World Health Organization

ANTIMICROBIAL STEWARDSHIP PROGRAMMES IN HEALTH-CARE FACILITIES IN LOW- AND MIDDLE-INCOME COUNTRIES

A WHO PRACTICAL TOOLKIT

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Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries. A WHO practical toolkit

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FOREWORD

On any given day, in a given country, a mother comes into a health-care facility when her child has a high fever, hoping that the child will get effective treatment and be cured. With increasing rates of antimicrobial resistance (AMR), treatment options diminish, and her hopes may be dashed if the bacteria have become resistant and available antibiotics no longer work.

Like access to clean water and air, we have taken antibiotics for granted for too long. Since the discovery of penicillin in 1928, antibiotics have significantly improved global health. Indeed, they have been a cornerstone of modern medicine, including cancer chemotherapy and advanced surgical procedures. And while decades of overuse and misuse of antibiotics have accelerated the emergence and spread of resistant bacteria, access to antibiotics remains a major issue in many parts of the world.

At the same time, not enough new antibiotics are being developed to fight resistant bacteria. Therefore, existing antibiotics must be used more responsibly and managed carefully to extend their lifespan while being made available to the patients who truly need them. They should be prescribed only when indicated, also because they may cause serious side effects. This practical toolkit for implementing antimicrobial stewardship (AMS) in health-care facilities is meant to help low- and middle-income countries achieve this goal. It provides practical guidance to support the implementation of Objective 4 of the Global Action Plan on AMR: optimizing the use of antimicrobial medicines.

The toolkit provides guidance on where to get started, including the structures and resources that should be put in place at the national and health-care facility level, through a stepwise approach in low-resource settings. As the ultimate goal of an AMS programme is sustainable behaviour change in physicians' antibiotic prescribing practices, the toolkit also provides detailed guidance on how to plan, perform and assess AMS interventions – including feedback on antibiotic use over time. Finally, the toolkit provides an overview of the competencies an AMS team needs to guide health-care professionals in changing their antibiotic prescribing behaviours.

It is my sincerest hope that this toolkit will be helpful to countries in implementing their national action plans on AMR, in particular in optimizing their use of antibiotics. Time is running out, but we still have a window of opportunity to turn the tide on AMR and ensure continued effective treatment of bacterial infections for future generations. Let us act now.

Dr Hanan Balkhy
Assistant Director-General for
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LIST OF ABBREVIATIONS

AMC	antimicrobial consumption
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
AWaRe	ACCESS, WATCH, RESERVE
CAP	community-acquired pneumonia
DDD	defined daily dose
DOTs	days of therapy
EML	essential medicines list
GLASS	Global Antimicrobial Resistance Surveillance System
GNI	gross national income
HCW	health-care worker
ICU	intensive care unit
IPC	infection prevention and control
IT	information technology
LMIC	low- and middle-income country
M&E	monitoring and evaluation
MDR	multidrug-resistant
PDR	pan drug-resistant
PPS	point prevalence survey
SMART	specific, measurable, achievable, relevant, time-bound
SSTI	skin and soft tissue infection
SWOT	strengths, weaknesses, opportunities and threats
TrACSS	Tripartite AMR country self-assessment survey
TWG	technical working group
UTI	urinary tract infection
WASH	water, sanitation and hygiene
XDR	extensively drug-resistant

GLOSSARY

Antibiotic: An agent or substance that is produced by or derived from a microorganism that kills or inhibits the growth of another living microorganism. Antibiotic substances that are synthetic, semi-synthetic, or derived from plants or animals are, strictly speaking, not antibiotics. However, for the purposes of the toolkit they are included. In this document "antibiotic" refers to an antimicrobial agent with the ability to kill or inhibit bacterial growth.[1]

Antimicrobial:[1] An agent or substance derived from any source (microorganisms, plants, animals, synthetic or semi-synthetic) that acts against any type of microorganism, such as bacteria (antibacterial), mycobacteria (anti-mycobacterial), fungi (antifungal), parasite (anti-parasitic) and viruses (antiviral). All antibiotics are antimicrobials, but not all antimicrobials are antibiotics.

Antimicrobial resistance (AMR):[2] Microorganisms such as bacteria, fungi, viruses and parasites change when exposed to antimicrobial drugs such as antibiotics (= antibacterials), antifungals, antivirals, antimalarials and anthelmintics. As a result, the medicines become ineffective.

Antimicrobial stewardship (AMS):[3,4] A coherent set of actions which promote the responsible use of antimicrobials. This definition can be applied to actions at the individual level as well as the national and global level, and across human health, animal health and the environment.

Antimicrobial stewardship programme (AMS programme): An organizational or system-wide health-care strategy to promote appropriate use of antimicrobials through the implementation of evidence-based interventions.

Community-acquired infection: An infection acquired in the community, outside of a health-care setting.

Competencies:[5] The development of observable ability of a person (or individual health worker) that integrates knowledge, skills and attitudes in their performance of tasks. Competencies are durable, trainable and, through the expression of behaviours, measurable.

Days of therapy (DOTs): The number of days a patient receives an antibiotic independent of dose.

Defined daily dose (DDD): Assumed average maintenance dose per day for a medicine used for its main indication in adults as established by the WHO Collaborating Centre for Drug Statistics and Methodology.

Empirical antibiotic treatment: Initial antibiotic treatment targeted at the most probable causative microorganism. The recommendations should be based on local susceptibility data, available scientific evidence or expert opinion, when evidence is lacking.

Health-care-associated infection (also referred to as "nosocomial" or "hospital infection"):[6] An infection occurring in a patient during care in a hospital or other health-care facility, which was not present or incubating at the time of admission. Health-care-associated infections can also appear after discharge. They represent the most frequent adverse event associated with patient care.

Low- and middle-income country (LMIC): A collective term for low income-, lower-middle-income- and higher-middle-income countries, based on the World Bank's grouping of countries according to gross national income (GNI) per capita for a specified year. For 2019, low-income countries are defined as having a GNI per capita of US$ 995 or less in 2017, and lower-middle-income countries a GNI per capita of US$ 996–US$ 3 895.

Multidrug-resistant bacteria:[7] Bacteria that are resistant to at least one agent in three or more antibiotic categories. Extensively drug-resistant (XDR) is non-susceptibility to at least one agent in all but two or fewer antibiotic categories (i.e. bacterial isolates remain susceptible to only one or two categories), and pan drug-resistant (PDR) is non-susceptibility to all agents in all antibiotic categories.

Outcome measures/indicators for AMS programmes: Outcome measures/indicators are used in AMS activities to capture quantitative change in e.g. patient or economic outcomes, but most of all in antibiotic use. Antibiotic consumption is expressed with a numerator indicating the quantity used (i.e. DDDs or DOTs) per defined denominator (i.e. patient-days, admissions, consultations), to enable comparisons over time in the same setting or with other settings.

Process measures/indicators for AMS programmes: Process measures/indicators aim to capture information about the key processes that contribute to achieving the desired outcome(s). An example in AMS would be the proportion of patients prescribed antibiotic treatment in compliance with standard treatment guidelines.

Situational or SWOT analysis: A SWOT (strengths, weaknesses, opportunities and threats) analysis (alternatively called a situational analysis) is a popular method of identifying internal and/or present strengths and weaknesses, and external and/or future opportunities and threats to aid a decision-making process.

Structural measures/indicators for AMS programmes: Structure refers to the characteristics (capacity, systems and processes) of the setting in which AMS programmes are conducted. Structures may be material or human resources, such as availability of financial resources, number of personnel, availability of guidelines, availability of information technology tools, etc.

1 Critically important antimicrobials for human medicine. 5th revision. Geneva: World Health Organization; 2017.
2 Antimicrobial resistance. Fact sheet. Geneva: World Health Organization; 2018 (https://www.who.int/en/news-room/fact-sheets/detail/antimicrobial-resistance, accessed 3 September 2019).
3 Mendelson M, Balasegaram M, Jinks T, Pulcini C, Sharland M. Antibiotic resistance has a language problem. Nature. 2017;545(7652):23-25; McGowan JE, Gerding DN. Does antibiotic restriction prevent resistance? New Horiz. 1996;4:370–6.
4 Dyar OJ, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? Clin Microbiol Infect. 2017;23(11):793–8.
5 Sioban Fitzpatrick, Health Workforce Department, Geneva WHO (personal communication).
6 Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016.
7 Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268–81.

1. INTRODUCTION

1.1 Background

For decades microbes, in particular bacteria, have become increasingly resistant to various antimicrobials. The World Health Assembly's endorsement of the Global Action Plan on Antimicrobial Resistance (AMR)[8] in May 2015, and the Political Declaration of the High-Level Meeting of the General Assembly on AMR[9] in September 2017, both recognize AMR as a global threat to public health. These policy initiatives acknowledge overuse and misuse of antimicrobials as a main driver for development of resistance, as well as a need to optimize the use of antimicrobials. The Global Action Plan on AMR sets out five strategic objectives as a blueprint for countries in developing national action plans (NAPs) on AMR:

Objective 1: Improve awareness and understanding of AMR through effective communication, education and training.

Objective 2: Strengthen the knowledge and evidence base through surveillance and research.

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures.

Objective 4: Optimize the use of antimicrobial medicines in human and animal health.

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

This toolkit aims to support countries in implementing Objective 4 of the Global Action Plan – ''optimize the use of antimicrobial medicines" – by providing practical guidance on how to implement antimicrobial stewardship (AMS) programmes in the human health sector at the national and health-care facility level in low- and middle-income countries (LMICs).

Antimicrobial stewardship programmes optimize the use of antimicrobials, improve patient outcomes, reduce AMR and health-care-associated infections, and save health-care costs amongst others.[10,11] According to the Organisation for Economic Co-operation and Development (OECD) report *Stemming the superbug tide: just a few dollars more,*[12] implementing AMS programmes together with other policies to reduce overuse of antibiotics and promote hospital hygiene could save up to 1.6 million lives by 2050 and US$ 4.8 billion per year in the 33 OECD countries.

1.2 Antimicrobial stewardship – an integral component of health systems

Stewardship is defined as "the careful and responsible management of something entrusted to one's care".[13] It was originally applied in the health-care setting as a tool for optimizing antimicrobial use, termed "antimicrobial stewardship" (AMS).[14] Stewardship has since been applied in the context of governance of the health sector as a whole, taking responsibility for the health and well-being of the population and guiding health systems at the national and global level.[15]

Today, AMS is one of three "pillars" of an integrated approach to health systems strengthening. The other two are infection prevention and control (IPC) and medicine and patient safety. When applied in conjunction with antimicrobial use surveillance, and the WHO essential medicines list (EML) AWaRe[16] classification (ACCESS, WATCH, RESERVE), AMS helps to control AMR by optimizing the use of antimicrobials. Linking all three pillars to other key components of infection management and health systems strengthening, such as AMR surveillance and adequate supply of quality assured medicines, promotes equitable and quality health care towards the goal of achieving universal health coverage (Figure 1).

AMS principles also apply to the use of antimicrobials in the animal and agriculture sectors, typically with an emphasis on the responsible and prudent use of these agents. Although increasing levels of viral, fungal and parasite resistance to antimicrobials are of concern, this document will focus on the public health challenges of bacterial resistance to antibiotics. The specific aim of the toolkit is to enable AMS in health-care facilities in LMICs.

8 Resolution WHA 68-7. Global action plan on antimicrobial resistance. In: Sixty-eighth World Health Assembly, Geneva, 26 May 2015. Annex 3. Geneva: World Health Organization; 2015.

9 A/RES/71/3. Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance. New York: United Nations; 2016.

10 Davey P, Brown E, Charani E, Fenelon L, Gould IM, Ramsay CR et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2013 Apr 30;4:CD003543. Update in Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2017 Feb 9;2:CD003543.

11 Schuts EC, Hulscher ME, Mouton JW, Verduin CM, Stuart JWTC, Overdiek HWPM et al. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. Lancet Infect Dis. 2016;16:847–56.

12 Stemming the superbug tide: just a few dollars more. Paris: OECD; 2018.

13 Global framework for development and stewardship to combat antimicrobial resistance: draft roadmap. Geneva: World Health Organization; 2017.

14 McGowan JE, Gerding DN. Does antibiotic restriction prevent resistance? New Horiz. 1996;4:370–6.

15 Towards better stewardship: concepts and critical issues. Geneva: World Health Organization; 2002.

16 WHO Model List of Essential Medicines, 20th List. Geneva: World Health Organization; 2017:8–15.

With rates of AMR increasing worldwide, and very few new antibiotics being developed, existing antibiotics are becoming a limited resource. It is therefore essential that antibiotics only be prescribed – and that last-resort antibiotics (AWaRe RESERVE group) be reserved – for patients who truly need them. Hence, AMS and its defined set of actions for optimizing antibiotic use are of paramount importance.[4,17]

Many countries around the world have developed and are implementing their NAPs on AMR,[18] in which AMS is a key priority. Although there is a scientific evidence base for AMS,[19] and national, regional and global guidance documents exist,[20,21,22,23] there is a growing need for more specific guidance on how to establish, implement and evaluate effective AMS programmes at the national and health-care-facility level, especially in LMICs.[24,25,26] To meet this need, WHO, in collaboration with global AMS experts, has developed this practical toolkit for implementing AMS programmes in health-care facilities in LMICs (summarized in Table 1). This is only the first step in a dynamic process of sharing the evidence and experience required to run these programmes effectively.

The aim of an AMS programme is:

- to optimize the use of antibiotics;
- to promote behaviour change in antibiotic prescribing and dispensing practices;
- to improve quality of care and patient outcomes;
- to save on unnecessary health-care costs;
- to reduce further emergence, selection and spread of AMR;
- to prolong the lifespan of existing antibiotics;
- to limit the adverse economic impact of AMR; and
- to build the best-practices capacity of health-care professionals regarding the rational use of antibiotics.

17 Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP et al. IDSA/SHEA guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis. 2007;44:159–77.

18 Antimicrobial resistance: a manual for developing national action plans. Geneva: World Health Organization; 2016.

19 Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infect Dis. 2017;17(9):990–1001.

20 Core elements of antibiotic stewardship programs in resource-limited settings. Atlanta, GA: US Centers for Disease Control and Prevention; 2018

21 Recommendations for implementing antimicrobial stewardship programs in Latin America and the Caribbean: manual for public health decision-makers. Washington, DC: PAHO, FIU; 2018.

22 A practical guide to antimicrobial stewardship programs in Ethiopian Hospitals. Addis Ababa: AFMHACA; 2018.

23 Antimicrobial stewardship program in hospitals. Manual of procedures. Manila: Department of Health; 2016.

24 Cox JA, Vlieghe E, Mendelson M, Wertheim H, Ndegwa L, Villegas MV et al. Antibiotic stewardship in low- and middle-income countries: the same but different? Clin Microbiol Infect. 2017; 23:812–8.

25 Van Dijck C, Vlieghe E, Cox A. Antibiotic stewardship interventions in low- and middle-income countries: a systematic review. Bull World Health Organ. 2018;96:266–80.

26 Wilkins A, Ebata A, MacGregor H. Interventions to reduce antibiotic prescribing in LMICs: a scoping review of evidence from human and animal health systems. Antibiotics. 2019;8(1):1–25.

FIGURE 1

Integrated approach to optimizing use of antimicrobials towards universal health coverage

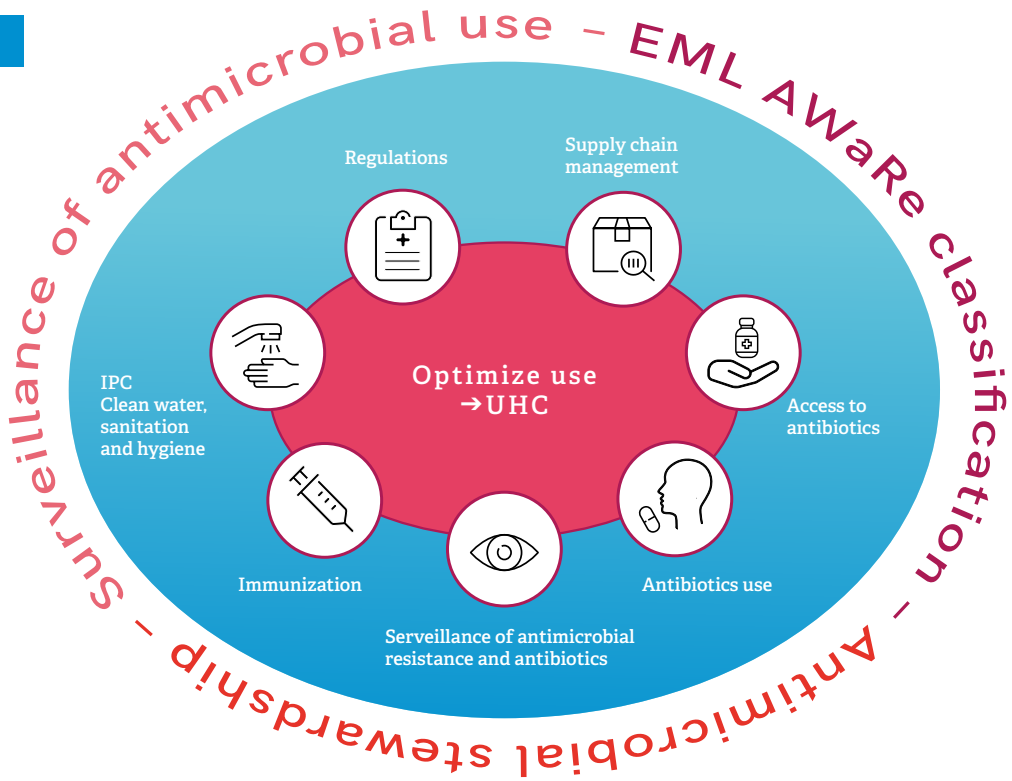


TABLE 1

WHO toolkit for AMS programmes in health-care facilities in LMICs

1. Structures	The core elements (Chapters 2 and 3) that should be in place to support AMS programmes at the national (state/regional) and facility level, i.e. AMS team, clinical treatment guidelines, and surveillance of resistance and antibiotics
2. Interventions	Guidance on how to plan, perform and assess AMS interventions in a health-care facility settings (Chapters 4–6)
3. Education and training	Outline of competencies for health-care professionals performing AMS activities (Chapter 7) Available online: Resources to support educational workshops and training programmes on AMS with educational material and a compilation of e-learning AMS resources relevant to LMICs

1.3 Establishing AMS programmes at a glance

To support readers and implementers at the national and health-care facility level to navigate the toolkit when implementing AMS programmes, Boxes 1 and 2 provide brief step-by-step guides on setting up, implementing and monitoring national and health-care facility AMS programmes, respectively.

AMS programmes can be driven through various processes and people. The key is to build on existing structures and to utilize entry points and champions. Box 3 describes how a health-care facility in Barbados set up its AMS programme based on an outbreak of a drug-resistant bacterium.

BOX 1

Key steps in establishing a national AMS programme to enable facility AMS

Audience: Ministry and/or department/s responsible for delivering quality-assured medical care and access to and rational use of medicines

1. Establish a governance structure – e.g. a national AMS technical working group (TWG) (Annex I) linked to the national AMR steering committee.
2. Review and prioritize the national core elements (Chapter 2):
   2.1. Identify what is already in place and the level of implementation required.
   2.2. Identify the short- and medium/long-term priority core elements.
   2.3. Identify the resources required.
3. Identify pilot health-care facilities (public and private) for initial AMS rollout:
   3.1. Tertiary teaching facilities;
   3.2. Regional/state and/or district facilities; and
   3.3. Primary care and/or community (as part of community AMS programmes not covered in this toolkit).
4. Develop a national AMS strategy* with national indicators.
5. Dedicate financial and human resources as required.
6. Monitor and evaluate implementation of the national AMS strategy (Chapter 6).
7. Facilitate access to and/or support pre- and in-service training on optimized antibiotic prescribing (Chapter 7).

* Include community and/or primary care AMS programmes (not covered in this toolkit).

BOX 2

Key steps to establishing a health-care facility AMS programme

Audience: Health-care facility leadership, AMS committee and/or AMS team

1. Undertake a facility AMS situational/SWOT analysis (Chapter 4) of:
    1.1. Health-care facility core elements – identify what is in place and the implementation level required (Chapter 3);
    1.2. Available data on antimicrobial consumption (AMC) and/or use, prescription audits and AMR surveillance data (Chapter 4); and
    1.3. Existing AMS competencies at the facility (Chapter 7).
2. Establish a sustainable AMS governance structure based on existing structures (Chapter 4; Annexes II and III).
3. Prioritize the health-care facility core elements based on the situational analysis (Chapter 3):
    3.1. Identify the immediate priorities.
    3.2. Identify the resources required.
4. Identify AMS interventions starting with the low-hanging fruit (Chapter 5):
    4.1. Identify who, what, where and when.
5. Develop a health-care facility AMS action plan that specifies the human and financial resources required (Chapter 4).
6. Implement AMS interventions (Chapter 5).
7. Monitor and evaluate AMS interventions (Chapter 6).
8. Offer basic and continued educational resources and training on optimized antibiotic prescribing (Chapter 7).

BOX 3

Case study: How a facility outbreak underpinned the establishment of facility AMS in Barbados

In a 600-bed health-care facility in Barbados, an outbreak of carbapenemase-resistant Klebsiella pneumoniae (KPC) resulted in the establishment of an AMS programme linked to the existing IPC programme. In 2012 **an all-facility PPS** (point prevalence survey) was undertaken which showed that one in five patients was colonized with KPC, and one in seven of the KPC-affected patients had an active infection. The results also showed a statistically significant correlation between KPC colonization and average length of hospital stay and antibiotic use of piperacillin/tazobactam and fluoroquinolones, resulting in increased hospital costs.

At the time of the outbreak, the facility's **IPC programme** consisted of a single nurse, but was then expanded with an infectious disease ID physician and a pharmacist. The IPC team used data to demonstrate to the hospital management that an **AMS programme** was critically needed and that it would involve minimal cost. **Leadership commitment** led to establishing an **AMS team** consisting of an infectious disease physician, pharmacist and microbiologist, as well as IPC-trained personnel who were all already employed in the facility.

The AMS team determined that the KPC outbreak and the three antibiotics associated with it accounted for 64% of the hospital costs of antibiotics during the preceding 6 months. The AMS set a **target** for decreasing the overall cost of antibiotics and hospital length of stay over the next 6–12 months. The AMS intervention began in the surgical intensive care unit (ICU) because of eager support from the head anaesthesiologist, an **AMS champion**. The targets were achieved faster than anticipated, and interest grew from other wards to be included in the AMS programme. A 60% decline in the use of carbapenems and vancomycin was documented.

