Telecommunication Union, in 2019 there were over 6.6 billion mobile cellar subscriptions in the developing world compared to 1.6 billion in the developed world and 46.7% of households in the developing world have access to the internet [1]. A study examined the effect of text messaging reminders among rural healthcare facilities in Kenya and demonstrated a statistically significant 23.7% increase in adherence to malaria treatment guidelines [1].

Research in antimicrobial resistance must be supported. Data must be generated in vivo and microorganisms must be identified. Unfortunately, publicly funded research in resource-limited settings is scarce, since health budgets are mostly devoted to medical assistance tasks [5]. Additionally, many hospitals lack access to a certified microbiology laboratory capable of providing timely information on antimicrobial resistance, further restricting research opportunities [5]. Support of health systems in resource-limited settings is needed. Resistance crosses borders. Microorganisms do not remain static in one region or continent. There are examples of resistant microorganisms that originated in one region and then spread to others [5]. Although it is logic and fair to hope for proactive measures in individual countries, the truth is that only international interest, cooperation and support will guarantee success for all in the future. In order for all to succeed, resource-limited settings must be particularly supported [5]. Initiatives like the Global Antimicrobial Stewardship Accreditation Scheme (GAMSAS) will be vital for the efforts to contain antimicrobial resistance risks around the world [5]. The development of AMR National Action Plans where absent, or their regular updates where present, needs to be supported, and strengthened through the inclusion of specific contingency plans for countries characterized by socio-political fragility which are known to harbour a high burden of AMR [3].

Conclusion

Antimicrobial resistance is an established and growing threat and LMICs share a disproportionate burden related to limited resources. It is vital that governments and health organizations

identify action to limit antimicrobial resistance as a top priority [1†L395-L396]. Antimicrobial stewardship involves the systematic deployment of evidence-based interventions designed to optimize antimicrobial use and slow the emergence of antimicrobial resistance [1]. Excellent resources exist (such as the World Health Organization Antimicrobial Stewardship Programmes in Health-Care facilities in low- and middle-income countries—A WHO Practical toolkit, 2019) that can help institutions develop and sustain ASPs and monitor outcomes [1]. If we agree that a global response to the increasing threat of antibiotic resistance is needed, we need to acknowledge that such response cannot be complete, let alone successful, without addressing the need for AMS in primary care settings also in countries affected by fragility and conflict [3]. More can be done: the time to act is now [3]. Multidisciplinary collaboration is essential for effective AMS implementation. Physicians, pharmacists, nurses, microbiologists, and infection prevention specialists each bring unique expertise to the stewardship team. Nurses' activities are already integrated in the day-to-day nursing practice and are grounded in the essence of nursing, being a patient advocate and showing nursing leadership in safeguarding the antimicrobial treatment process [7]. Educating, engaging and empowering nurses in this already integrated role, could lead to a solid, impactful nursing contribution to AMS [7]. The implementation of effective IPC and ASP guidelines remains a major challenge at all levels. By enforcing sustained implementation by dedicated healthcare personnel with a broad skill set, a reduction in HAIs and multidrug-resistant pathogens can be achieved and, as a result, ultimately improve patient safety [6]. Addressing AMR is not merely a clinical necessity; it is a critical imperative for global health security.

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