Additional core elements that led to the success of AMS in the facility included facility-wide training on AMS; development of a facility antibiogram with regular feedback to the prescribers; a strong relationship and trust built between health-care professionals and the laboratory, which allowed for timely delivery of laboratory reports to inform prescribing; and media engagement.

2. STRUCTURES FOR NATIONAL (STATE/REGIONAL) AMS PROGRAMMES

Key audience: Ministry and/or department/s responsible for delivering quality-assured medical care and access to rational use of medicines

2.1 Introduction

Experience shows that AMS programmes can be successfully implemented when certain structures are in place.[27] A list of essential national core elements (Figure 2) has been developed to help countries build the necessary structures at the national (state/regional) level to enable health-care facility AMS programmes, taking into account the local context.

Putting key stewardship elements in place is essential to enabling sustainable action in this area.[28] The checklist of national (state/regional) core elements aims to guide countries in identifying the most critical elements for their national context, supporting the implementation of the NAP on AMR and subsequently AMS (Table 2). However, the list is a guide, and it is important for countries, states and regions to build on structures that are already in place and to use them as entry points for AMS initiatives, e.g. basic health-care package review and implementation, national EMLs and treatment guideline reviews. Ultimately, it is up to each country to decide how best to set priorities at the local, regional and/or national level. The core elements have been stratified as basic, which require fewer resources, and advanced, which require more resources, but these elements may vary for each country.

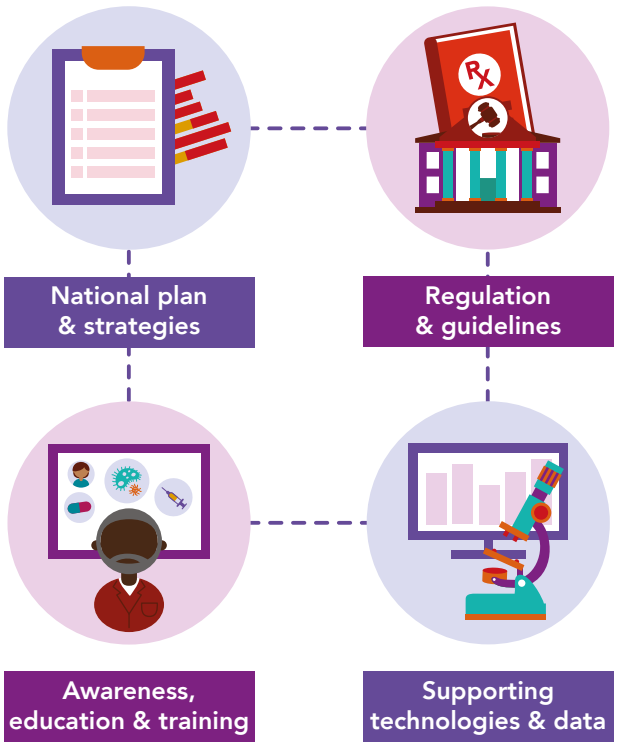
> *"Overall, the first priority will be on antimicrobial stewardship, because when there is antimicrobial stewardship instituted in the hospitals and the Ministry as a whole, then everything – the monitoring, the surveillance – everything comes after that."*
>
> (Bhutan, Government Official)

2.2 Selecting the national core elements

In developing the essential national core elements, a group of international experts conducted a literature review to identify key publications.[19,20,29,30,31,32,33] A structured consensus procedure (>80%) was then used to identify core elements relevant to national AMS programmes to enable health-care facility AMS, and these elements were stratified based on the resources required (basic and advanced).

FIGURE 2

National (state/regional) core elements for AMS programmes in LMICs



[27] Core elements of hospital antibiotic stewardship programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014.
[28] Pulcini C, Binda F, Lamkang AS, Trett A, Charani E, Goff DA et al. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. Clin Microbiol Infect. 2018;25:20-25.
[29] Draft WPRO – AMS training package. Geneva: World Health Organization; 2019.
[30] Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines. New Delhi: World Health Organization; 2011.
[31] Drug and therapeutics committees – a practical guide. Geneva: World Health Organization; 2003.
[32] Promoting rational use of medicines: core components. Geneva: World Health Organization; 2002.
[33] WHO guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016.

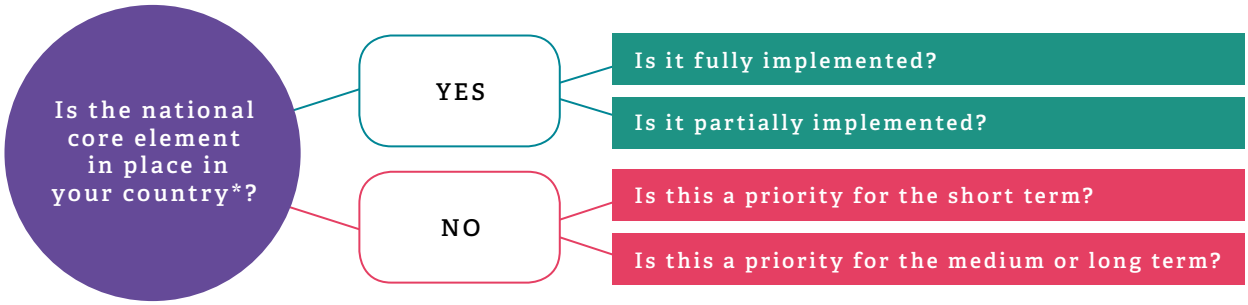
2.3 How to use the national core elements list

Decision makers responsible for national AMS programmes are encouraged to go through the checklist, identify what is already in place and the level of implementation (Figure 3), which core elements require accelerated implementation (partially implemented) and what is missing. A stepwise short- and medium/long-term implementation plan should be developed for the core elements that are prioritized as important based on the country context.

A recommended place to start for establishing a national (state/regional) AMS programme is to ensure leadership commitment to AMS by providing dedicated funding and human resources for NAP and AMS activities, and by putting in place a national TWG on AMS, education and training, surveillance of antibiotic use as part of a national monitoring system and standard treatment guidelines.

FIGURE 3

Guide to navigating the national core elements checklist to identify, prioritize and develop a stepwise implementation plan over the short and medium/long term



* "Country" can be substituted by "state" or "region" depending on the context.

TABLE 2

Checklist of essential national* core elements for AMS programmes in LMICs – basic (light grey) and advanced (dark grey) core elements

	NATIONAL CORE ELEMENTS	Yes	No
1. NATIONAL PLAN AND STRATEGIES	**1. National action plan on AMR that states AMS is a priority** The government endorses a national action plan on AMR explicitly stating that AMS is a national priority.	☐	☐
	2. Dedicated funding for the national action plan on AMR The national action plan on AMR has been costed and includes national activities for implementing AMS activities in the short to medium term (1–3 years) and/or long term (5 years).	☐	☐
	3. Technical working group on AMS established with clear terms of reference The national multisectoral coordination group has established a TWG or subcommittee on AMS that includes at least one ministry of health focal point and is linked to the AMC and AMR surveillance and IPC technical working groups. For sample terms of reference, see Annex I.	☐	☐
	4. National AMS implementation plan or policy endorsement An achievable national implementation plan for AMS with defined goals, outcomes, timelines, structures (national and hospital core elements) and responsibilities has been developed. It is linked to the national IPC plan or policy if it exists and is integrated into the government's annual action plan as appropriate.	☐	☐
	5. Monitoring and evaluation mechanism in place for the national action plan on AMR A mechanism is in place to monitor and evaluate progress on implementing the national action plan on AMR with the explicit inclusion of AMS and IPC activities.	☐	☐
2. REGULATION AND GUIDELINES	**6. Integration of the AWaRe classification of antibiotics in the national EML and formulary** Develop or review and adapt the antibiotics contained in the national EML and the national formulary with reference to the WHO EML AWaRe groups of antibiotics and outline AMS strategies for each group.	☐	☐
	7. Up-to-date clinical guidelines that include AMS principles and integrate the AWaRe classification of antibiotics The government endorses and makes available up-to-date standard treatment guidelines for infection management, based on national susceptibility surveillance data (where possible) to assist with antibiotic selection for common clinical conditions. These guidelines should be based on and explicitly include stewardship principles. Incorporate the WHO EML AWaRe classification of antibiotics into the next update of the guidelines. Where guidelines exist, a first step is to review them and to identify missing guidelines with an initial focus on empirical treatment. Where guidelines do not exist, the government provides human and financial resources to support the development of such national standard treatment guidelines and their dissemination as a priority activity. Coherence between guidelines and EMLs should be ensured.	☐	☐
	8. Regulations on fixed-dose combinations of antibiotics The government puts in place regulations that ban fixed-dose antibiotic combinations not approved by national or international guidelines.	☐	☐
	9a. Regulations on prescription-only sale of antibiotics[i] The government puts in place legislation or regulations that require antibiotics to be dispensed only on prescription by a qualified health-care professional (where access to health care is not an issue).	☐	☐
	9b. Regulation and enforcement of prescription-only dispensing of antibiotics[i] Legislation or regulation is actively implemented and enforced that requires antibiotics to be dispensed only on prescription by a qualified health-care professional (where access to health care is not an issue).	☐	☐
	10. Measures in place to ensure continued availability of quality-assured antibiotics[i] The government acts to ensure that available antibiotics are of suitable quality and that substandard or falsified drugs are not being sold.	☐	☐
	11. Measures in place to ensure affordability of essential antibiotics[i] The government acts to ensure that antibiotics are made available in suitable dosages (including paediatric formulations when appropriate) at a reasonable price to the public.	☐	☐

	NATIONAL CORE ELEMENTS	Yes	No
3. AWARENESS, TRAINING AND EDUCATION	**12. Regular public antibiotic awareness campaigns** Antibiotic awareness campaigns such as World Antibiotic Awareness Week and other targeted campaigns are regularly organized to address specific national or local issues and communities.	☐	☐
	13. Education in schools on basic infection principles The government ensures that schools provide education on basic IPC principles, including hand hygiene.	☐	☐
	14. Training on AMS competencies for AMS team members The government and/or health-care facilities facilitate access to in-service training in antimicrobial prescribing and stewardship for AMS team members in facilities. Use existing core competencies and set standards or adapt curricula.	☐	☐
	15. Education and training for all health-care professionals on AMS The government and/or other relevant bodies (e.g. professional societies) facilitate access to and/or support pre- and in-service training on how to optimize antibiotic prescribing, dispensing and administration for all relevant health-care professional groups (e.g. doctors, pharmacists, nurses). Use existing core competencies and set standards or adapt curricula (e.g. adaptation of the WHO core competencies and the AMR education and training curriculum guide).	☐	☐
	16. Incentives to support implementation of AMS programmes in all health-care facilities, including staffing standards, training and accreditation The government sets staffing standards for the AMS programme, makes implementation of AMS programmes in all facilities (public and private) a requirement, ensures that the health-care facility core elements (detailed in Chapter 3) are in place (e.g. by requiring certification/accreditation) and sets criteria to secure specific government funding for AMS in all facilities.	☐	☐
4. SUPPORTING TECHNOLOGIES AND DATA	**17. National surveillance system on AMC in place**[i,ii] The government supports programmes to compile and analyse appropriate data on the quantity and types of antibiotics purchased or distributed in the country (distinguishing between the health-care facility and community sector, if possible), following the WHO methodology on surveillance of AMC.	☐	☐
	18. National surveillance system on AMR in place with laboratory capacity to guide optimal use of antibiotics in clinical practice and update clinical guidelines Laboratory capacity is in place at the health-care facility or off-site (reference laboratory) to identify pathogens and their antibiotic susceptibility, to guide optimal use of antibiotics in clinical practice and to update guidelines. The laboratory further supports identification of key pathogens or syndromes to target AMS interventions. The government supports programmes to collate, compile and compare data from different facilities to identify trends over time and possibly to identify facilities that are outliers and might warrant investigation and assistance.	☐	☐
	19. Diagnostic tests available and capacity building undertaken to optimize antibiotic use Governments are encouraged to procure and promote the use of relevant diagnostic tests to optimize antibiotic use. The government acts to ensure that relevant and essential investigations (e.g. biology, microbiology, imaging) are available for all health-care facilities (either on-site, or with available access off-site).	☐	☐

* "National" can be substituted by "state" or "region" depending on the context.
[i] Indicator in the Tripartite M&E framework for the Global Action Plan on AMR.
[ii] Indicator tracked on an annual basis through the TrACSS.

The Tripartite M&E framework for the Global Action Plan on AMR[34] includes outcome indicators for optimizing use of antimicrobials (Table 3) that may be useful in monitoring national AMS programmes. These indicators are also expected to aid reporting to the annual Tripartite AMR country self-assessment survey[35] (TrACSS), in particular regarding a "national monitoring system for consumption and rational use of antimicrobials in human health".

[34] World Health Organization, Food and Agriculture Organization of the United Nations, World Organisation for Animal Health [the Tripartite]. Monitoring and evaluation of the Global Action Plan on Antimicrobial Resistance: framework and recommended indicators. Geneva: World Health Organization; 2019.

[35] Global database for antimicrobial resistance: country self assessment. Geneva: World Health Organization; 2018 (https://www.amrcountryprogress.org/, accessed 3 September 2019).

TABLE 3

Indicators from the Tripartite M&E framework for the Global Action Plan on AMR relevant to AMS programmes[32]

MEASUREMENT	INDICATOR NAME	SOURCE OF DATA AT THE GLOBAL LEVEL
4.1 Use of antimicrobials in humans	a. Total human consumption of antibiotics for systemic use (Anatomical Therapeutic Chemical classification code J01) in DDDs per 1000 population (or inhabitants) per day (b-d. see ref. 34.)	GLASS (Global Antimicrobial Resistance Surveillance System) Cross-sectional PPS
4.2 Access to antibiotics	Percentage of health facilities that have a core set of relevant antibiotics available and affordable on a sustainable basis	Sustainable Development Goal indicator 3.b.3, with ACCESS antibiotics disaggregated
4.3 Appropriate use of antimicrobials	Percentage of inpatient surgical procedures with appropriate timing and duration of surgical antibiotic prophylaxis	PPSs
4.7 Optimize antimicrobial use and regulation	Legislation or regulation that requires antimicrobials for human use to be dispensed only with a prescription from an authorized health worker	TrACSS

3. STRUCTURES FOR HEALTH-CARE FACILITY AMS PROGRAMMES

Key audience: Health-care facility leadership, AMS committee and/or AMS team

3.1 Background

At the health-care facility level, different contexts and types of facilities will face different challenges. A list of health-care facility core elements has been developed (Figure 4) to guide facility management in building the structures needed to enable implementation of sustainable AMS programmes in their facility.

3.2 Selecting the health-care facility core elements

In developing the health-care facility core elements for AMS programmes in LMICs, an international group of experts reviewed the key literature,[18,19,20,21,21,22,23,24,25] in particular the approach of Pulcini et al.,[28] suggesting additions and deletions and taking into account the low- and middle-income setting. Following the first round of suggestions, a structured consensus procedure (>80%) was undertaken to develop the final list of core elements for health-care facilities. The list was then stratified based on the resources required (basic or advanced).

3.3 How to use the health-care facility core elements list

The essential health-care facility core elements in the checklist shown in Table 4 have been stratified into basic core elements requiring fewer resources and more advanced core elements requiring more resources. However, this differentiation may vary from country to country and facility to facility based on size, needs, priorities, resources and context. Even within a small facility, the health-care facility administrator/manager, AMS committee and/or AMS team/person are encouraged to go through the checklist, identify which core elements are already in place and the level of implementation, what requires accelerated implementation and what is missing (Figure 5).

FIGURE 4

Health-care facility core elements for AMS programmes in LMICs

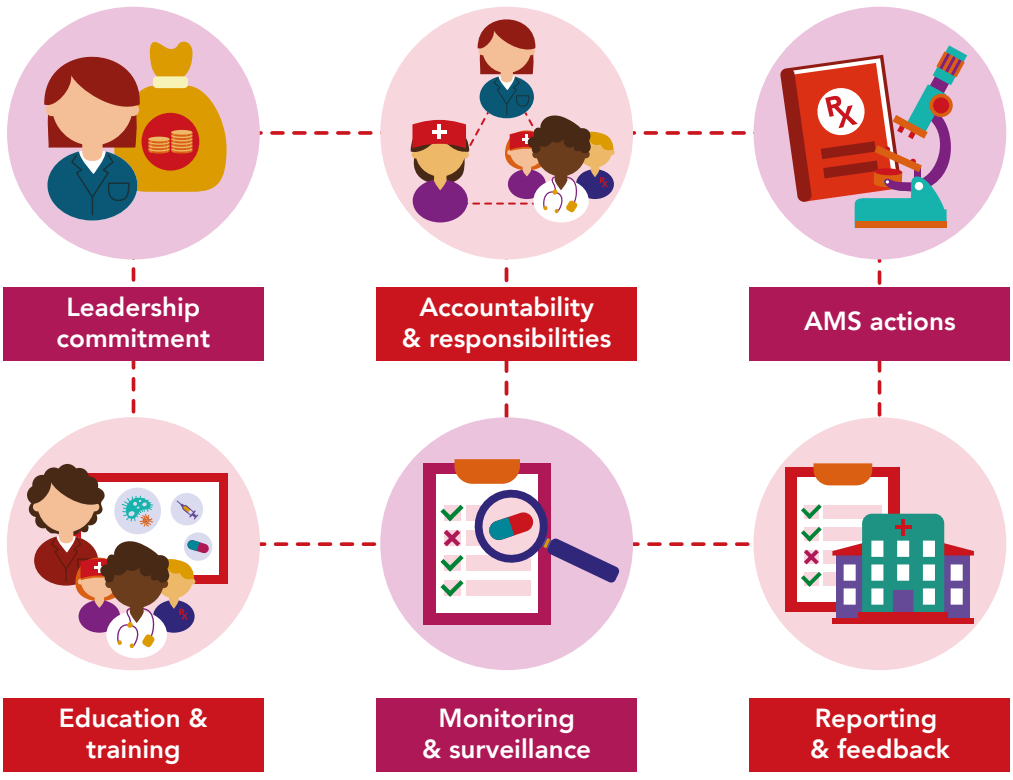
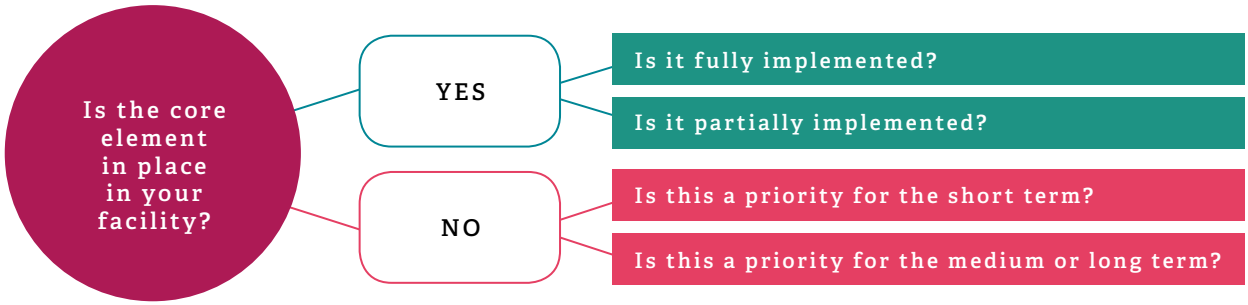


FIGURE 5

Guide to navigating the health-care facility core elements checklist to identify, prioritize and develop a stepwise implementation plan over the short and medium/long term



This information will help in developing a stepwise implementation plan over the short and medium/long term for the prioritized missing core elements and accelerate implementation of existing ones. For a small facility, it may be necessary to collaborate with other health-care facilities to put certain core elements in place, e.g. AMS expertise, education and training, standard treatment guidelines and AMC surveillance.

TABLE 4

Checklist of essential health-care facility core elements for AMS programmes in LMICs – basic (light grey) and advanced (dark grey) core elements

	HEALTH-CARE FACILITY CORE ELEMENTS	Yes	No
1. LEADERSHIP COMMITMENT	**1. AMS identified as a priority for health-care facility management** The facility management has formally identified AMS as a priority objective for the facility and included it in its key performance indicators. Financial and human resources have been allocated for AMS activities.	☐	☐
	2. Health-care facility AMS action plan endorsed that prioritizes activities and measures progress and accountability A health-care facility AMS action plan is endorsed that prioritizes activities and measures progress and accountability for ensuring appropriate antibiotic use, based on existing national or international guidelines and/or an existing national strategy. The AMS action plan is updated regularly as required.	☐	☐
	3. Dedicated financial support for the health-care facility AMS action plan There is dedicated, sustainable and budgeted financial support for AMS activities in the action plan (e.g. support for salary, training and information technology (IT) support).	☐	☐
2. ACCOUNTABILITY AND RESPONSIBILITIES	**4. Multidisciplinary AMS leadership committee in place with clear terms of reference*** This AMS committee can be either stand-alone or embedded in another existing committee structure (e.g. drug and therapeutics committee, pharmacy committee, infection control committee, patient safety committee). If embedded in another committee, AMS must be a standing item on the committee's agenda. The AMS committee is explicitly in charge of setting and coordinating the AMS programme/strategy according to its terms of reference.	☐	☐
	5. Dedicated AMS leader/champion identified for the health-care facility A health-care professional has been identified as a leader/champion for AMS activities at the facility and is responsible for leading the AMS team in implementing the AMS programme.	☐	☐
	6. Multidisciplinary AMS team with terms of reference* An AMS team of multidisciplinary health-care professionals who will implement the day-to-day AMS activities in the health-care facility. In resource-limited settings or small facilities it is often difficult to have an AMS team, and an AMS champion can be identified instead. The composition of the AMS team is flexible and should be based on existing recommendations and adapted to the local context: • option 1: >2 health-care professionals constituting a multidisciplinary team (e.g. tertiary hospitals); • option 2: a prescriber and a nurse or pharmacist (e.g. secondary or small hospitals); or • option 3: an AMS champion, e.g. a physician, nurse or pharmacist leading the stewardship programme, with access to expert advice.	☐	☐
	7. Other health professionals identified and involved in AMS activities Other health-care professionals apart from the AMS team (e.g. from the ICU, internal medicine and surgery, health informatics, or pharmacy or nursing personnel) participate in AMS activities based on the priorities of the health-care facility AMS action plan.	☐	☐
	8. Clearly defined collaboration between the AMS and IPC programmes A document clearly specifies the process of collaboration between the AMS team/committee and the IPC programme and/or committee. In many low-resource settings the IPC and AMS committees may be merged into one.	☐	☐
	9a. Regular (descriptive) activity reports on the implementation of the AMS programme Regular activity reports are produced and disseminated to health-care facility personnel and regional/national AMS TWGs. These reports include data on antibiotic use/consumption and describe the interventions implemented by the AMS team.	☐	☐
	9b. Regular activity reports (status and outcomes) on the implementation of the AMS programme Regular activity reports are produced and disseminated to health-care facility personnel and regional/national AMS TWGs with timelines for measurable short- and long-term targets/goals, based on analysis of local antibiotic use and evaluation of the impact of stewardship interventions.	☐	☐

	HEALTH-CARE FACILITY CORE ELEMENTS	Yes	No
3. AMS ACTIONS	**10. Up-to-date standard treatment guidelines** The health-care facility has available, up-to-date recommendations for infection management based on international/national evidence-based guidelines and local/national susceptibility patterns (where possible), to assist with antibiotic selection for common clinical conditions (indication, agent, dose, route, interval, duration). A process is in place for regular review and updating of the guidelines based on new evidence or other external input.	☐	☐
	11. Regular AMS team review/audit of specified antibiotic therapy or clinical conditions at the health-care facility Depending on available resources, this can be conducted by prioritizing wards or specific patient conditions.	☐	☐
	12. Advice/feedback from AMS team members is easily accessible/available to all prescribers This can be achieved through various methods, including facility ward rounds, bedside consultations and dedicated telephone lines.	☐	☐
	13. The AMS team conducts regular ward rounds and other AMS interventions in select health-care facility departments The AMS team conducts regular ward rounds (in one or more wards) and other AMS interventions in select facility departments (one or more) identified in the health-care facility AMS action plan.	☐	☐
	14a. Health-care facility formulary with a list of approved antibiotics The health-care facility has a formulary with a list of approved antibiotics that may be based on national recommendations or the WHO EML.	☐	☐
	14b. Health-care facility formulary with a list of restricted antibiotics The health-care facility has a formulary with a list of antibiotics approved for use in the facility and specifies a list of restricted antibiotics that require approval by the designated AMS team member (or infectious disease physician if available, physician or AMS champion) when used and/or are only permitted for specific conditions, e.g. the WATCH and RESERVE groups of antibiotics.	☐	☐
	15. Laboratory and imaging services accessible to support AMS interventions The health-care facility has access to (on-site or off-site) laboratory and imaging services, and to timely, quality-assured results to support diagnosis of the most common infections.	☐	☐
	16. Health-care facility access to IT services to support AMS activities The specific requirements need to be defined at local/regional/national level. This could include, for example, measurement of antibiotic use.	☐	☐
	17a. Standardized facility prescription chart and medical records The health-care facility ensures the availability and use of standardized prescription charts, medical records and transfer notes.	☐	☐
	17b. Health-care facility policy for documenting prescribed medicines The health-care facility has a written policy that requires prescribers to clearly document the indication and antibiotics prescribed (agent, dose, route, interval, duration and review dates) in the prescription chart, medical record and transfer notes to other health-care institutions.	☐	☐

HEALTH-CARE FACILITY CORE ELEMENTS		Yes	No
4. EDUCATION AND TRAINING	**18. Basic training in optimal antibiotic use for health-care professionals** The health-care facility offers basic induction training (e.g. sensitization on AMR and use of standard treatment guidelines) to staff on how to optimize antibiotic prescribing, dispensing and administration.	☐	☐
	19. Continued training in optimal antibiotic use for health-care professionals The health-care facility offers continued educational resources (e.g. regular training on infection management) to train staff on how to optimize antibiotic prescribing, dispensing and administration.	☐	☐
	20. Initial and regular training of the AMS team in infection management The health-care facility offers initial and regular training of the AMS team in infection management (diagnosis, prevention and treatment) and AMS. This training is usually not offered at the facility level, but is likely to be available at the regional, national or international level. The facility should, however, ensure that members of the AMS team are adequately trained, according to local/national requirements.	☐	☐
5. MONITORING AND SURVEILLANCE	**21. Monitoring appropriateness of antibiotic use at the unit and/or facility-wide level through audits or PPSsi** The AMS team undertakes audits or PPSs, at the unit and/or health-care facility level, to assess the appropriateness of infection management and antibiotic prescription (e.g. indication, agent, dose and duration of antibiotic therapy in specific infectious conditions such as pneumonia or surgical prophylaxis) according to policy/guidance.	☐	☐
	22. Monitoring quantity and types of antibiotic use (purchased/prescribed/dispensed) at the unit and/or facility-wide level In collaboration with the facility pharmacy, the AMS team monitors the quantity and types of antibiotic use (purchased/prescribed/dispensed) at the unit and/or health-care-facility level.	☐	☐
	23. Monitoring of antibiotic susceptibility and resistance rates for a range of key indicator bacteria The AMS team monitors antibiotic susceptibility and resistance rates for a range of key indicator bacteria at the health-care facility-wide level, in alignment with national and/or international surveillance systems (e.g. GLASS).	☐	☐
	24. Monitoring compliance of AMS interventions by the AMS committee The AMS committee monitors compliance with one or more of the specific interventions put in place by the AMS team (e.g. indication captured in the medical record for all patients on antibiotics).	☐	☐
6. REPORTING AND FEEDBACK	**25. Regular evaluation and sharing of health-care facility data on antibiotic use with prescribers** Health-care-facility reports on the quantity of antibiotics purchased/prescribed/dispensed are reviewed and analysed, and key findings are shared with prescribers along with specific action points.	☐	☐
	26. Regular evaluation and sharing of health-care facility resistance rates with prescribers The facility reports on antibiotic susceptibility rates are reviewed, and analyses and key findings are shared with prescribers along with specific action points.	☐	☐
	27. Evaluation of appropriateness of data on antibiotic use is shared with prescribers Findings from audits/reviews of the quality/appropriateness of antibiotic use are communicated directly to prescribers along with specific action points.	☐	☐
	28. Health-care facility antibiogram for key antibiotics informed by data on antibiotic use and resistance The health-care facility aggregate antibiogram is developed and regularly updated based on a review and analysis of facility antibiotic use and antibiotic-resistant bacteria. The antibiogram may help to inform updates of clinical guidelines.	☐	☐

* In resource-limited settings, the functions of the AMS committee and AMS team may fall under the same team.

[i] Indicator in the Tripartite M&E framework for the Global Action Plan on AMR.

4. PLANNING AN AMS PROGRAMME IN A HEALTH-CARE FACILITY

Key audience: Health-care facility leadership, AMS committee and/or AMS team

4.1 Introduction

AMS programmes in health-care facilities should not be vertical programmes. Rather, they should cut across other existing programmes to optimize antibiotic use, thereby improving quality of care and infection management.

Health-care facilities are often differentiated as follows:

- private, not for profit, or public health-care facilities;
- district, regional, tertiary or quaternary/central health-care facilities (size, patient mix and available resources);
- health-care facilities with or without a fixed financial budget;
- health-care facilities with or without their own pharmacy; and
- health-care facilities with or without an on-site microbiology laboratory.

Independent of the characteristics of the health-care facility, including size, an AMS programme should be adapted to the facility's human, financial, structural and organizational resources, and to the patient mix. An AMS programme in a large tertiary hospital with different specialities will necessarily be larger and more complex than one in a district hospital. It is therefore important that health-care facility management and an AMS committee and/or AMS team together decide which strategies best fit their local setting, based on a situational analysis and development of an action plan (Table 5). The implementation of an AMS programme is a step-by-step dynamic process, with each facility building on what they already have in place. This chapter provides insights that can help inform the design of health-care-facility AMS programmes.[36]

[36] Mendelson M, Morris A, Thursky K, Pulcini C. How to start an antimicrobial stewardship programme in a hospital. Clin Microbiol Infect. 2019 Aug 21. [Epub ahead of print]

TABLE 5

Preparation for developing and implementing an AMS programme in a health-care facility

Situational or SWOT analysis	Conduct a situational or SWOT analysis using the checklist of health-care facility core elements to identify existing and missing (but priority) elements, as well as possible enablers for and barriers to implementing a facility AMS programme. Pay attention to: • *Structures, policies and guidelines:* Identify which structures, policies and guidelines are in place and which are critically in need of being put in place according to the checklist of facility core elements (see Chapter 3). • *Human resources:* Identify the existing and required human resources (including competencies) needed for a functioning governance structure for AMS, including the AMS committee and/or AMS team, and clinical and other staff to be involved in implementing the AMS activities. • *Antimicrobial use and resistance data:* Review data on antimicrobial consumption and/or use, and identify challenges related to antibiotic prescribing practices in the facility and/or departments. Review existing surveillance data on AMR and aggregate antibiograms from the facility. • *AMS activities:* Identify any existing AMS activities (including ad hoc) in the facility/wards that can be built on and made sustainable.
Facility AMS action plan	Based on the situational analysis, develop a health-care facility AMS action plan to ensure accountability, prioritize activities and measure progress. This should include the following key components: • *Core elements:* Determine priority core elements to be implemented in the short and medium term, including accountability, timeline and indicator. • *Governance:* Identify leadership commitment and oversight, and establish an AMS committee (new or incorporated into an existing structure) and an AMS team that is endorsed by the facility leadership. • *AMS activities:* Identify areas for improvement, implement AMS interventions (who, what, where, when and how), monitor and evaluate, and report and feed back the results. • *Health-care facility-wide engagement:* Ensure facility-wide engagement in the AMS programme, and empower the AMS committee and/or AMS team to undertake the AMS interventions and monitor their implementation. • *Education and training:* Identify competencies that need to be strengthened to effectively implement AMS, and develop a facility AMS education and training plan. • *Budget:* Develop a budget for the AMS programme, including human and financial resources required for the day-to-day running of the programme as well as for education and training on AMS of the AMS team and health-care professionals. The budget should be endorsed by the health-care facility leadership.

4.2 Conducting a situational or SWOT analysis

Before an AMS programme is developed and implemented, a situational or SWOT analysis should be performed. For AMS programmes, this information is important in determining what needs to be done and what can be done. This analysis does not need to be a complex exercise, but rather a pragmatic one that includes the following:

- mapping which core elements are in place in the facility;
- undertaking a baseline antibiotic use analysis;
- identifying main challenges related to antibiotic prescribing and use; and
- identifying available human and financial resources.

The situational analysis should include:

- strengths, weaknesses, opportunities and threats (SWOT) at different levels in the facility; and
- possible barriers and enablers for the full participation of the different health-care professionals and departments in the AMS programme.

The situational and/or SWOT analysis will help the health-care facility in developing a stepwise AMS action plan that identifies what is already in place (health-care facility core elements), what needs to be put in place over time (short- and medium/long-term priorities), the human resources needed (including champions), the composition of an AMS team and other core elements (including guidelines) based on the facility core elements checklist and priorities.

Figure 6 provides an example of a SWOT analysis for planning an AMS programme in a health-care facility. It lays out the strengths, weaknesses, opportunities and threats involved in determining how ready the facility is to implement AMS and paves the way for developing a facility AMS action plan.

Putting the core elements in place in the facility enables sustainable action on AMS, even if that means through collaboration with neighbouring facilities. For example, if there is no facility antibiotic guideline or a pharmacist to analyse antimicrobial consumption data, an option may be to adopt the guideline from a neighbouring facility with a similar context and collaborate with their pharmacist to analyse the AMC data.

FIGURE 6

Example of a SWOT analysis for AMS readiness in a health-care facility

	HELPFUL	HARMFUL
INTERNAL/PRESENT FACTORS	**Strengths** *Core elements:* • AMR and AMS are a leadership priority. • IPC programme/committee is active. *Human resources:* • There is enthusiasm for AMS in the facility/wards. • There is clinical knowledge of AMS. *Antimicrobial use and resistance data:* • Prescription audit is conducted in one ward. • Facility aggregate antibiogram is available. *AMS activities:* • A pharmacist is involved in some AMS activities in one ward.	**Weaknesses** *Core elements:* • No medical record or prescription pad is available. *Human resources:* • No dedicated health-care professional is available to lead the AMS team. *Antimicrobial use and resistance data:* • The supply of microbiology reagents is poor. • The supply of antibiotics is poor. *AMS activities:* • Health-care professionals have competing priorities and little time for AMS work.
EXTERNAL/FUTURE FACTORS	**Opportunities** *Core elements:* • Active implementation of the NAP on AMR • Increasing national awareness of AMR and its consequences for health *Human resources:* • Incorporating AMS responsibility into the IPC committee *Antimicrobial use and resistance data:* • Funds for conducting a facility PPS *AMS activities:* • Presenting findings from AMS activities to other wards/ health-care professionals	**Threats** *Core elements:* • Unstable access to essential antibiotics • Increased costs for antibiotics • Prioritization of issues other than AMS in the facility • Low facility budget *Human resources:* • Too many nonfunctional committees in the health-care facility *Antimicrobial use and resistance data:* • Increasing AMR rates, including carbapenem-resistant Enterobacteriaceae (CRE) *AMS activities:* • Opposition from clinical leaders

SWOT

4.3 Identifying human resources

It is essential to have a governance structure (Figure 7) that includes the different functions needed to effectively implement a health-care facility AMS programme.[37] The governance structure may vary in size and complexity depending on the facility. Most important is to identify the responsibility and accountability of the hospital management, and of those who are to coordinate and implement the AMS programme.

The health-care facility leadership/management should formally endorse the facility AMS action plan and provide organizational and structural support by allocating the required financial and human resources for AMS activities. It is essential that the health-care facility leadership/management endorse the health-care facility AMS governance structure to empower the AMS committee, AMS team and/or AMS champions to implement the AMS programme effectively.

An **AMS committee** in the health-care facility should provide leadership and overall coordination of the AMS programme. The AMS committee can be a stand-alone committee or be integrated into an existing structure, such as the infection control, patient safety or drug and therapeutics committee with clear terms of reference. It can be an opportunity to revitalize or empower existing committees. If integrated into an existing committee, AMS must be a standing item on the committee's agenda (see the sample AMS committee terms of reference in Annex II). The chair of the AMS committee (representing the facility management) should be responsible for providing leadership support and is accountable for the overall implementation of the AMS programme.

A **multidisciplinary AMS team** (or individual, depending on availability and the size of the health-care facility) of different health-care professionals[17] should be established, who collectively possess the competencies and undertake functions to successfully deliver and implement AMS programmes in health-care facilities. Ideally, the AMS team should comprise a prescribing clinician, a pharmacist, a nurse and a (clinical) microbiologist or laboratory technician in facilities with a microbiology laboratory (see the checklist of health-care facility core elements in Chapter 3). If available, an infectious disease physician, a clinical pharmacologist, and/or a nurse with expertise in infections or IPC are also recommended. The AMS team should have a clear terms of reference (see the sample terms of reference for an AMS team in Annex III). The nominated staff in the team need dedicated time to implement the programme, and their AMS role should be in their job description and performance contract.

In addition, a **clinical leader** for the AMS team should be identified who has sufficient training in AMS or infection management to manage the most common issues.

In smaller health-care facility, the AMS clinical leader may sometimes be the only member of the AMS programme. Where the AMS clinical lead is not a doctor, one (inside or outside the facility) should be identified (on-site or off-site) to provide medical advice and support to the AMS team, which can be led by a pharmacist or nurse, when required. Similarly, if a pharmacist is not a member of the AMS team on-site, it is useful to identify a pharmacist (inside or outside the facility) from whom advice can be sought.

In many settings a hierarchical health-care facility structure may pose a barrier for this kind of teamwork. In such cases it may be important to formally endorse pharmacists and nurses as part of the AMS team. Moreover, the AMS team members should be given the responsibility and authority required to perform AMS activities, recognizing a team of different individuals and professions with complementary competencies provides for more opportunities to perform AMS interventions adapted to local clinical settings. In this regard, health-care facility administrative and managerial support is essential.

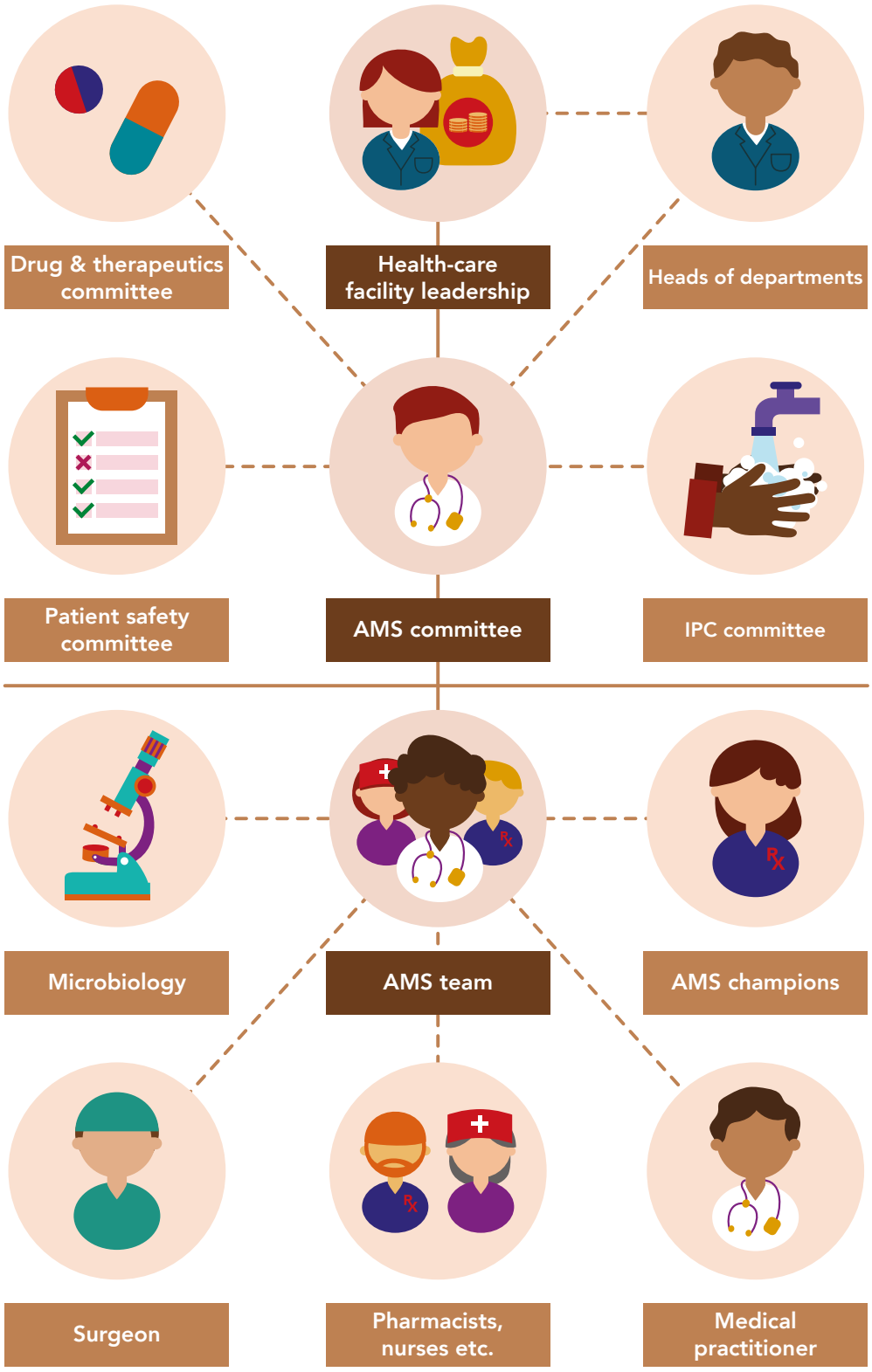
The **skill sets of professionals** who traditionally undertake roles in AMS are defined below. How these human resources are secured and how AMS tasks are assigned depend on the local context, needs, resources, health-care landscape and availability of expertise. Roles often require adaptation, with different professionals taking on different or multiple roles. Nevertheless, the emphasis must be to ensure that whoever undertakes the core tasks has the required generic skill sets and competencies (see Chapter 7).

Expertise in infection management is provided by an infectious disease or infection specialist, or a physician with interest and experience in infectious diseases. In the AMS team this person is the main source for supporting prescribers in diagnosing and managing patients, including optimal use of antibiotics to treat infections.[38] In addition, the infection management expert supports guideline development, pre-authorization and post-prescription AMS interventions, including review and feedback, and solicited or unsolicited consultations, as well as review and analysis of progress reports. The person also supports the development, coordination, dissemination, delivery and evaluation of educational programmes, which are then included in the implementation of the AMS education strategy and

[37] Colligan P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. Lancet Planet Health. 2018;2:e398–e405.

FIGURE 7

Example of an AMS governance structure for health-care facilities in LMICs



framework (see Chapter 7). The physician often leads the AMS team. But increasingly pharmacists and nurses are taking on this role, while recognizing the need to be able to consult with a physician in certain areas of infection management.

Expertise in antimicrobials is often the domain of a pharmacist or pharmacologist (if available).[39] In health-care facilities they traditionally help to develop guidelines and formularies and oversee the purchasing and supply of antimicrobials, dispense antimicrobials in wards/units and review the prescription order, identify and find solutions to stock-outs and shortages, perform surveillance of AMC and use (e.g. AMC data, PPS or prescription audits), and participate in their analyses. In wards they perform reviews of antibiotics prescribed (through prospective or retrospective audit with feedback), optimize antibiotic dosing in patients with organ dysfunction and comorbidities, and promote best practice in prescribing, dispensing and administering medicines, including antibiotics.

Expertise in patient care is typically provided by nurses.[40] They are considered crucial because they have first-hand information about patients. Focusing more on supporting optimal care and patient safety rather than strictly on antibiotic prescriptions may facilitate greater engagement from nurses, as this is part of quality nursing care.[41] This AMS team member should promote timely antibiotic administration without missing doses, therapeutic drug monitoring (if available), quality microbiological sampling and communication of laboratory results to prescribers to support antibiotic prescription decisions. Furthermore, nurses should encourage monitoring of patients' clinical progress and the side effects or ineffectiveness of medicines, identify opportunities to switch antibiotics from IV to oral and to monitor the correct handling of patients' invasive devices. Nurses may engage in data collection for audits and surveillance of antimicrobial consumption and use, and educate patients, families and colleagues (if empowered by the health-care facility leadership to do so) about optimal antimicrobial use as well as recommended IPC and water, sanitation and hygiene (WASH) behaviours and practices.

Expertise in microbiology is often provided by a microbiologist or laboratory technician to process samples for diagnosis and antibiotic susceptibility testing, and to feed back the results to the prescribers as well as to develop and regularly update the health-care facility's aggregate antibiogram. Not all health-care facilities have a microbiology laboratory; for smaller health-care facilities, this service could be provided through collaboration with other facilities.

For effective and sustainable stewardship initiatives, the roles individual team members undertake may naturally change over time. For example, a nurse who initially had a supporting role in the AMS programme may develop skills that will allow him or her to undertake surveillance, or an education or safety role, and a pharmacist may move from implementation to more of a governance role over time.

Additional expertise is essential to complement the skills of the AMS team, such as local champions and health-care professionals who can participate in performing and facilitating stewardship interventions on their wards. Also, if a health-care facility has a quality improvement, patient safety or IPC programme (Box 3) with dedicated staff, securing some of their time to focus on AMS activities is advantageous.

4.4 Link between IPC and AMS

The case study from Barbados (Box 3) is a good illustration of how AMS programmes are often initiated in facilities or even countries due to an outbreak of multidrug-resistant (MDR) bacteria. Likewise, it is often the same people involved in issues related to IPC and AMS both at the facility level and the national (state/regional) level. This is because IPC and AMS are two sides of the same coin when it comes to development and spread of AMR, optimizing antibiotic use and providing quality health care, as shown in Figure 8 and Box 4.

[39] Goff DA, Rybak MJ. Global antimicrobial stewardship: challenges and successes from frontline stewards. Infect Dis Ther. 2015;4:1–3.

[40] Brink A, Van den Bergh D, Mendelson M, Richards GA. Passing the baton to pharmacists and nurses: new models of antibiotic stewardship for South Africa? S Afr Med J. 2016;106(10):947–8.

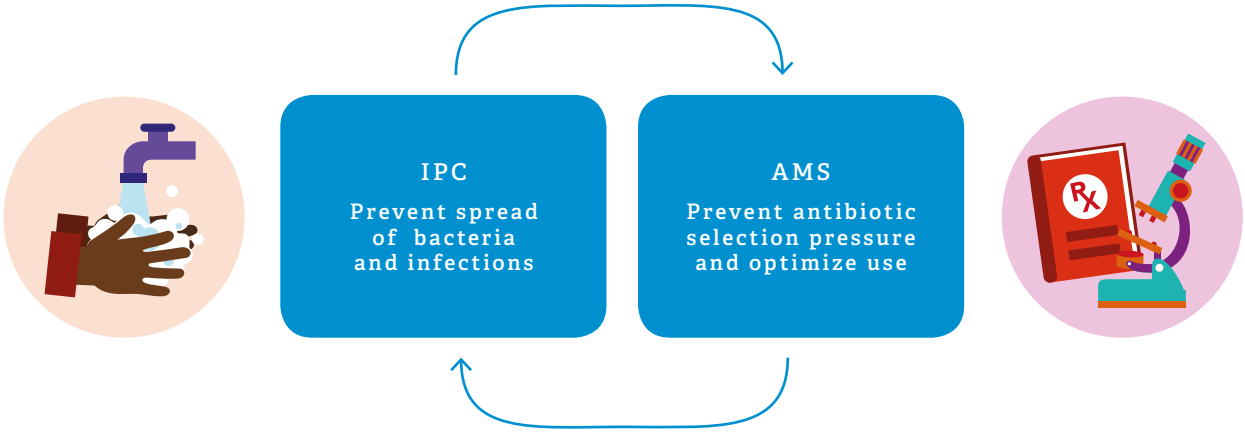
[41] Cotta MO, Robertson MS, Marshall C, Thursky KA, Liew D, Buising KL. Implementing antimicrobial stewardship in the Australian private hospital system: a qualitative study. Aust Health Rev. 2015;39:315–22.

[42] Improving infection prevention and control at the health facility. Interim practical manual supporting implementation of the WHO Guidelines on Core Components of Infection Prevention and Control Programmes. Geneva: World Health Organization; 2018 (https://www.who.int/infection-prevention/tools/core-components/en/, accessed 3 September 2019).

[43] Adapted from Figure 2 in ref. 42 (https://www.who.int/infection-prevention/tools/core-components/ipc-cc_visual.pdf?ua=1, accessed 3 September 2019).

FIGURE 8

Links between IPC and AMS in delivering quality health care and optimizing antibiotic use



BOX 4

Core components of IPC and the link to AMS

IPC is a practical, evidence-based approach which aims to prevent patients and health-care workers (HCWs) from being colonized with bacteria or getting infections. The implementation of IPC interventions not only prevents health-care-associated infections and deaths, but also saves money, reduces the spread of AMR and supports high-quality, people-centred health services. Comprehensive and effective IPC consists of establishing IPC programmes with strong links to other programmes, e.g. AMS programmes and other initiatives addressing AMR. According to the relevant WHO core components guidelines, implementing IPC promotes adoption of appropriate IPC practices during health-care delivery, thus enhancing patient safety and quality of care[42] (Figure 9). This approach is complementary to that of AMS, which aims to prevent the spread of MDR bacteria and infections by reducing overuse and misuse of antibiotics. Both IPC and AMS are interdependent programmes that require coordinated efforts and interventions to achieve the greatest impact.

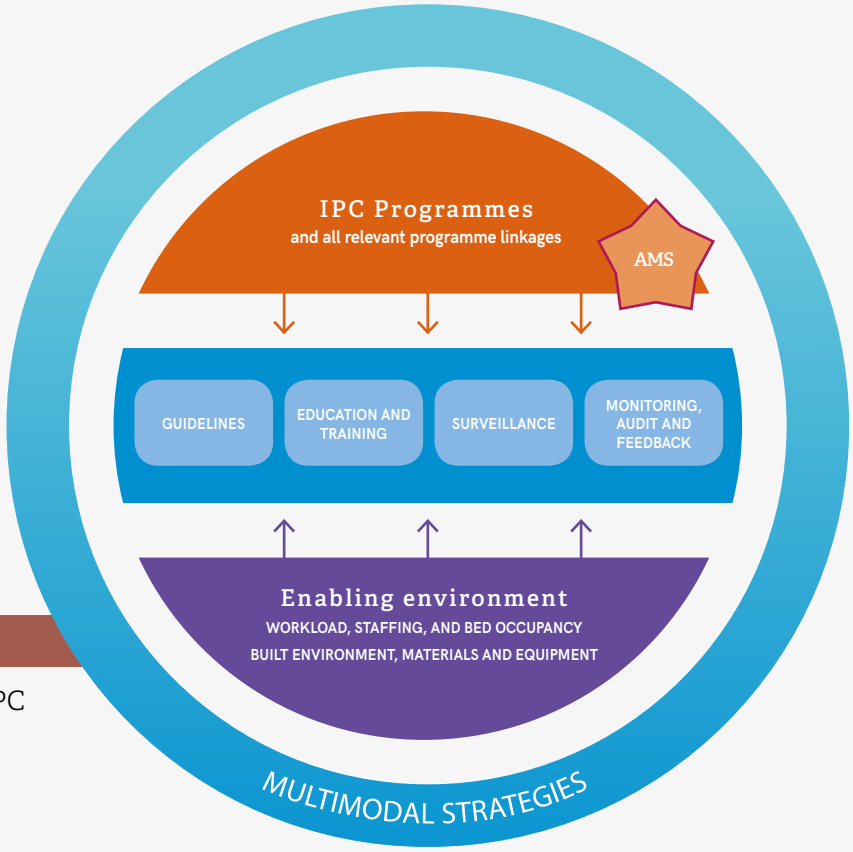


FIGURE 9

Linkage of AMS and the IPC core components[43]

4.5 Use of antibiotics in health-care facilities

The main purpose of collecting data on the use of antibiotics is to assess the extent and quality of antibiotic use, identify problematic prescribing practices, and compare appropriate use across health-care facilities and within a health-care facility, department or ward over time. Measuring the quantity and appropriateness of antibiotic prescribing and use will identify where there is room for improvement in targeting and monitoring AMS interventions.

The human and IT resources required for collecting this data are often regarded as a barrier to effective measurement. Therefore, it is advised to collect only the data essential for providing feedback to health-care professionals on their antibiotic use and to try to get them involved in the data collection. Integrating data collection as part of the requirements for other initiatives (e.g. infection control, patient safety and antisepsis programmes) is also an efficient way to collect critical data without duplication. Data should be collected according to a protocol, and the data quality should be validated. Although electronic data collection is ideal, paper-based collection is very common and acceptable.

Three main types of antibiotic data are used to provide baseline information and evaluate AMS interventions. Each type of data – antibiotic consumption, antibiotic use and antibiotic audit data – has advantages and disadvantages (see Chapter 4.5.1-3). Different data sets require different data sources, as shown in Figure 10 on antimicrobial consumption vs antibiotic use data sources.

Using these data for AMS programmes requires certain drug expertise as well as knowledge and training in data collection, management and analysis. For more detailed information on how to assess the impact of AMS programmes, see the structural indicators detailed in the health-care facility core elements checklist (Table 4), and advice on assessing AMS programmes in Chapter 6.[44]

4.5.1 Quantity – AMC data

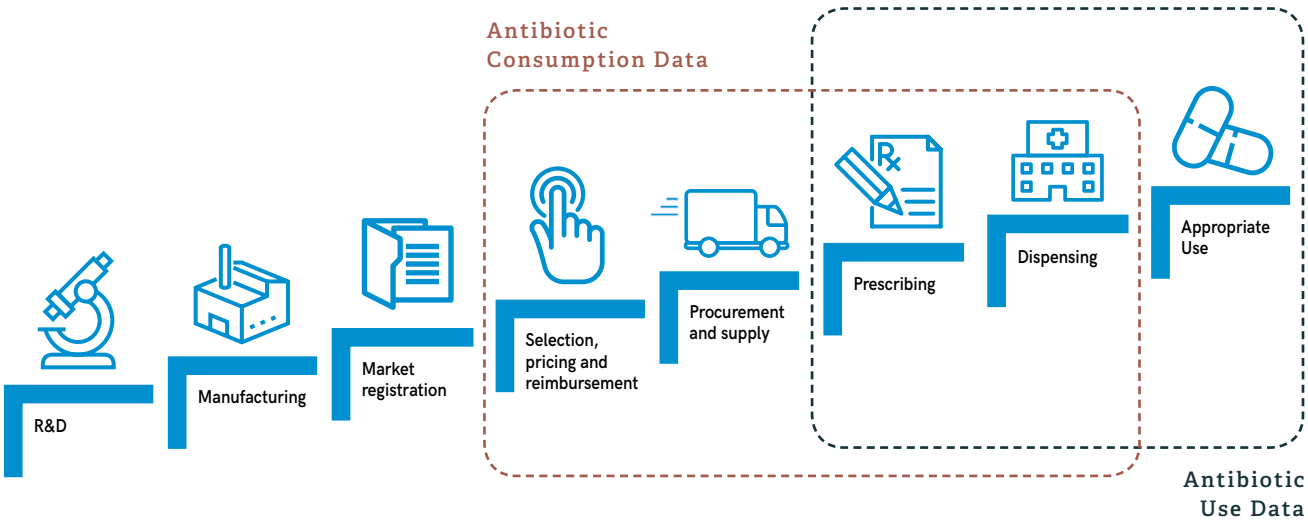
The term "consumption" refers to estimates that are derived from aggregated data sources, mainly procurement and dispensing data, and serves as a proxy for actual antibiotic use. These data sources do not contain any patient information or treatment indications, but they can provide an estimate on the quantity and types of medicines consumed at the national, subnational or facility level over time. Data should be collected according to a protocol from a recognized international methodology such as the WHO methodology on national/hospital surveillance of AMC.[45] This can be collected at the national or health-care facility level and stratified using the AWaRe classification and/or other relevant clinical categories. A step-by-step guide on setting up a national AMC surveillance programme at the facility level is shown in Box 5.

[44] Harbarth S, Hackett J. Introduction: DRIVE-AB's definitions and indicators to monitor responsible antibiotic use. J Antimicrob Chemother. 2018;1:vi2.

[45] WHO methodology for a global programme on surveillance of antimicrobial consumption. Version 1.0. Geneva: World Health Organization; n.d. (http://www.who.int/medicines/areas/rational_use/WHO_AMCsurveillance_1.0.pdf, accessed 4 February 2019).

FIGURE 10

Pharmaceutical value chain indicating potential data sources for surveillance of antimicrobial consumption and use



BOX 5

Step-by-step guide for setting up an AMC surveillance programme at the facility level[46]

Step 1: Structures and governance

- Appoint a person/team to manage and coordinate the local surveillance system at the facility level (part of an already existing structure such as the AMS or IPC committee).
- Assign tasks and responsibilities with clear terms of reference.

Step 2: Objectives and methodology

- Define the objectives and outputs of the facility surveillance programme.
- Determine the surveillance framework with respect to hospital structure, antimicrobial classes and frequency of data collection.
- Identify the sources of consumption data and the type of hospital activity indicator.

Step 3: Data collection and validation

- Collect consumption and hospital activity data.
- Validate and clean the data.

Step 4: Data analysis and reporting

- Identify the target groups for the results.
- Analyse and report data, taking into account the identified target groups.
- If applicable, report the data to the national surveillance system.

Step 5: Use of the data and follow-up

- Support the AMS and hospital medicines management in analysing the data.
- Improve the system to meet the requirements of the target groups.

Benefit: Data on antimicrobial consumption are often readily available and measured using the WHO ATC/DDD (Anatomical Therapeutic Chemical Classification/ Defined Daily Dose) methodology. This method refers to routine surveillance of existing data at no additional cost. Data at the facility level are collected from procurement, and dispensing data are ascertained from the facility pharmacy or other available sources along with the number of occupied beds or patient admissions during the study period.

Limitation: Independent of how the data are obtained, there are several possible sources of error. For example, the facility purchase data may not capture all the antibiotics used in the facility, or the facility may accept donations outside the formal procurement process. If there is no fixed population per health-care facility, it may be difficult to calculate the denominator.[47] Because the information is not as detailed as in a PPS or audit study, and the indication is missing, consumption data ensure only the quantity and types of antibiotics, not the quality of prescribing. Nonetheless, this method still provides a valuable estimate, especially for analysing trends. Expressing antimicrobial consumption in DDDs for paediatric populations is biased, as dosage is often age and weight dependent, with marked differences to adult DDDs.

4.5.2. Quality – antibiotic use data (PPS)

The expression "antibiotic use data" refers to estimates derived from individual patient data and may include information on patient characteristics and indications for treatment. Collection of use data is more resource demanding than consumption data, but the additional information provided is important for e.g. AMS programmes and to identify areas for improving antibiotic use. "Point prevalence survey" refers to the collection of antibiotic treatment data from hospitalized inpatients (all patients or a sample) at a point in time according to a recognized international methodology such as the WHO methodology for PPS on antibiotic use in hospitals.[48] A step-by-step guide for setting up a health-care facility PPS is shown in Box 6.

[46] Draft WHO methodology for antimicrobial consumption surveillance in hospitals. Geneva: World Health Organization; 2019.

[47] Chandy S et al. Patterns of antibiotic use in the community and challenges of antibiotic surveillance in a lower-middle-income country setting: a repeated cross-sectional study in Vellore, South India. J. Antimicrob Chemother. 2013;68(1):229–36.

[48] WHO methodology for point prevalence survey on antibiotic use in hospitals. Version 1.1. Geneva: World Health Organization; 2019.

Benefit: Facility PPS data provide an overview of how antibiotics are used in a facility. A PPS also allows assessment of compliance to guidelines because it includes more specific data, such as indications for antibiotic treatment, prescribed antibiotic(s), dosage, timing of administration of first dose, dose interval and drug administration route, though not duration of treatment. It is recommended that local PPSs be performed regularly. A PPS can be integrated with other surveys (e.g. of surgical site infections) to optimize resources.

Limitation: Data are collected at a point in time (5–7 days) and may not be representative, as less frequent practices might be missed. Conversely, if data are collected during outbreaks, higher use would be reported. Doing a PPS is more resource-intensive than collecting antimicrobial consumption data, as data are collected on individual patients.

4.5.3. Quality – antibiotic audit data

"Auditing" refers to the prospective (real-time) or retrospective collection of antibiotic prescription data on hospitalized patients. The data are analysed and then fed back to the prescribers. Though auditing may sometimes be laborious, it is an essential part of any AMS programme and should be encouraged.[49] This method can begin with weekly or bimonthly quick audits (only a few patients) during ward rounds, with real-time feedback to the prescribers, similar to a repeated and small-scale PPS. For more detailed information and examples, see Chapter 5.8 on prospective and retrospective audit with feedback.

4.7 The EML and AWaRe classification

The WHO EML AWaRe[50] classification of commonly used antibiotics into three groups – ACCESS, WATCH and RESERVE – provides a tool to support antibiotic monitoring and AMS activities, with recommendations on when to use

[49] Ivers N, Jamtvedt G, Flottort S, Young JM, Odgaard-Jensen J, French SD et al. Audit and feedback: effects on professional practice and healthcare outcomes. Cochrane Database Syst Rev. 2012 June 13;6:CD00259.

[50] Executive summary: the selection and use of essential medicines 2019. Geneva: World Health Organization; 2019.

BOX 6

Step-by-step guide for setting up a health-care facility PPS[48]

Step 1: Structures and governance

- Identify the team/committee in the facility with the overarching responsibility for the PPS, often the committee also responsible for AMS.
- As part of this team/committee, appoint a facility PPS focal point responsible for coordination and day-to-day management of the survey and investigators (surveyors).

Step 2: Objectives and methodology

- Define the objectives and output of the PPS in the facility.
- Select a standardized PPS protocol for the survey, e.g. WHO PPS protocol, Global PPS.
- Train the hospital PPS focal point, team and investigators in the methodology.

Step 3: Preparation

- Obtain ethical approval and other necessary permissions to undertake the survey.
- Agree on the days for conducting the surveys in the respective wards.
- Prepare the necessary materials for undertaking the survey.

Step 4: Data collection and validation

- Undertake a pilot survey in one ward to validate the data, and operationalize the survey procedures.
- Conduct the survey in all wards according to predefined timelines.
- ransfer data from paper to electronic format when applicable, and validate the data.

Step 5: Data analyses and reporting

- Clean and analyse the data based on a predefined data analysis plan according to target groups.
- Report results to the responsible team/committee, the facility management, etc.
- Identify areas for improving antimicrobial prescribing and use based on results, and agree on AMS interventions to address these areas.
- Monitor and evaluate the AMS interventions with e.g. a targeted PPS or audits.

FIGURE 11

Overview of the WHO AWaRe groups and essential antibiotics on the WHO EML[50]

ACCESS GROUP

This group includes antibiotics and antibiotic classes that have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistance potential than antibiotics in Watch and Reserve groups. Access antibiotics should be widely available, affordable and quality-assured to improve access and promote appropriate use.

Selected Access group antibiotics (shown here) are included on the WHO EML as essential first-choice or second-choice empirical treatment options for specific infectious syndromes.

- Amikacin
- Amoxicillin
- Amoxicillin + clavulanic acid
- Ampicillin
- Benzathine benzylpenicillin
- Benzylpenicillin
- Cefalexin
- Cefazolin
- Chloramphenicol
- Clindamycin
- Cloxacillin
- Doxycycline
- Gentamicin
- Metronidazole
- Nitrofurantoin
- Phenoxymethylpenicillin
- Procaine benzylpenicillin
- Spectinomycin
- Sulfamethoxazole + trimethoprim

WATCH GROUP

This group includes antibiotics and antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials (CIA) for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. Watch group antibiotics should be prioritized as key targets of national and local stewardship programmes and monitoring.

Selected Watch group antibiotics (shown here) are included on the WHO EML as essential first-choice or second-choice empirical treatment options for a limited number of specific infectious syndromes.

- Azithromycin
- Cefixime
- Cefotaxime
- Ceftazidime
- Ceftriaxone
- Cefuroxime
- Ciprofloxacin
- Clarithromycin
- Meropenem
- Piperacillin + tazobactam
- Vancomycin

RESERVE GROUP

This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi drug-resistant organisms, and treated as "last-resort" options. Their use should be tailored to highly specific patients and settings, when all alternatives have failed or are not suitable. They could be protected and prioritized as key targets of national and international stewardship programmes, involving monitoring and utilization reporting, to preserve their effectiveness.

Selected Reserve group antibiotics (shown here) are included on the WHO EML when they have a favourable risk-benefit profile and proven activity against "Critical Priority" or "High Priority" pathogens identified by the WHO Priority Pathogens List, notably carbapenem-resistant Enterobacteriaceae.

- Ceftazidime + avibactam
- Colistin
- Fosfomycin (intravenous)
- Linezolid
- Meropenem + vaborbactam
- Plazomicin
- Polymyxin B

the antibiotics in each category. Selected AWaRe antibiotics are included on the WHO Model EMLs as recommended treatment options for specific infectious syndromes (Figure 11).

The full AWaRe database, along with further guidance on how to apply the WHO AWaRe classification for developing and updating national EMLs, developing and updating treatment guidelines, and for monitoring antimicrobial consumption and use (including more intense surveillance of the RESERVE antibiotics), will be made available on the WHO website. However, some examples of how the AWaRe classifications can be incorporated at the national level to enable health-care facility AMS include the following:

- review/update national EMLs with AWaRe groups;
- review/update Sustainable Development Goals with AWaRe groups;
- align empirical antibiotic treatment guidelines with ACCESS antibiotics;
- target WATCH and RESERVE groups for AMS;
- review antimicrobial consumption and use surveillance data with AWaRe; and/or
- include in health professional curricula.

Stratifying total antimicrobial consumption data by the AWaRe groups can be undertaken at multiple levels, including at the national (state/regional), facility and ward level. This allows benchmarking and overall monitoring of national and global progress towards WHO's goal of increasing the proportion of global consumption of antibiotics in the ACCESS group to ≥60%.[51] Figure 12 shows an example of how the AWaRe groups can be integrated into national AMC surveillance data to highlight the proportion of antimicrobial consumption across the categories.

4.7 Microbiology

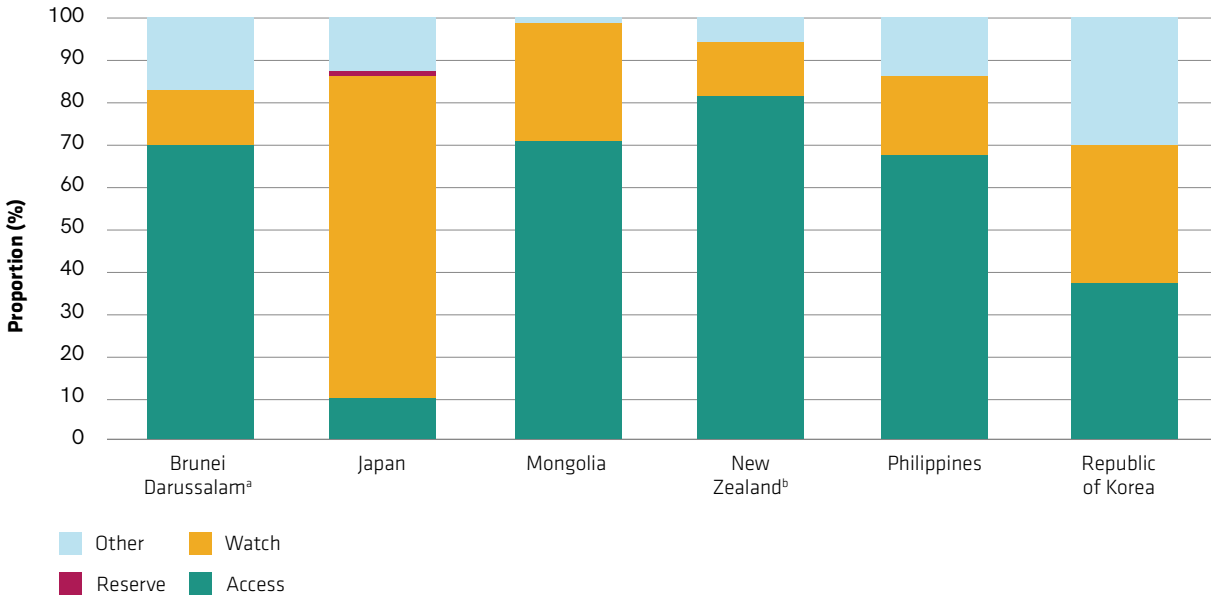
Most patients, both in health-care facilities and in primary health-care settings, receive initial antibiotic treatment based on a clinical assessment, without the use of microbiological tests. Treatment is chosen according to which microbes are most likely to cause different infections. This strategy works well when resistance rates are low, or AMR surveillance can guide recommendations for empirical antibiotic treatment. There is a great need for affordable, sensitive, specific and rapid diagnostic tests that provide prescribers with quality-assured information about whether or not a patient has a bacterial infection, and which antibiotics the causative bacteria are sensitive to. Microbiology laboratories play a key role in informing the appropriate use of (ACCESS) antibiotics, ensuring first- and second-line antibiotics are used whenever possible. The quality of the clinical diagnosis is still essential, as the tests need to be interpreted in light of it.

Many countries lack microbiology laboratories with external quality assurance and microbiology expertise altogether. However, with the implementation of national action plans on AMR, countries are encouraged to collect and analyse local resistance data and establish national AMR surveillance systems reporting to GLASS.[53] A brief introduction to GLASS is provided in Box 7.

[51] Thirteenth general programme of work 2019–2023. Geneva: World Health Organization; 2018.
[52] WHO report on surveillance of antibiotic consumption: 2016–2018 early implementation. Geneva: World Health Organization; 2018.
[53] Global antimicrobial resistance surveillance system (GLASS): manual for early implementation. Geneva: World Health Organization; 2015.

FIGURE 12

Proportional consumption (%) of antibiotics by AWaRe classification in six countries of the Western Pacific Region, 2015[52]



[a] Only public sector reported.
[b] Only community consumption reported.

BOX 7

Snapshot of GLASS[53]

Launched in 2015, GLASS is being developed to support the Global Action Plan on AMR. The aim is to support global surveillance and research in order to strengthen the evidence base on AMR and antimicrobial use and to help inform decision-making and drive national, regional and global actions.

GLASS promotes and supports a standardized approach to the collection, analysis and sharing of AMR and antimicrobial use data at a global level. GLASS does this by encouraging and facilitating the establishment of national AMR surveillance systems capable of monitoring AMR and antimicrobial use trends and producing reliable and comparable data.
GLASS objectives:

- foster national surveillance systems and harmonized global standards;
- analyse and report global data on AMR and antimicrobial use on a regular basis;
- estimate the extent and burden of AMR globally by selected indicators;
- detect emerging resistance and its international spread;
- inform implementation of targeted prevention and control programmes; and
- assess the impact of interventions

Countries benefit from participation in GLASS through enhanced capacity building, access to training and implementation tools, and support in collecting AMR and antimicrobial use data at the local and national level.

Efforts are being made to meet country needs, including capacity building for specimen collection, antibiotic susceptibility testing and IT systems for analysing AMR patient data.[54]

The main function of microbiologists (or laboratory technicians) in an AMS programme is to interpret and communicate microbiology results to prescribers, and to develop and update antibiograms and communicate their value and limitations. An example of an aggregate antibiogram (only for gram- negative bacteria) can be found in Annex VIII. Microbiologists also serve to support the AMS team in developing antibiotic guidelines and policy based on local resistance surveillance, and to educate clinical staff on quality sampling for microbiology testing and AMR rates. In addition, microbiologists require support from the AMS team to ensure they receive basic demographic and clinical data to help in analysing laboratory results. Finally, where possible, microbiologists support the AMS team by reporting on MDR organisms and selectively reporting susceptibility data to the facility management and prescribers.

[54] Diagnostic stewardship: a guide to implementation in antimicrobial resistance surveillance sites. Geneva: World Health Organization; 2016.

5. PERFORMING AMS INTERVENTIONS IN A HEALTH-CARE FACILITY

Key audience: AMS team

5.1 Implementing an AMS programme

One main outcome of performing AMS interventions in a health-care facility is behaviour change in antibiotic prescribing practices, leading to more responsible use of antibiotics. Implementing AMS programmes is a strategy for changing this behaviour over time.[55]

The **health-care facility core elements** reflect some of the evidence that has been shown to inform clinical/professional practice, e.g. leadership commitment, data on antimicrobial consumption and use, standard treatment guidelines, and AMS teams and champions. **SWOT analysis** is important in highlighting possible barriers and enablers to implementation of an AMS programme (e.g. data on antimicrobial consumption and use), helping to identify areas for improvement and monitoring use over time. The **health-care facility AMS action plan** provides an overview of the facility AMS programme with overall goals, how they will be reached and by whom, and how progress will be measured. However, having a plan is not enough – it has to be implemented.

> *"It is not just what you do, it is how you do it."*
>
> (Dr Hanan Balkhy, Assistant Director-General for Antimicrobial Resistance, WHO)

5.2. Implementing AMS interventions and behaviour change

It is said that using evidence-based interventions is no guarantee of success, because success depends on implementing the interventions. Implementation research is defined as "methods to promote the uptake of proven clinical treatments, practices, organizational and management interventions into routine practice, and hence to improve health." It identifies the behavior of healthcare professionals and healthcare organizations as key sources of variance requiring improved empirical and theoretical understanding before effective uptake can be reliably achieved[56] Hence, implementing evidence-based AMS interventions[10] to change prescribing behaviour means taking into account factors that influence prescribing and use at the facility/department/ward level. Many structural and organizational factors, also called extrinsic factors, are addressed in developing a facility AMS programme/action plan.[57]

However, intrinsic factors may also influence antibiotic prescribing behaviour and need to be addressed. Examples of intrinsic factors include the following:[58]

- perception that AMR is an immediate threat (lack of awareness and knowledge about AMR);
- fear of losing a patient;
- belief that broad-spectrum antibiotics are very effective and low risk;
- influence of a senior physician's preferences on a junior physician's prescribing;
- physician autonomy in prescribing what he or she thinks is best; and
- uncertainty due to inadequate microbiology services.

Consequently, when performing AMS interventions, implementation requires that they be tailored to address the different factors that may influence antibiotic prescribing and use in a specific context.[59] Two ways of tailoring AMS interventions are to involve clinical staff in identifying local targets for improving antibiotic use (Chapter 5.3) and to have a systematic approach to implementing AMS interventions, review progress over time and make changes when appropriate (Chapter 5.4).

[55] Hulscher MEJL, Prins JM. Antibiotic stewardship: does it work in hospital practice? A review of the evidence base. Clin Microbiol Infect. 2017;23:799–805.

[56] Implementation Science (https://implementationscience.biomedcentral.com/about, accessed 3 September 2019).

[57] Teixeira Rodrigues A, Roque F, Falcão A, Figueiras A, Herdeiro MT. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies. Int J Antimicrob Agents. 201e;41:203–12.

[58] Krockow EM, Colman AM, Chattoe-Brown E, Jenkins DR, Perera N, Mehtar S et al. Balancing the risks to individual and society: a systematic review and synthesis of qualitative research on antibiotic prescribing behavior in hospitals. J Hosp Infect. 2019;101:428–39.

[59] Flottorp SA, Oxman AD, Krause J, Musila NR, Wensing M, Godycki-Cwirko M et al. A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice. Implement Sci. 2013;8:35.

5.3 Identifying local targets for improving antibiotic use

Table 6 lists some common, very generic areas for improving antibiotic prescribing. In a smaller facility, the overall goal identified in the AMS action plan may be sufficient, and the same AMS interventions may be implemented over the whole facility. However, in a larger facility, a surgical department may have different priorities to a medical department. In that case, it is more meaningful for each department to set their own SMART (specific, measurable, achievable, relevant, time-bound) goals.

5.4 A systematic approach to implementing AMS interventions

The continuous quality improvement model[60] provides a systematic approach for involving clinical staff in AMS team efforts to set SMART goals for change, tailoring and implementing interventions appropriate for the local context, and assessing their success (Figures 13–15). This model can be applied at the facility level in small facilities or at departmental or ward level in larger facilities. For assessing the outcomes of AMS interventions, see Chapter 6. It is important to agree on a set time period (e.g. 3–6 months) for reviewing the impact of the AMS interventions and adjusting them.

Key message:
AMS interventions should be implemented in a stepwise approach, build on existing structures and reporting, maximize teamwork, and encourage champions and clinical staff – including prescribers – to participate. Start small and keep it simple and doable.

[60] Langley GL, Moen R, Nolan KM, Nolan TW, Norman CL, Provost LP. The improvement guide: a practical approach to enhancing organizational performance. 2nd edition. San Francisco: Jossey-Bass; 2009.

TABLE 6

Nine common areas for improving antibiotic prescribing

PRESCRIPTIONS	WHAT TO IMPROVE
1. Overprescribing	Antibiotics are prescribed when not needed, e.g. fever without evidence of infection, asymptomatic urinary tract colonization, viral infections, malaria, inflammatory conditions.
2. Overly broad spectrum	More broad-spectrum antibiotics (WATCH and RESERVE antibiotics) are prescribed than are necessary (e.g. surgical prophylaxis).
3. Unnecessary combination therapy, including certain fixed-dose combinations	Multiple antibiotics are used, particularly with overlapping spectra and in combinations that have not been shown to improve clinical outcomes.
4. Wrong antibiotic choice	Wrong antibiotic(s) are prescribed for particular indications/infections.
5. Wrong dose	Antibiotics are prescribed with the wrong dose (over- or underdosing).
6. Wrong dose interval	Antibiotics are prescribed with the wrong dose interval (too much time between doses).
7. Wrong route	Antibiotics are prescribed by the wrong route (e.g. IV instead of oral).
8. Wrong duration	Duration of antibiotic treatment should be optimized (e.g. antibiotics prescribed for too long a period, prolonged surgical prophylaxis).
9. Delayed administration	Administration of the antibiotic(s) is delayed from the time of prescription. Repeat doses are not administered in a timely way, which is critical in the case of septic shock and other serious infections.

FIGURE 13

Questions to address when applying the quality improvement model for AMS interventions

What are you trying to achieve ?	Set a goal for change in antibiotic use that is SMART (i.e. specific, measurable, achievable, relevant and time-bound).
How will you know that the change is an improvement?	Determine what quantitative measures to use to show improvement (measurements).
What changes can you make that will result in improvement?	Not all changes are an improvement. Identify the behaviour changes that will result in improvement (AMS interventions).

FIGURE 14

The quality-improvement model following the continuous improvement cycle: Plan, Do, Study, Adjust

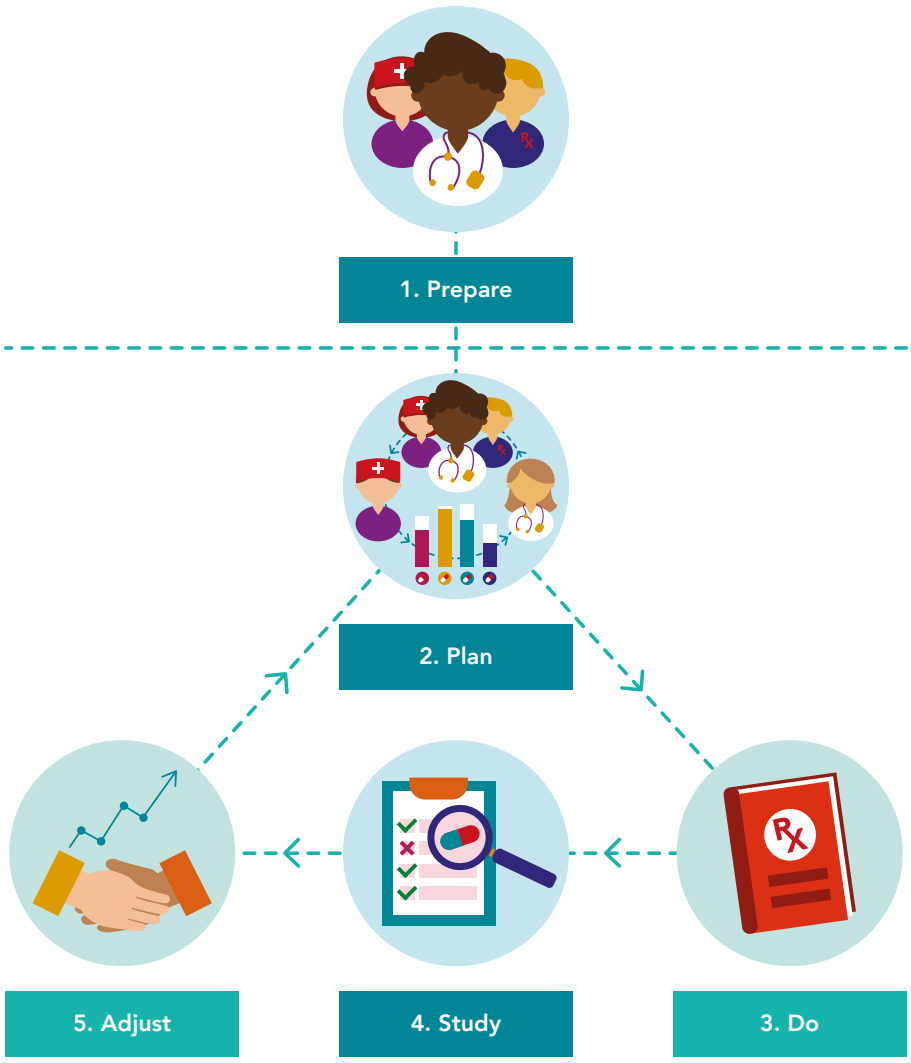
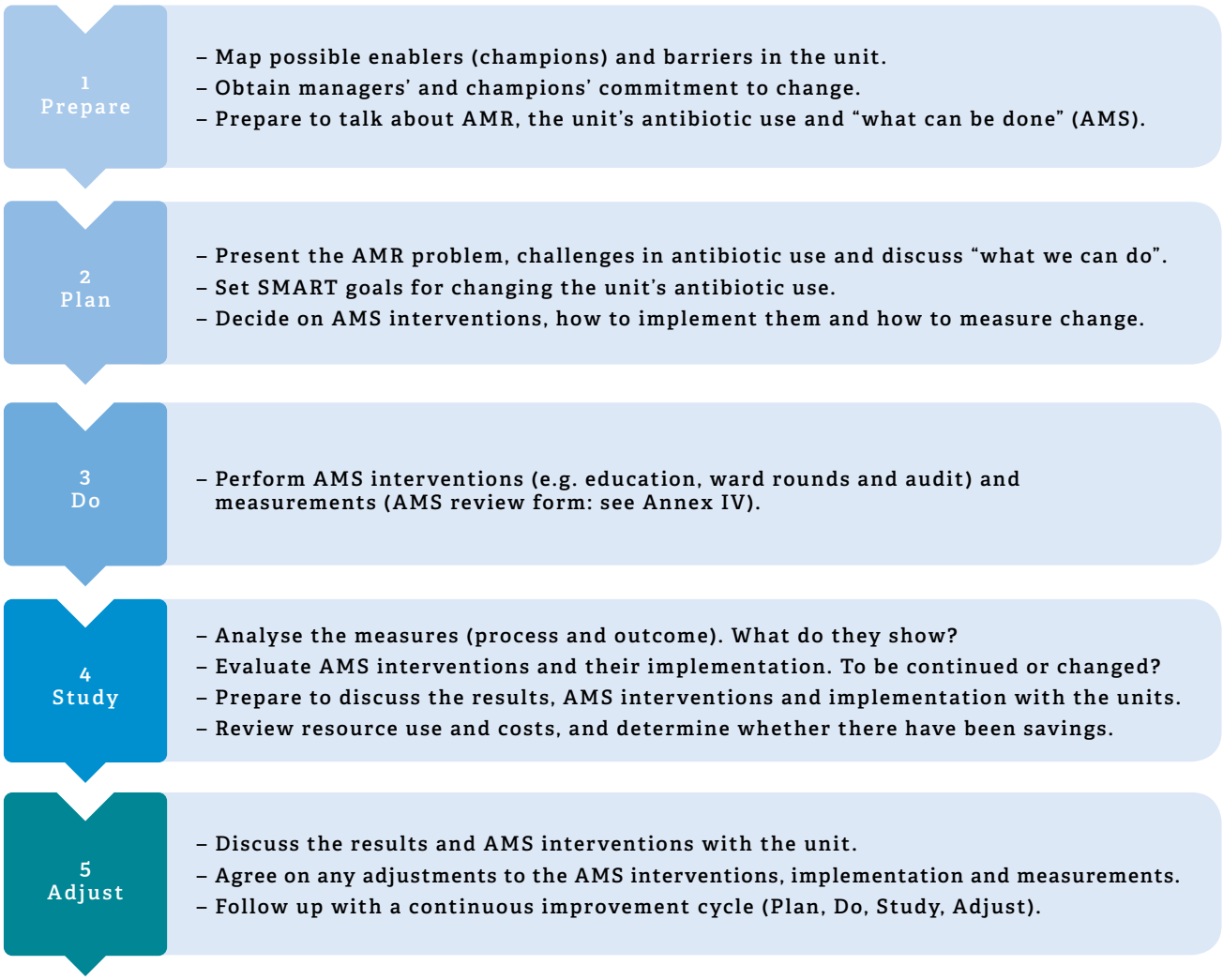


FIGURE 15

The quality-improvement model in more detail



5.5. Basic AMS interventions

AMS interventions can be performed in all types of health-care facilities. The interventions should align with local needs and address areas where observations or data suggest the need for improvement, and/or where the outcomes of the implemented interventions are measurable.

In facilities where many core elements are not yet in place, the simple interventions shown in Box 8 may be a place to start to improve antibiotic prescribing. These interventions can be implemented one at a time or in a bundle.

The AMS review form in Annex IV can be used/adapted to collect data needed to measure change in the areas listed in Box 8 for improvement involving reviews.

BOX 8

Basic AMS interventions

1. Educate prescribers and health personnel involved in antibiotic use (see Chapter 7).
2. Develop and update a standardized medical record and medical chart to ensure that information on patients' medicines is all in one place (see Annex VI).
3. Review whether patients who receive antibiotic treatment have written indications.
4. Review antibiotic treatment for patients prescribed three or more broad-spectrum antibiotics.
5. Review the dose of antibiotics prescribed.
6. Review surgical antibiotic prophylaxis where it is prescribed for >24 hours and where a single dose is appropriate.
7. Develop local guidelines for surgical prophylaxis and treatment of common clinical conditions such as community-acquired pneumonia, UTIs, skin and soft tissue infection (SSTIs), as well as common health-care-associated infections such as pneumonia, UTIs and catheter-related infections.
8. Work to ensure leadership and identify expertise in infection management.
9. Improve the supply and management of medicines, including essential antibiotics, e.g. by establishing a drug and therapeutics committee.
10. Work to establish basic microbiology laboratory facilities.
11. Work to establish regular surveillance activities (e.g. AMR, AMC, health-care-associated infections).

5.6 Moving beyond basic AMS interventions

To fully benefit from an AMS programme, facilities should aspire to put core elements for health-care facilities in place, including to secure supplies of essential antibiotics, provide treatment guidelines and establish a multidisciplinary AMS team. An option for smaller health-care facilities may be to collaborate with other health-care facilities on certain areas, i.e. developing guidelines, expertise, microbiology laboratory services, etc. This will facilitate the necessary structures, expertise and skills to implement more AMS interventions aimed at improving antibiotic prescribing[61] related to treatment – diagnosis, and prescribe, review and stop treatment (Figure 16) – and to surgical prophylaxis – indication, and prescribe and stop prophylaxis (Figure 17). This in turn will improve not only antibiotic prescribing, but also dispensing and use.

[61] Tamma PD, Miller MA, Cosgrove SE. Rethinking how antibiotics are prescribed: incorporating the 4 moments of antibiotic decision making Into clinical practice. JAMA. 2019;321(2):139-40.

FIGURE 16

Appropriate antibiotic treatment – indication and prescribe, review and stop treatment

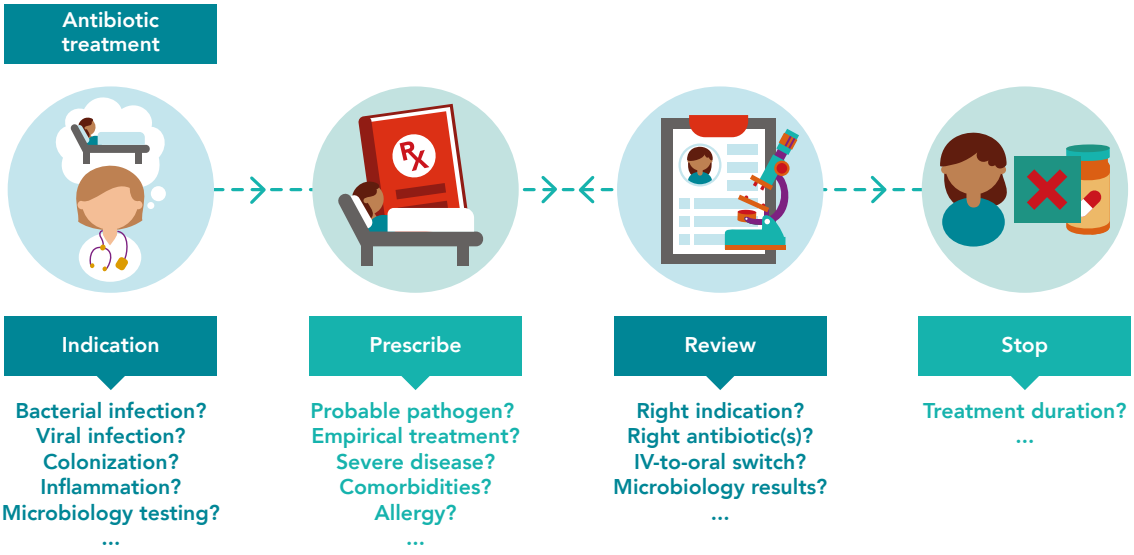
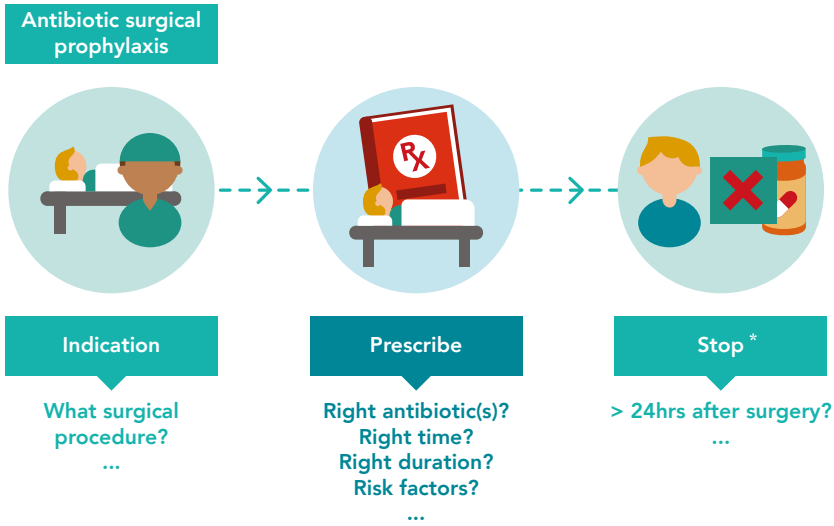


FIGURE 17

Appropriate antibiotic surgical prophylaxis – indication, and prescribe and stop prophylaxis



* Antibiotic prophylaxis should not be prescribed for more than 24 hours after surgery. Beyond that, evidence is lacking to show reduced rates of complications, including surgical site infections.

5.7. More detailed AMS interventions to improve antibiotic prescribing

Different types of AMS interventions (Table 7) included in facility AMS programmes to improve antibiotic prescribing have proven successful.[10] To bring about change in antibiotic prescribing, a bundle[62] of AMS interventions is often implemented. These may include (Table 8) educational outreach[63] (formal or informal), and/or audit and feedback activities (real-time, either written or oral, or retrospective),[64] and/or restrictive interventions, such as pre-authorization of targeted antibiotics. Restrictive interventions have been shown to provide quick positive results in reducing antibiotic use. However, after around 6 months, restrictive and persuasive interventions are equally effective. Finally, structural interventions – which often refer to IT interventions – have also proven to promote more appropriate antibiotic prescribing.

It may be useful to change things up over time, either to switch the target for change and/or what interventions are performed, and/or how they are performed. This is where local context and local expertise come in play. Each facility, department and ward can try different ways to target change, and tailor the AMS interventions to their own setting.

Table 8 identifies AMS interventions to improve antibiotic prescribing practices. The ease or difficulty of implementation will depend on the availability of local resources and competencies. Facilities need to prioritize interventions based on resources available, and to ensure that local or regional networking and sharing of resources, including e-learning resources,[65] are considered to support their implementation.

[62] Pulcini C, Defres S, Aggarwal I, Nathwani D, Davey P. Design of a "day 3 bundle" to improve the reassessment of inpatient empirical antibiotic prescriptions. J Antimicrob Chemother. 2008;61:1384–8.

[63] Gyssens IC. Role of education in antimicrobial stewardship. Med Clin North Am. 2018;102:855–71.

[64] Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ et al. Implementing an antibiotic stewardship program: guidelines by the IDSA/SHEA. Clin Infect Dis. 2016;62:e51–77.

[65] Nathwani D, editor. Antimicrobial stewardship: from principles to practice. British Society for Antimicrobial Chemotherapy; 2018 (http://www.bsac.org.uk/antimicrobialstewardshipebook/BSAC-AntimicrobialStewardship-FromPrinciplestoPractice-eBook.pdf, accessed 3 September 2019).

TABLE 7

Types of AMS interventions for improving antibiotic prescribing practices

INTERVENTION	WHAT IT IS
Persuasive (education)	• Educational meetings (e.g. basics on antibiotic use, case-based discussions, morbidity and mortality, significant event analysis, lectures on specified topics) • Distribution of and training on educational material (e.g. clinical practice guidelines) • Using local key opinion leaders (champions) to advocate for key messages • Reminders provided verbally, on paper or electronically • AMS e-learning resources made available to all health-care personnel • AMS education as part of continuing medical education
Persuasive (feedback)	• Audit with feedback to prescribers on their prescribing practice • AMS as a component of ward rounds (real-time feedback with educational component) • Patient handover meetings between two shifts with real-time feedback by consultants • Local consensus processes for changes in antibiotic treatment or surgical prophylaxis
Restrictive	• Formulary restrictions • Restricted prescribing of identified antibiotics (expert approval prior to prescription) (see Annex V) • Compulsory order forms for targeted antibiotics • Automatic stop orders (e.g. after a single dose of surgical prophylaxis) • Selective susceptibility reporting from the lab
Structural	• Rapid laboratory testing made available • Therapeutic drug monitoring

TABLE 8

Comprehensive list of AMS interventions for improving antibiotic prescribing practices

INTERVENTION	HOW TO DO IT	ADVANTAGES	DISADVANTAGES
INTERVENTION			
EDUCATION[66] Formal or informal teaching and training to engage prescribers and other HCWs in improving antibiotic prescribing, dispensing and administration practices.	Basic and continuous education of clinical staff, clinical case discussions, classes and regular sharing of information, reminders and AMS e-learning resources.	Can be performed by well-informed HCWs in informal settings (i.e. ward rounds). Necessary for better adoption of most AMS interventions. Results in improved prescribing behaviours when combined with other AMS interventions (bundle).	Few AMS team members a barrier for formal training of HCWs.
TREATMENT GUIDELINES Facility treatment recommendations for common infection syndromes based on national or facility clinical guidelines, and on local susceptibility data, if available.	WHO manual for developing antibiotic policy guidance.[67,68]	Empirical antibiotic prescribing guidelines and standard treatment guidelines lead to improved, standardized care for common infectious diseases, help prescribers select initial therapy, improve antibiotic use, and decrease cost and length of stay.	Requires broad dissemination through multiple formats and channels to ensure uptake.
SURGICAL PROPHYLAXIS GUIDELINES Facility recommendations for common surgical procedures.	Adapt surgical prophylaxis guidelines to local needs, providing antibiotic choice, dose and duration. Disseminate well: poster in the operating theatre, leaflet, apps, electronic platform. Automatic stop orders might be incorporated (see below).	Ensure timely administration and stop of appropriate antibiotic(s). Significantly reduce surgical site infections. Easier to implement than other guidelines due to few controversies around the recommendations. Need to be disseminated to surgeons and/or anaesthetists, and supervised by pharmacists. Low-hanging fruit: once the process is optimized, only periodic monitoring and feedback are required.	Require coordination and collaboration of many disciplines in the facility.

[66] Nathwani D, editor. Antimicrobial stewardship: from principles to practice. British Society for Antimicrobial Chemotherapy; 2018 (http://www.bsac.org.uk/antimicrobialstewardshipebook/BSAC-AntimicrobialStewardship-FromPrinciplestoPractice-eBook.pdf, accessed 3 September 2019).

[67] Pulcini C, Gyssens IC. How to educate prescribers in antimicrobial stewardship practices. Virulence. 2013;4:192–202.

[68] Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines. Geneva: World Health Organization; 2011 (http://apps.who.int/medicinedocs/documents/s19184en/s19184en.pdf, accessed 4 February 2019).

INTERVENTION	HOW TO DO IT	ADVANTAGES	DISADVANTAGES
FEEDBACK INTERVENTIONS			
AUDIT WITH FEEDBACK[69] Refers to the assessment of prescribed antibiotic treatment, with feedback on antibiotic treatment considered as inappropriate. Prospective (preferred) or retrospective assessment of antibiotic therapy in in-patients, performed by trained HCWs or AMS team members.	See Annex IV: AMS review form and Chapter 5 for details on how to perform audits, with feedback and examples.	Essential to prescribers' education; provides specific feedback on what antibiotics they prescribe and how they prescribe them. Identifies antibiotic prescribing challenges in the unit, and shows the impact of AMS interventions on antibiotic prescribing and use (e.g. de-escalation, duration). Data may include information on indication for treatment, prescribed antibiotic(s), dosage, interval, administration route, timing of administration of first dose and duration if collected after stop of treatment. Can be performed from very basic (only indication and antibiotics prescribed per patient) to more advanced.	Time-consuming. Can be perceived as intrusive; if so, ensure data is only used confidentially for improvement in the unit.
WARDS ROUNDS[70,71] Real-time assessment of antibiotics to be prescribed, or which are already prescribed, with instant feedback to prescriber.	Assess appropriateness of prescribed antibiotics for all inpatients or a group of patients (ICU, surgery, etc.), and provide real-time feedback. AMS members do ward rounds preferably with clinical staff, providing oral or written feedback. Issues to consider are redundant therapy, antibiotics prescribed (compliance with guidelines or microbiology test results), dose optimization, IV-to-oral switch and duration (see below) (see also Annex IV: AMS review form).	Provide real-time feedback on inpatient antibiotic treatment and training of prescribers. Can be performed by clinical experts who are not AMS team members (e.g. on handover meetings between shifts).	Ward rounds are often performed by AMS teams. Frequency of ward rounds depends on human resources and burden of antibiotic use.
ANTIBIOTIC SELF-REVISION BY PRESCRIBERS Scheduled re-assessment of need for and choice of antibiotics.[62]	Involves prescribers performing a post-prescription review of antibiotics, combined with audit and feedback. A checklist may improve compliance (see Annex IV: AMS review form). Consider indication for treatment, redundant therapy, antibiotics prescribed (compliance with guidelines or microbiology test results), dose optimization, IV-to-oral switch, duration (see below).	Directly involves prescribers in charge of patients in reviewing prescribed antibiotic treatment. Facilitates prescriber education and maintains prescriber autonomy. Less resource-intensive than audit and feedback.	Opposition from prescribers and lack of facility policy for implementing it. May not happen if prescribers are not prompted or comfortable with making changes. May not lead to improved appropriateness if prescribers lack expertise in infection management.

[69] Akpan MR, Ahmad R, Shebl NA, Ashiru-Oredope D. A review of quality measures for assessing the impact of antimicrobial stewardship programs in hospitals. Antibiotics (Basel). 2016;5:5.

[70] Li DX, Cosgrove SE. Efficacy and implementation of strategies to address antimicrobial overuse and resistance. In: Pulcini C, Ergönül Ö, Can F, Beović B, editors. Antimicrobial stewardship. Amsterdam: Elsevier; 2017:13-28.

[71] Chung GW. Antimicrobial stewardship: a review of prospective audit and feedback systems and an objective evaluation of outcomes. Virulence. 2013;4:151-7.

INTERVENTION	HOW TO DO IT	ADVANTAGES	DISADVANTAGES
FEEDBACK INTERVENTIONS			
REDUNDANT THERAPY Review of antibiotic therapy, revealing unnecessary or undesirable therapy.	A quick review of a patients' antibiotic therapy may reveal undesirable antibiotic combinations: duplication of treatment, overlapping bacterial spectra (e.g. metronidazole and clindamycin) or interactions with other medicines.	A relatively easy target for AMS interventions. Cost savings on antibiotics, and potentially reduces AMR. Reduces adverse events (e.g. nephrotoxicity, gastrointestinal side effects).	Need for trained staff who can review antibiotic therapy and provide expert advice.
REVIEW OF PRESCRIBED ANTIBIOTICS 1. DE-ESCALATION by prescribers.	1. Self-revision by prescriber irrespective of time and availability of microbiology test results.	Can reduce costs for broad-spectrum antibiotics, and potentially reduces AMR and further facility and patient costs.	1-2. May not occur if prescribers are not prompted or are not comfortable making changes.
2. DE-ESCALATION according to guidelines.	2. Self-revision by prescribers or review on ward rounds on whether empirical treatment is according to guidelines (diagnosis, drug, dose, interval, administration route, duration) and patient characteristics.		
3. DE-ESCALATION according to microbiology test results +/- 48 hours after prescription.	3. When microbiological results become available, antibiotic treatment should be streamlined accordingly: choose the most active antibiotic(s) with least toxicity, narrowest spectrum and lowest cost.[72] De-escalation is safe for sepsis and septic shock, and is associated with decreased mortality.[73]		3. Requires that microbiology sampling be done correctly, as well as quality-assured microbiology testing, timely release of results and good communication with trained prescribers.
DOSE OPTIMIZATION Review of antibiotic doses based on infection, patient characteristics, antibiotic(s) and guidelines.	Optimize dose based on age, weight, organ dysfunction (kidney) and tissue penetration. Consider therapeutic drug monitoring, if available, especially for nephrotoxic antibiotics (aminoglycosides). Evaluate the need for loading dose and/or prolonged/continuous infusions. Integrate into pharmacists' review during ward rounds or other audit processes.	Improves patient outcomes, and reduces suboptimal drug concentrations and adverse events (mainly nephrotoxicity).	Requires patient-specific data to perform the assessment, e.g. weight, renal function, indication and recommendations for dosing in special patient populations (e.g. obesity, renal dysfunction), which are not always available. May also require microbiology laboratory results (minimum inhibitory concentration) for correct dose.

[72] Levy Hara G, Kanj SS, Pagani L, Abbo L, Endimiani A, Wertheim HF et al. Ten key points for the appropriate use of antibiotics in hospitalized patients: a consensus from the AMS and Resistance Working Groups of the International Society of Chemotherapy. Int J Antimicrob Agents. 2016;48:239-46.

[73] Garnacho-Montero J, Gutiérrez-Pizarraya A, Escoresca-Ortega A, Corcia-Palomo Y, Fernández-Delgado E, Herrera-Melero I et al. De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock. Intensive Care Med. 2014;40:32-40.

INTERVENTION	HOW TO DO IT	ADVANTAGES	DISADVANTAGES
FEEDBACK INTERVENTIONS			
IV-TO-ORAL SWITCH Promotes the use of oral antibiotics instead of IV when clinically indicated.	Consider based on: • clinical condition and availability of adequate oral antibiotic; • oral intake and gastrointestinal absorption (not impaired); • adequacy of oral intake in terms of diagnosis (e.g. not in the case of endocarditis or meningitis).[74]	Reduces unnecessary days of IV lines and common complications. Reduces length of stay, as patients can complete antibiotic treatment at home.	May meet opposition from prescriber (and patient).
DURATION Review (real-time or retrospective) of stop dates for antibiotic treatment in patients.	Can be performed: • by prescribers during self-revision; • the entire AMS team during ward rounds; • pharmacists collecting prescriptions in every unit; • retrospectively.	Addresses a common area for improvement with regard to antibiotic prescribing. Improves patient outcomes, and prevents selection of MDR bacteria and adverse events (i.e. Clostridium difficile infection and nephrotoxicity).	May need to be individualized in e.g. immune-compromised patients or patients with central nervous system or bone infection.
RESTRICTIVE INTERVENTIONS (LIMITATIONS TO PRESCRIBING TARGETED ANTIBIOTICS)			
RESTRICTION Restricted dispensing of targeted antibiotics on the hospital's formulary, according to approved criteria (e.g. use the AWaRe categories). Use of restricted antibiotics may be limited to certain indications, prescribers, services, patient populations or a combination of these.	Restrictions on antibiotics are by diagnosis or unit. Selection of restricted antibiotics is done by facility authorities, the AMS team and heads of units based on spectrum, cost or toxicities. Antibiotics are restricted before use; ensures expert approval before initiation. Practical approach that allows attending physician to use the drug pending approval by physician or AMS team after +/- 48 hours. See Annex V for an example of a pre-authorization form.	Controlling targeted antibiotics defined by the AMS team or hospital formulary. Shown to be highly effective, especially in the early stages of an AMS programme, in an outbreak situation or as part of a response to an increase in or current high use of certain antibiotics in the facility.[10] Has been shown to reduce medicine costs for hospitals over time.	May delay initiation of treatment. Opposition from prescribers due to lack of autonomy. Risk of misusing other antibiotics that do not require authorization.[64] Labour-intensive and time-consuming because it requires enforcement to be effective.
Selective susceptibility reporting.	Report susceptible first-line narrow-spectrum antibiotics to regular wards.	May reduce use of broad-spectrum antibiotics.	Opposition from prescribers, lack of guidelines, poor system support, insufficient resources.
AUTOMATIC STOP ORDERS Stop dates automatically applied to an antibiotic order when the duration is not specified to ensure that antibiotics are continued no longer than necessary.	Automatic stop orders are mostly used for a single dose of surgical antibiotic prophylaxis, or prescribing some antibiotics. Useful in small facilities and with limited pharmacy staff. Use only in a context with good control mechanisms to avoid unsafe treatment interruptions.[27] Nurses can play a role in alerting the attending physician.	A simple measure, considering the high burden of antibiotics unnecessarily used for surgical prophylaxis.	IT is needed, which is often missing. Unintended treatment interruptions if not properly supervised by the AMS team.

[74] van den Bosch CM, Geerlings SE, Natsch S, Prins JM, Hulscher ME. Quality indicators to measure appropriate antibiotic use in hospitalized adults. Clin Infect Dis. 2015;60:281–91.

INTERVENTION	HOW TO DO IT	ADVANTAGES	DISADVANTAGES
RESTRICTIVE INTERVENTIONS (LIMITATIONS TO PRESCRIBING TARGETED ANTIBIOTICS)			
RAPID LABORATORY TESTING Stop dates automatically applied to an antibiotic order when the duration is not specified to ensure that antibiotics are continued no longer than necessary.	Rapid diagnostic tests allow for more accurate diagnosis and targeted antibiotic treatment.	Provides quicker diagnostic results than traditional microbiology testing	Tests are often expensive and/or require advanced, expensive equipment that is not available in many facilities.
THERAPEUTIC DRUG MONITORING To be performed for concentration-dependent antibiotics when used >3 days.	There should be a standardized procedure for collecting blood samples. The concentration of the antibiotic is measured in blood to allow for optimal adjustment of daily dose.	Fewer adverse events related to specific antibiotic treatments.	Therapeutic drug monitoring is not available in many health-care facilities.
COMPUTERIZED PHYSICIAN ORDER ENTRY (CPOE) Replaces a facility's paper-based ordering system with an electronic one.	Allows users to place electronic orders, and the facility to maintain an online medical record.	Orders made and the online medical records, incl. medical charts, can be read and reviewed by HCWs attending to a patient.	Requires health-care IT systems which are not available in many health-care facilities.
ANTIBIOTIC ALLERGY ASSESSMENTS[75] Replaces a facility's paper-based ordering system with an electronic one.	Establish guidance for antibiotic allergy assessment, e.g. a penicillin allergy assessment protocol, with recommendations on which patients might benefit from skin testing.	Promote the use of old narrow-spectrum antibiotics, which are also potentially more effective.	Equipment and/or expertise to perform allergy testing may not be available in the facility.

[75] Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. Lancet. 2019;393:183–198.

5.8. Audit with feedback

5.8.1 Prospective (real-time) audit with feedback

Prospective audit with feedback (e.g. on ward rounds) involves the assessment of antibiotic therapy by trained individuals (usually physicians and/or pharmacists), who make recommendations to prescribers in real time when therapy is considered suboptimal.

A prospective audit should be prioritized over a retrospective audit. It may be performed alongside clinical personnel on ward rounds, providing oral recommendations for changes in antibiotic treatment in real time. Alternatively, the physician and/or pharmacist in the AMS team may perform ward rounds on their own, providing written recommendations for changes in antibiotic treatment. See Annex IV for an AMS review (audit) form and Chapter 5.8.4 for an example of patient audit data.

5.8.2 Retrospective audit with feedback

Retrospective audit with feedback is a method of collecting antibiotic data to evaluate the impact of AMS interventions (baseline and follow-up data) on antibiotic use, but is inferior to a prospective audit and real-time feedback. An audit involves assessing antibiotic therapy in hospitalized patients, and is often coordinated by a physician or administrator but performed by pharmacists and/or nurses. Antibiotic audit data are collected as follows:

- at baseline to identify areas for improvement of antibiotic prescribing for the whole hospital, a department or ward;
- for a defined period of time to evaluate any improvements; and
- to provide regular and structured feedback both on the quality and quantity of antibiotic prescribing and use to prescribers.

Audit with feedback provides an opportunity for clinical staff to discuss their own prescribing practices, to identify priority areas for change and to set specific goals for themselves at the facility, department and/or ward level.

5.8.3 Selecting one or more infections for audit

To what degree are infections treated according to guidelines?

The audit should provide figures on compliance with the guidelines and suggest where there is room for improvement. Data are collected on ward rounds or directly from patients' medical charts. A sample medical record form can be found in Annex VI.

How to choose which infections to audit?

- Common infections, such as community-acquired pneumonia (CAP), UTIs, and SSTIs.
- When a problem is detected, a specific intervention might be designed. For example, an increase in infections after surgery or in urine cultures referred to the microbiology lab, which might indicate that patients with asymptomatic bacteriuria are wrongly being treated for UTIs.
- Infections treated for a long duration (e.g. >7 days).

Example #1:

The AMS team pharmacist notes that during the past week, three patients admitted to the internal medicine unit with non-severe CAP received a combination of ceftriaxone and clarithromycin. Clinical guidelines at your hospital recommend ampicillin alone for most non-severe CAPs.

What can be done?

1. List all patients admitted with non-severe CAP to the internal medicine unit during the last 2–3 months.

2. If samples (i.e. sputum, blood cultures) have been submitted, review medical records for severity (e.g. CRB-65) as well as microbiology test results. Also note down recorded reasons for prescribing ceftriaxone/clarithromycin and whether a review (de-escalation) of treatment has been carried out.

3. Hold a meeting with a smaller group of prescribers on the ward to discuss your initial findings. Discuss further steps and possible actions (training of health personnel, ward rounds, audit, etc.).

4. Hold a further meeting with the heads of the unit and all the medical staff (including residents and fellows) to discuss why broad-spectrum antibiotics and frequent combinations should be avoided for CAP. Agree on further action, such as targets for changes to prescribing, training and other AMS interventions.

5. Continue active surveillance through audit for a specified time period and meet again with the unit to discuss progress.

Example #2:

During ward rounds or in specific patient consultations, a member of the AMS team has the impression that many patients with urinary catheters are being treated with antibiotics.

What can be done?

1. Together with ward staff, list all patients with a urinary catheter. Draw up a chart (table) that includes the main variables to be evaluated (see the following points).

2. Review every patient history looking for signs of UTI, including fever or sepsis without another focus of infection.

3. Determine which patients (with or without clinical signs of infection) have had urine samples taken for culture, to find out whether patients without clinical signs of UTI have had urine cultures taken as well as whether no urine or blood culture has been taken when a true infection is suspected.

4. Review any prescription of antibiotics for patients with a urinary catheter, whether asymptomatic or symptomatic. Again, this will detect the prevalence of prescriptions in both circumstances.

5. For patients with clinical signs of UTI, assess whether the treatment is appropriate according to local epidemiology and/or guidelines (selection of antibiotic(s), dose, de-escalation and duration).

6. Depending on sample size, extend the assessment retrospectively (e.g. 1 month) by searching patient medical records.

7. Once these first analyses are done, discuss the results with the medical staff on the ward, suggesting targets for change and which data to collect for a specified time period. Agree on further interventions (i.e. any necessary training and follow-up) and on when to meet again to discuss the results of the new audit.

5.8.4 Selecting antibiotic(s) for audit

To what degree is an antibiotic used according to guidelines?

The audit should provide figures on who is receiving antibiotic(s), indications for treatment and whether the patient is receiving the right antibiotic treatment (see the audit sample below).

How to choose which antibiotics to audit?

- Antibiotics where consumption has increased significantly over time.
- Antibiotics with a higher potential of inducing and propagating resistance (e.g. WATCH and RESERVE antibiotics).
- Broad-spectrum antibiotics (e.g. piperacillin/tazobactam, ticarcillin/clavulanate, carbapenems).
- Last-resort antibiotics (e.g. polymyxins, linezolid).
- Expensive antibiotics.

Note: Keep in mind that restricting one antibiotic may increase the use of others

Depending on the strategy adopted in the facility, audit might be done via ward rounds, pharmacy alerts, a process of pre- or post-authorization, self-revision by physicians or a combination of all of these.

Department/ward: **Year:**

Week	*Pat. ID*	*Age*	*Gender (M/F)*	*Indication*	*Medicine(s)*	*Dose*	*Adm. interval*	*Adm. route*	*Guideline compliance*	*Comments: allergy, etc.*
15	01	55	M	Cellulitis	Ceftriaxone	1 g	x 1	IV	No	No allergy
"	02	18	M	Meningitis	Ceftriaxone	2 g	x 2	IV	Yes	
"	02	42	F	Gastro-enteritis	Ceftriaxone	1 g	x 1	IV	No	No fever or bloody stool
"	02	25	F	UTI	Ceftriaxone	1 g	x 1	IV	Yes	
"	03	36	M	CAP	Ceftriaxone	1 g	x 1	IV	No	CRB65 = 1

Example #1:

The pharmacist who picks up medication request forms in the ICU has noted that for some time now, there has been an increase in the use of meropenem in higher doses and of colistin.

What can be done?

1. Hold a meeting with the head of the ICU to convey your concern and suggest a meeting to gather most of the ICU staff, including physicians who only are on call in the ICU.

2. Discuss with prescribers their perception of this increase (e.g. more severe septic patients, an increase in MDR gram-negative pathogens).

3. Review and discuss the patients receiving treatment with one or both antibiotics studied.

4. Perform a retrospective audit of patients who were treated with one or both antibiotics.

5. Analyse with the AMS team the appropriateness of the prescriptions: indication, dose, duration, microbiology test results and the existence (or not) of alternative treatments with regard to both ecology and cost.

8. Once this analysis is done, meet again with the ICU medical team to discuss the results. Try to reach agreement regarding what changes are feasible, what training and other interventions might be useful, and how to measure change through active surveillance (audit) for a specified time period.

9. Meet once again to discuss the results of the new audit.

Example #2:

As part of the stewardship strategy, the AMS team decides to assess what is happening with antibiotic surgical prophylaxis. Your hospital has not yet updated clinical practice guidelines for this indication, but national guidelines are in place.

What can be done?

1. Review the list of all surgical procedures done or performed over at least the last 2 weeks (depending the number of surgical procedures performed by different specialties).

2. Produce a form (e.g. Excel or electronic platform) that includes essential issues for evaluation: indication (type of surgery), gender and age of the patients, main comorbidities, antibiotic(s) prescribed as prophylaxis, dose, time of administration and duration.

3. Review the appropriateness of the prophylaxis: the antibiotic(s) prescribed, dose, timing and duration.

4. Hold a meeting with the surgical services and anaesthesia for feedback on the findings. The meeting might be general (the whole surgical department) or by specialty depending on the results and the size of the department.

5. Adapt national or international guidelines to your facility situation (epidemiology and drug availability), and involve every specialty in developing the guidelines to increase ownership.

6. Repeat the audit after a specified time (e.g. 4–6 months) after implementing new guidelines for surgical antibiotic prophylaxis in the facility.

5.9 Role of IT in an AMS programme

Even a successful AMS programme needs to be adequately measured to be efficient. The use of proper and updated information is essential. Often data can be collected and analysed without technology. Point prevalence surveys are an example of this. Table 9 identifies areas where IT can be of additional benefit.

TABLE 9

Areas where IT can benefit AMS interventions

BASIC LEVEL	INTERMEDIATE LEVEL	ADVANCED LEVEL
Database on procurement and ward dispensing at the facility pharmacy level Database of AMR surveillance in different units	Calculation of antimicrobial consumption (e.g. in DDD/1000 inpatients/day) Alerts on specific antibiotic use Time-sensitive automatic stop orders for surgical prophylaxis Electronic guidelines (via electronic mailings to prescribers, intranet) Apps for doing a PPS	CPOE system Estimations of clinical outcomes related to antibiotic treatment Apps for national, regional or facility guidelines Point-of-care access to microbiological results from all units Clinical decision-support systems (commercial or self-developed) of different levels of complexity Computerized patient dispensing billing data Automatic submissions/reporting of computerized facility-level data to the national centre

6. ASSESSING AMS PROGRAMMES

Key audience: Health-care facility leadership, AMS committee and/or AMS team

6.1 Introduction

Data play an important role in assessing AMS interventions (to identify problems or evaluate the benefits of AMS interventions), although qualitative improvement can be achieved even in the absence of data (Chapter 5.5). However, from a mid- to long-term perspective, efficiently prioritizing interventions and allocating resources for AMS requires data to identify key challenges in antibiotic use and to demonstrate the impact of targeted interventions. Indicators of antibiotic use are thus an essential part of any AMS strategy.[64]

This chapter aims to advise on metrics (Figure 18) for assessing the impact of AMS interventions. Because assessing all indicators is unrealistic,[76,77] the collection of indicators shown in Tables 10–12 is not intended to be comprehensive. AMS programmes are encouraged to select the most relevant and feasible metrics for a particular local setting. Note also that the resources required for assessing the indicators will vary, depending on the setting and the available infrastructure. Nonetheless, given the complexity of antibiotic use, a single indicator will probably not suffice. How to assess structural indicators of AMS programmes (e.g. leadership commitment, human resources and guidelines) is covered in Chapters 2 and 3. Finally, in as much as local indicators will vary, this toolkit does not specify targets or methods, which are available in reviews.[78]

6.2 Structural measures/indicators

Structural measures are used to assess the capacity, systems and processes in a facility or an organization. The national and health-care facility core elements present essential structures for implementing national and health-care facility level AMS programmes.

6.3 Process measures/indicators

The implementation of AMS interventions aims to optimize antibiotic prescribing and use. It is therefore recommended to also include process indicators as a proxy measure for improvement (Table 12). Process measures may specify how patient medical charts are reviewed (e.g. how many times a week over a given period of time) and how antibiotic prescribing and use is improving. Apply the process indicator that corresponds to the AMS intervention(s) implemented. For an example, see Chapter 6.5.

[76] Kallen MC, Prins JM. A systematic review of quality indicators for appropriate antibiotic use in hospitalized adult patients. Infect Dis Rep. 2017;9:6821.

[77] Stanic Benić M, Milanič R, Monnier AA, Gyssens IC, Adriaenssens N, Versporten A et al. Metrics for quantifying antibiotic use in the hospital setting: results from a systematic review and international multidisciplinary consensus procedure. J Antimicrob Chemother. 2018;73:vi50–vi58. .

[78] De Kraker MEA, Abbas M, Huttner B, Harbarth S. Good epidemiological practice: a narrative review of appropriate scientific methods to evaluate the impact of antimicrobial stewardship interventions. Clin Microbiol Infect. 2017;23:819–25.

[79] Donabedian A. Quality of care. JAMA 1988;12:1743–8.

FIGURE 17

Structural, process and outcome measures for assessing AMS programmes[79]

6.4 Outcome measures/indicators

The aim of an AMS programme is often achieved by reducing overall AMC and perhaps reducing overall use of specific (broad-spectrum) antibiotics. However, it is equally important to document that this reduction is not associated with unintended negative **patient outcomes**. Furthermore, AMS aims not only to prevent negative patient outcomes, but also to improve patient outcomes, providing further arguments for assessing outcome measures.

In health-care settings without established surveillance programmes for AMR and health-care associated infections, or electronic health records, it may be difficult to obtain reliable data about **clinical outcome** measures (Table 11). Given the sound evidence for the safety and effectiveness of AMS programmes, it may be justifiable as a first step to focus on **outcome measures related to antimicrobial use** (Table 10).[10,11,19]

Regardless of whether electronic prescribing is available, many facilities have pharmacy systems that can provide information on antimicrobials supplied to wards and other clinical areas. These data can be collected manually and used as a proxy for antimicrobials given to patients. In an AMS programme, when it comes to measuring and expressing antibiotic use in numerical terms, a standardized measure is required. The most common standardized measure is DDDs. Other outcome measures used are described in Tables 11 and 12.

The potential cost savings (direct and indirect) as a result of the shift from more expensive broad-spectrum to less expensive first-line narrow-spectrum antibiotics should be partly used/reinvested in sustaining/maintaining the AMS programme in the facility.

6.5 How to begin assessing AMS programmes

Below is an example of a stepwise approach for applying different indicators when assessing an AMS programme.

Structural measures/indicators:
The national and health-care facility core elements can be used as checklists for assessing the structures of national and health-care facility AMS programmes.

Initial outcome measures/indicators:
An essential part of any AMS programme, both national and facility, is to study antibiotic prescribing and use over time. Either antimicrobial consumption surveillance data, PPS data or audit data can be applied. The most sustainable and least laborious way to measure antibiotic use over time is through routine collection of antimicrobial consumption data. The study of the indicators DDD per 100(0) patient-days and/or DDD per admission should be prioritized. A simple way to initiate further analyses of the consumption data is to look at the proportion of DDDs in AWaRe and OTHER groups or any other relevant clinical categories. It is recommended that antibiotic use should be expressed in at least two metrics simultaneously.

Other outcome measures/indicators:
Although evidence shows that AMS interventions do not lead to increased mortality, study of *clinical patient outcomes* – e.g. mortality and length of stay – is recommended to ensure that implemented interventions do not have unintended consequences for patients.

Process measures/indicators:
Process indicators are often used as a proxy measure of improvement, e.g. that antibiotic prescribing practices are moving in the right direction. For example, if the target is to improve adherence to recommended empirical treatment of a particular infection, a corresponding process measure would be the proportion of all patients with this particular infection who receive recommended empirical treatment.

TABLE 10

Outcome measures/indicators related to antimicrobial use

INDICATOR	INDICATOR CONSTRUCTION	POSSIBLE D ATA SOURCES	COMMENT
DDD per 100(0) patient-days	**Numerator:** DDD of an agent (based on ATC code) purchased/ dispensed/consumed in a period of time (i.e. total antibiotic used) **Denominator:** Total number of patient-days within that period of time **Multiplier:** x 100(0) to obtain data per 100(0) patient-days	Pharmacy dispensing data Health-care facility purchasing data Nursing chart administrative data (paper) Electronic drug administrative data E-prescribing records	DDD per 100(0) patient-days is the most commonly used quantity measure of antibiotic use, because the data needed to calculate it are available in many settings (unlike days of therapy, DOTs); no individual-level data are needed. It should, however, be noted that differences in data sources and definitions may influence this indicator, for instance: • the list of antibiotics included (e.g. all ATC class J01 antibiotics, or subsets of ATC class J01, or additional antibiotics and antimicrobials not included in ATC class J01); • the data source used – it has, for example, been shown that pharmacy dispensing data tend to overestimate antibiotic use compared with actual drug administration data;[80] and • how patient-days are calculated (e.g. "days present", an alternative measure).[81] Detailed guidance on how to calculate DDDs is available elsewhere.[82] DDDs can be calculated for overall use, specific antibiotic, classes or other categories (such as AWaRe). It is very important to clearly define how the metric is calculated (i.e. antibiotics included, data sources, ATC version and year, calculation of patient-days) and to be consistent over time.
DDD per admission	**Numerator:** See above **Denominator:** Total number of patients admitted within a period of time	See above	DDD per admission gives different information than does DDD per patient-days. The length of stay may affect patient days and admissions differently.
DOTs per 1000 patient-days	**Numerator:** Days of therapy with an agent during a period of time **Denominator:** Total number of patient-days within that period of time **Multiplier:** x 1000 to obtain data per 1000 patient-days	Nursing chart administrative data (paper) Electronic drug administrative data E-prescribing records	The major disadvantage of DOTs compared with DDDs is the need for individual-level patient data (instead of aggregated data, such as pharmacy data, which are sufficient to calculate DDDs). (On the other hand individual-level data make it possible to assess the duration of treatment, redundant therapy, etc.).

[80] Dalton BR. Assessment of antimicrobial utilization metrics: days of therapy versus defined daily doses and pharmacy dispensing records versus nursing administration data. Infect Control Hosp Epidemiol. 2015;36:688–94.

[81] Moehring RWl. Denominator matters in estimating antimicrobial use: a comparison of days present and patient days. Infect Control Hosp Epidemiol. 2018;39:612–15.

[82] DDD indicators. In: Essential medicines and health products: ATC/DDD toolkit. Geneva: World Health Organization; n.d. (http://www.who.int/medicines/regulation/medicines-safety/toolkit_indicators/en/index1.html, accessed 4 February 2019).

INDICATOR	INDICATOR CONSTRUCTION	POSSIBLE DATA SOURCES	COMMENT
Proportion of DDDs in AWaRe and OTHER groups	Classify DDDs according to AWaRe and OTHER groups, and calculate the percentage of each	Pharmacy dispensing data Hospital drug purchase data Nursing chart administrative data (paper) Electronic drug administrative data E-prescribing records	

TABLE 11

Outcome measures/ indicators related to patients and microbiology

INDICATOR	INDICATOR CONSTRUCTION	POSSIBLE DATA SOURCES	COMMENT
Patient outcomes	**In-hospital mortality:** Number of deaths during hospitalization / Total number of hospitalizations	In-hospital mortality: hospital administrative data 30-day mortality: population office administrative data Infection-specific mortality: chart review and administrative data	Can be assessed as in-hospital mortality (i.e. death during hospitalization) or mortality at a specific time point after admission (e.g. 30 days). The latter has better face validity since it is not influenced by differences in length of stay, but the data needed to calculate it are more difficult to obtain in most settings. Ideally, infection-specific mortality rates (e.g. for CAP) would also be calculated. Since it is difficult to assess whether a specific death was caused by an infection or by AMR, the assessment of infection-specific mortality can be tricky (and time-consuming). The numerator and denominator must be clearly defined.
	Length of stay: Days of hospitalization by type of infection / Total number of patients with that infection	Infection-specific chart review and administrative data	There are many different ways of defining length of stay. It is important to use consistent definitions over time.
	Readmission within 30 days after discharge: Patients with infections readmitted <30 days after discharge / Total number of patients discharged with that specific infection	Infection-specific chart review and administrative data	Only unscheduled readmissions should be counted (e.g. a planned admission for a surgical intervention should not be counted).

INDICATOR	INDICATOR CONSTRUCTION	POSSIBLE DATA SOURCES	COMMENT
Microbiology outcomes	***Clostridium difficile:*** Number of health-care-associated *C. difficile* infections in a period of time / Total number of patient-days within that period x 100 000 **MDR organisms (e.g. MRSA, ESBL-E/CPE, MDR *Pseudomonas* and *Acinetobacter* spp., vancomycin-resistant enterococci):** Number of health-care-associated infections in a period of time / Total number of patient-days within that period x 100 000	• Microbiology data • Epidemiology data • Infection control surveillance data • Administrative data • Chart review • Microbiology data • Epidemiology data • Infection control surveillance data • Administrative data • Chart review	*C. difficile* definitions may vary, and a detailed discussion is beyond the scope of this document. Interested readers may consult the respective surveillance protocols and guidelines.[83,84] A detailed discussion is beyond the scope of this document. See also GLASS (http://www.who.int/glass/en/).

[83] European surveillance of Clostridium difficile infections. Surveillance protocol version 2.3. Stockholm: European Centre for Disease Prevention and Control; 2017 (https://ecdc.europa.eu/sites/portal/files/documents/European-surveillance-clostridium-difficile-v2point3-FINAL_PDF3.pdf, accessed 8 February 2019).
[84] McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE et al. Clinical practice guidelines for Clostridium difficile infection in adults and children: 2017 update by the IDSA and SHEA. Clin Infect Dis. 2018;55:e1–e48 (https://academic.oup.com/cid/advance-article/doi/10.1093/cid/cix1085/4855916, accessed 8 February 2019).

TABLE 12

Process measures/indicators of antimicrobial use

INDICATOR	INDICATOR CONSTRUCTION
Documented indication for antibiotic use	Number of patients with a written indication for antibiotic treatment / Total number of patients treated with antibiotic(s)
Stop/review date	Number of patients with a written stop/review date for antibiotic treatment / Total number of patients treated with antibiotic(s)
Compliance with current clinical treatment guidelines	Number of patients with an indication receiving empirical treatment with antibiotic(s) according to clinical guidelines / Total number of patients with this indication
Length of therapy by indication	Total number of days of antibiotic treatment for a specific indication / Total number of patients treated with antibiotic(s) for that indication
48-hour review	Number of patients where a 48-hour review is performed / Total number of patients treated with antibiotic(s) hospitalized >48 hours
De-escalation	Number of patients where a de-escalation from the initial therapy is performed / Total number of indicated empirical treatments
IV-to-oral switch	Number of regimens switched to oral route / Total number of regimens that can be switched to oral route based on predefined criteria
Compliance with current guidelines for surgical prophylaxis (antibiotics)	Number of patients receiving surgical antibiotic prophylaxis according to guidelines / Total number of surgical patients receiving antibiotic prophylaxis
Surgical prophylaxis within the previous 60 minutes	Surgeries with prophylaxis administered within 60 minutes prior to surgery / Total number of surgeries that require prophylaxis
Surgical prophylaxis stopped within 24 hours after surgery	Surgeries with prophylaxis stopped within 24 hours after surgery / Total number of surgeries that require prophylaxis

7. EDUCATION AND TRAINING

Key audience: Ministries and/or departments, health-care facilities, institutions and/or related entities responsible for planning and delivering pre-service and in-service education and training.

7.1 AMS competencies

Competencies[5] are defined as the development of observable ability of a person (or individual health worker) that integrates knowledge, skills and attitudes in their performance of task. Competencies are durable, trainable and, through the expression of behaviours, measurable. AMS competencies are the guiding set of knowledge, skills and attitudes that result in durable, trainable and measurable behaviours facilitating better prescribing of antibiotics (Table 13).

Some of the key concepts to keep in mind when prescribing antibiotics include the following:

- awareness of the health-care facility's standard treatment guidelines;
- the importance and rationale for using recommended empirical antibiotic agents for patients, but also the potential immediate and long-term harm of broad-spectrum therapy;
- the benefit and safety of de-escalation antibiotic treatment after cultures; and
- the opportunity and benefits of IV-to-oral switching.

Individuals must objectively assess their current level of knowledge and skills (basic, competent, advanced) related to the topics and their ability to apply them in practice. Table 13 provides a comprehensive set of competencies in five core domains at three different levels. Local programmes need to decide what level of competency is expected depending on the health-care professional. These competencies may change or evolve over time depending on the job function/role.[85,86,87] Once a realistic assessment of competencies (knowledge, skills and attitudes) has been established, learning needs (e.g. training curricula[88] and learning materials), and how these needs can be met, are then determined.

[85] WPRO-AMS training package. Geneva: World Health Organization; 2018.
[86] WHO global interprofessional AMR competency framework for health workers education and training. Geneva, World Health Organization; 2018.
[87] Dyar O, Beović B, Pulcini C, Tacconelli E, Hulscher M, Cookson B et al. ESCMID generic competencies in antimicrobial prescribing and stewardship: towards a European consensus. Clin Microbiol Infect. 2019;25:13–19.
[88] WHO competency framework for health workers' education and training on antimicrobial resistance. Geneva: World Health Organization; 2018.

TABLE 13

Competencies for HCWs involved in AMS programmes in health-care facilities in LMICs

LEVEL OF COMPETENCY:
- **Basic:** The professional is aware of, has knowledge of or understands the core principles of an area.
- **Intermediate:** The professional is aware of the core principles of an area, understands them and knows how to apply them in his/her practice.
- **Advanced – expert:** The professional is aware of the core principles of an area, understands them, knows how to apply them in his/her practice, can show others how to apply them and provides leadership, expertise or support to others in this area.

TOPIC	
1. Introduction to AMR	
Global situation of AMR and AMS	Understand the morbidity, mortality and economic threat of AMR to human health.
Drivers of AMR	• Use of antibiotics in humans, animals, plants and environment: • Understand the development and main drivers of AMR. • Know the importance of optimizing use of antimicrobials in the human and animal sectors to prevent development of resistance. • Understand that travel, recent hospitalization or previous microbiology findings of resistant bacteria are factors that predispose to colonization/infection with a resistant pathogen.
WASH and IPC	Advocate for WASH and scaling up vaccines for common infections. Understand the link between AMS and IPC. Understand the infection chain: organism, source, route of transmission and susceptible host, and the importance of practicing hand hygiene to prevent transmission.
Call for action	Promote awareness of AMR and appropriate antimicrobial use amongst all HCWs, patients and the general public to protect the effectiveness of antimicrobials as a public good.
2. Antibiotics	
Different antibiotic classes	Understand the clinically relevant spectrum of activity for commonly prescribed antibiotics, and use this knowledge when prescribing. Understand the mechanisms of actions for commonly prescribed antibiotics.
PK/PD, formulations and patient characteristics	Understand the basic principles of pharmacokinetics and pharmacodynamics (PK/PD), and use this knowledge when prescribing. Understand the use of antibiotics in special care groups (e.g. paediatrics, pregnancy, breastfeeding, renal diseases and obese persons).
Prescribing principles Prophylaxis, empirical therapy, definitive therapy and drivers of excess antibiotic use	Understand the principles of empirical, syndromic or culture-based treatment options in relation to the selection of antibiotics. Understand single prophylactic antibiotic dosing for surgical and other procedures for which prophylaxis has been shown to be effective, and use this knowledge when prescribing. Understand that an inflammatory response can be due to both infectious and noninfectious causes (e.g. acute pancreatitis). Understand when not to prescribe antibiotics (e.g. for viral infections, or when there is bacterial colonization). Understand best practices for some infections may not include antibiotic treatment (e.g. incision and drainage of abscesses, removal of foreign material, most upper respiratory tract infections). Understand key elements for initiating antibiotic therapy: • Indication for antibiotic therapy, including assessment of the severity of the infection (sepsis syndrome recognition) to inform urgency of therapy. • Bacterial infection, infection site, probable causative bacteria. • Antibiotic choice, dosage, interval, duration, preparation and administration of antibiotics, review and stop dates. • Importance of avoiding unnecessary use of antibiotics. • Empirical treatment guided by local antibiotic susceptibility patterns. • Broad- and narrow-spectrum antibiotics and the importance of avoiding unnecessary use, especially of those with broad-spectrum activity.

2. Antibiotics	
Documentation and communication on antibiotic prescription and use	Understand the need to document important details of the antibiotic treatment plan (e.g. agent, dosing, administration route, clinical indication, duration and review dates) in the prescription chart, medical records and transfer notes to other health-care institutions. Ensure appropriate documentation of antibiotics dispensed, including route, time, dose, therapeutic drug monitoring and response for individual patients. Be able to communicate with patients on the appropriate use of antibiotics, including patient counselling etiquette, discussion techniques and psychology for patient communication: • Promote better patient understanding of all treatment issues, such as safety concerns (including alerts) and adherence. • Promote a standard for the appropriate use of antibiotics, and manage patient expectations and demands especially when the use of antibiotics is not indicated.
Allergies, cross-reactions, adverse effects	Understand the significance of common antimicrobial and drug/food interactions, and utilize strategies to avoid interactions. Understand that optimizing antimicrobial use can limit common side effects and collateral damage related to treatment (e.g. disruptive effects on host normal flora, which may lead to *C. difficile* infection, superinfection with Candida spp.). Understand common side effects of antimicrobials, including allergy, and use this knowledge when prescribing: • Understand allergy types: immediate, non-life-threatening, severe adverse drug reactions (e.g. Stevens-Johnson syndrome). • Understand the mechanisms and risks of beta-lactam cross-reactions. Understand how to monitor common side effects, and use this knowledge when prescribing. Understand what to do when common side effects of antimicrobial therapy are suspected (e.g. documenting allergic reactions in patient records, reporting side effects).
EML and the AWaRe classification	Encourage adherence to antimicrobial formulary/protocol restrictions. Discourage use of fixed-dose combinations of different antibiotics that have not been shown to improve clinical outcome. Ensure regular and timely supply of appropriate medicines. Understand that antimicrobials have different resistance potential (AWaRE groups). Understand the importance of promoting appropriate use of antimicrobials according to their AWaRe groups to implement specific resistance-prevention actions for these antimicrobials.
3. Microbiology	
Important terms	Understand the differences between colonization (e.g. isolation of bacteria from a skin wound or urine with no sign of inflammation or infection) and infection. Understand the difference in microorganisms and resistance patterns for infections acquired in the community compared with hospital settings.
Common causative agents and resistance mechanisms	Understand the common and important gram-positive and gram-negative bacteria (WHO priority pathogens list plus *C. difficile*). Understand the nature and classification of microorganisms that commonly cause infections in humans. Recognize common mechanisms of resistance within an institution for different antimicrobial/organism combinations. Understand their impact on resistance to other antimicrobials. Understand local AMR epidemiology, resistance and susceptibility patterns.
Data collection and analysis	Be able to collect microbiology samples correctly. Ensure timeliness in the handling of microbiology samples and communication of susceptibility results. Act as first line of surveillance in the correct use and reporting of microbiological tests and diagnostic tools. Be able to interpret and use basic antimicrobial susceptibility testing results (in settings where they are commonly used) and other microbiology testing tools: blood cultures, urine samples, wound samples and screening cultures. Be able to interpret and use new, more advanced microbiology samples, biomarkers, point-of-care tests: • Understand how to use and interpret investigations that can help inform diagnosis of an infection (e.g. microbiological investigations, biomarkers, point-of-care tests). • Understand how to use and interpret investigations (e.g. microbiological investigations, biomarkers, point-of-care tests) that can help in monitoring the response to treatment of infections.

3. Microbiology	
Selective sensitivity reporting/antibiogram	Advocate for and comply with guidelines regarding antimicrobial susceptibility testing. Understand how to implement selective sensitive reporting to minimize broad-spectrum antimicrobial use. Understand the basic principles of antibiograms and other reporting tools and their interpretation. Understand the use of antibiograms in detecting and reporting AMR patterns.
Bug-drug combination chart	Understand the common microbiological etiology and treatment of human infections.
4. Clinical syndromes	
Guidance and best practice in antibiotic prescribing	Understand how and where to access relevant guidance on antimicrobial prescribing and AMS, and use this knowledge when prescribing. Understand that empirical treatment should be guided by local antimicrobial susceptibility patterns. Promote best practice approaches by developing and implementing guidelines and/or clinical pathways.
Common infections	Understand the decision process for appropriate antibiotic use: clinical assessment and clinical symptoms→ probable diagnosis, causative agents, diagnostics incl. microbiology sampling, patient characteristics incl. comorbidities and risk factors for AMR, whether or not to treat with antibiotics, and how to choose antibiotics to treat or prevent common infections incl. but not limited to: • CAP • UTI • Diarrhoea • SSTI • Sepsis • Surgical antibiotic prophylaxis • Bacterial infections that resolve by themselves e.g. sinusitis and otitis media • Influenza, malaria and other nonbacterial infections • Symptoms not indicative of a bacterial infection, e.g. nonspecific uro-gynaecological symptoms • Common health-care-associated infections e.g. UTIs, surgical site infections, catheter-related infections
5. AMS	
Planning an AMS programme	Plan AMS activities: • Provide clear mechanisms for the governance of AMS, including addressing responsibility and accountability for the quality and quantity of antimicrobials prescribed within a system. • Ensure that health workers have the knowledge and awareness of effective approaches/interventions to control AMR, and have the skills to implement change according to their role. • Understand basic principles of behaviour change in the context of prescribing antimicrobials and model good prescribing behaviour to colleagues. • Understand the use of quality-improvement frameworks to address gaps and to improve antimicrobial use.
Performing AMS interventions	Understand the key elements of a logical approach to continuation and appropriateness of antimicrobial therapy and be able to implement AMS interventions: • Adjusting doses (e.g. for patients with renal impairment), and where to seek advice about this. • Monitoring antibiotic levels when indicated, and where to seek advice about this. • Reviewing antibiotic therapy at 48–72 hours and regularly thereafter in hospitalized patients, and in appropriate situations in the community. • Switching antibiotics from intravenous to oral administration as soon as possible when indicated (according to guidelines). • Changing antibiotics, ideally to a narrower spectrum (de-escalation) or broader (escalation) spectrum, according to microbiology results and clinical condition. • Stopping antibiotics if there is no evidence of infection based on clinical findings and investigations, e.g. negative microbial cultures, imaging reports.

5. AMS	
Assessing an AMS programme	• Understand the types of indicators (structure, process and outcome measures). • Identify sources of data, recognizing the benefits and limitations of each. • Be able to use PPSs. • Understand how to measure and calculate antimicrobial use metrics (DDDs, DOTs, etc.). • Ensure timely and appropriate feedback to prescribers and other care groups. • Understand and engage with any locally or nationally agreed quality measures for assessing antibiotic prescriptions (e.g. compliance with guidance, adverse events, reviews of antibiotic therapy at 48–72 hours in hospitalized patients). • Understand the principles of AMR surveillance and the use of surveillance data. • Understand and implement balancing measures. • Understand the importance and stages of evaluation. • Be able to monitor and report on the performance of hospital AMR and related AMS programmes.

7.2 Education and training

Once the facility has outlined the competencies required for the different staff groups, it needs to develop a training delivery plan, in other words, identify a leader, teachers and participants, and make a time plan.[89] The opportunity to use real-world clinical opportunities for training (e.g. ward rounds, clinical case discussions) should be emphasized. In addition, those in training should be encouraged to access external training opportunities, including available e-learning options (Figure 19).

Key message: Integrated learning translates into integrated practice.

Pre- and in-service training

AMS linked with IPC should be incorporated or strengthened in preservice training, curricula and textbooks.[88] Voluntary or mandatory in-service training on AMS and IPC is also encouraged, such as through inclusion of relevant AMS and IPC competencies in continuing medical education.

Face-to-face workshops

A possible structure for a face-to-face workshop, with content aligned with the required competencies for AMS, is presented in Table 12. However, this is a "menu" of options which can be used to design a local training programme that meets local needs, contexts and resources.

Blended learning

Blended learning, with its mix of technology and traditional face-to-face instruction, is an approach that is commonly used. Blended learning combines classroom learning with online learning[90,91] and is becoming increasingly popular, as students can partly control the time, pace and place of their learning.

Practical training at centres of excellence

As centres of excellence and WHO collaborating centres for AMS are established globally, AMS teams and AMS champions are encouraged to gain practical hands-on training through these centres. Countries can also set up twinning or mentoring programmes with successful counterparts, using context-relevant examples to support the establishment, implementation and monitoring of stewardship interventions.

On the job learning

A common approach to successful training makes use of both existing structures and opportunities that arise in the clinical environment. For example, a member of the AMS team is reviewing a patient with sepsis who has been started empirically on broad-spectrum antibiotics (piperacillin/tazobactam), in contradiction to the antibiotic combination recommended by the local treatment guidelines (amoxicillin/gentamicin and metronidazole). The empirical treatment was continued despite blood cultures that revealed *Escherichia coli* susceptible to amoxicillin. A brief discussion with the attending physicians and nurses could provide an opportunity for training in one or more areas:

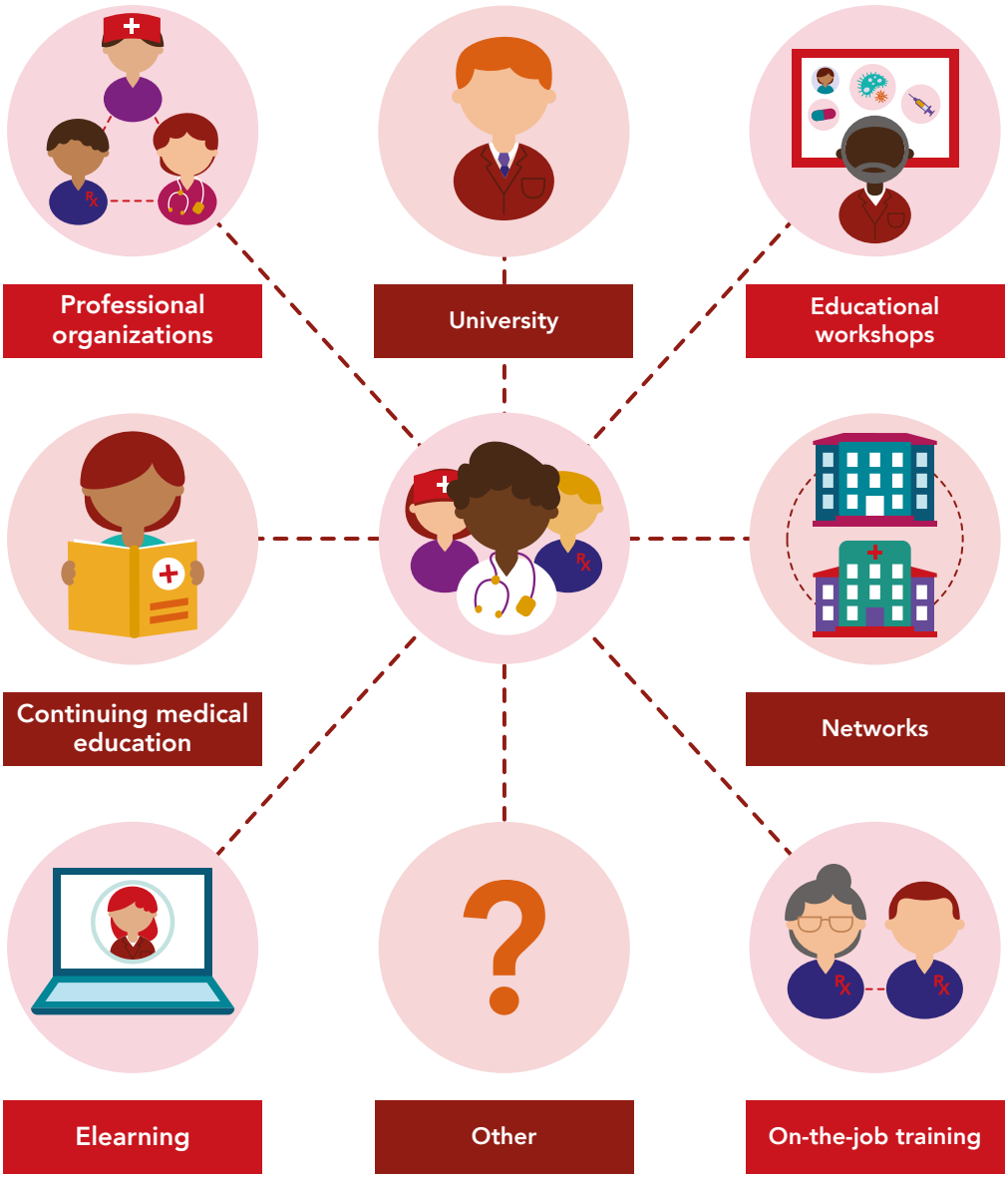
[89] Practical approach to care kit – PACK. London: BMJ Publishing (https://pack.bmj.com/, accessed 4 February 2019).

[90] Antimicrobial resistance and stewardship. BSAC Virtual Learning Environment. British Society for Antimicrobial Chemotherapy (http://bsac-vle.com/, accessed online 3 September 2019).

[91] Antimicrobial stewardship: a competency-based approach. WHO e-learning course. Geneva: World Health Organization; n.d. (https://openwho.org/courses/AMR-competency, accessed 3 September 2019).

FIGURE 18

Education and training delivery modes for AMS-related competencies



- raising awareness of the facility's standard treatment guidelines;
- the importance and rationale for using recommended empirical agents for patients, but also the potential immediate and long-term harm of broad-spectrum therapy;
- the benefit and safety of de-escalation antibiotic treatment following cultures; and
- the opportunity and benefits of IV-to-oral switching.

As described in Chapter 5, holding ward rounds jointly with the unit health personnel and the AMS team is among the most dynamic instances of learning. Every member of the team attending to the patient has the opportunity to give their opinion, debate the pros and cons of each diagnostic or therapeutic decision, and understand what is best for this and future patients.

Recently, the organizational, resource-related and fiscal benefits of learning for health-care professionals have been outlined in an excellent systematic review.[92] This pragmatic approach to on-the-job training and its relevance for optimal patient management can be instructive, valued and is often retained.

E-learning

The importance of directing participants to local, national and international e-learning resources is important in ensuring the long-term sustainability of these educational activities, and various resources already exist.[91,93] Indeed, e-learning has been commended as one important form of effectively delivering education in AMS. However, e-learning is a means to an end, rather than the end in itself. Using e-learning can result in greater educational opportunities for students while simultaneously enhancing faculty effectiveness and efficiency. However, this potential of e-learning assumes a certain level of institutional readiness in human and infrastructural resources that is not always present in LMICs. Institutional readiness for e-learning adoption ensures the alignment of new tools to the educational and economic context.[94]

Other

Other examples of facility structures and meetings where training could be provided include morbidity and mortality meetings, audit meetings, quality improvement and safety briefs, significant event analysis, risk management meetings and journal clubs. Where possible and relevant, using team-based or multidisciplinary teaching and training events also provides an excellent opportunity for interprofessional learning. As infection prevention and management is very much a team-based approach, it enhances the philosophy of learning together and delivering care together to achieve better patient outcomes.

The challenge for AMS facility training is to ensure that the capacity and capability exist for delivering a quality, effective and sustainable programme or course. Therefore, having a simple model to ensure implementation of this programme is important (Box 9).

[92] Al-Shorbaji N, Atun R, Car J, Majeed A, Wheeler E, editors. eLearning for undergraduate health professional education: a systematic review informing a radical transformation of health workforce development. Geneva: World Health Organization; 2015 (https://whoeducationguidelines.org/sites/default/files/uploads/eLearning-healthprof-report.pdf, accessed 4 February 2019).

[93] JAC-Antimicrobial Resistance. Open access journal on education and research in AMS and AMR (https://academic.oup.com/jacamr, accessed 3 September 2019).

[94] Frehywot S, Vovides Y, Talib Z, Mikhail N, Ross H, Wohltjen H et al. E-learning in medical education in resource constrained low- and middle-income countries. Hum Resour Health. 2013;11:4.

BOX 9

Core steps for implementing an educational programme

1. Programme leaders (often the AMS team) are identified and should have acquired the advanced competencies to lead and deliver local or regional training.
2. Training of programme leaders may require 2–3 days of face-to-face workshops using local, regional, national or external resources.
3. Access to e-learning resources to support this is recommended. These leaders will require skill sets that have been identified in train-the-trainer models.
4. The programme leaders in each facility or region identify a multidisciplinary faculty of trainers for advanced training in AMS. Again, access to e-learning resources to support this effort is recommended. The faculty will develop the local programme. It is always helpful to include at least one prescribing non-specialist as part of this group.
5. The faculty identifies the broad needs of the prescribing and related health-care professionals in their facility or network. They devise a programme cycle that includes the target audience, course content and evaluation.

7.3 Effectiveness of different training and education delivery

While face-to-face training methods are the norm in many LMICs, more active methods such as e-learning are increasingly used. Furthermore, blended programmes that encompass some or many components of e-learning to augment traditional face-to-face training are becoming more popular. There is evidence that the use of online and mobile digital education in the management of antibiotics for post-registration health-care professionals is associated with increased professional knowledge compared with traditional education.[95] E-learning approaches have been shown to provide flexible, low-cost, user-centred and easily updated learning.[96] However, the effectiveness of e-learning varies from context to context and has been shown to make considerable demands on users' motivation, levels of "digital literacy" and on the capacity of providing institutions. These considerations must be taken into account when developing e-learning courses.

A range of teaching methods, described in Table 14, are used to deliver training. Broadly speaking, active methods are more effective than passive methods in changing prescribing behaviour.

[95] Kyaw BM, Car LT, van Galen LS, van Agtmael MA, Costelloe CE, Ajuebor O et al. Health professions digital education for antibiotic management: systematic review and meta-analysis by the Digital Health Education Collaboration. J Med Internet Res., accepted (http://dx.doi.org/10.2196/14984, accessed 3 September 2019).

[96] E-learning for undergraduate health professional education: a systematic review informing a radical transformation of health workforce development. Geneva: World Health Organization; 2015.

TABLE 14

Teaching methods for AMS interventions

CATEGORY	METHOD
Passive	• Printed educational materials • Clinical practice guidelines • Formal lectures • Seminars, conferences • Educational courses • Reminders • Distance learning, e-learning
Active	• Discussion groups, journal clubs • Educational outreach visits and academic discussions • Audit and feedback • Interactive role play, case scenarios, interactive educational workshops • Sequenced educational sessions (learn-work-learn), learning by working (practice) • Distance learning, e-learning

ANNEXES

Annex I: Sample terms of reference – national AMS technical working group

Purpose

- Provide strategic leadership on AMS (and IPC) measures under the national action plan on AMR.
- Provide a coordinated approach for national, health-care facility and community AMS (rational use of antimicrobials) programmes.
- Support national and international efforts as appropriate.

The overall aim of the AMS TWG is to optimize the use of existing antimicrobials and prevent the spread of resistant infections.

Accountable to

- National AMR Steering Committee
- Professional organizations and others as applicable

Responsibilities and activities

- Oversees and co-ordinates the development and implementation of national strategy and/or policy for controlling AMR by optimizing the use of antimicrobials through the implementation of AMS programmes.
- Ensures sufficient resources (human and financial) to achieve the objectives and outcomes of the national AMS strategy or policy.
- Ensures that relevant education and training on AMS are provided to pre- and in-service health-care professionals.
- Undertakes M&E of AMS interventions at the national, health-care facility and community level based on the national AMS strategy or plan on an annual or biannual basis.

Membership (to be adapted based on the country context)

The membership of the national AMS TWG should be composed of members representing the relevant departments within the ministry of health responsible for the selection, procurement, supply, distribution, prescribing and use of antimicrobials at the national level. Inclusion of additional sectors, notably the animal health, food and environment sectors, is advisable. Representatives should be given sufficient authority by their institutions to make decisions. The TWG should remain small enough to be functional, striking a balance between full representation and the functionality of the group to coordinate a national AMS strategy, policy or plan and be linked with other relevant groups/TWGs (AMR and AMC surveillance, etc.).

Frequency of meetings

The meeting format and rules should conform to national norms. Standard operating procedures may be elaborated transparently and according to the principles of best practice to guide the activities of the TWG. A chairperson should be selected based on his or her expertise in leadership. Rotation of the chair among members of the TWG could be considered. The TWG should meet on a regular basis, at a minimum quarterly or biannually.

Conflict of interest

It is recommended that the group have a mechanism (with appropriate records) to ensure that its members have no conflicts of interests and that the work of the TWG in the interests of public health is transparent.

Annex II: Sample terms of reference – health-care facility AMS committee

Purpose

The health-care facility AMS committee provides oversight and coordination of the implementation and review of the AMS programme at the facility. The AMS programme involves a systematic approach to optimizing the use of antimicrobials in the facility to improve patient outcomes, reduce inappropriate antimicrobial prescribing and reduce adverse consequences of antimicrobial use (including AMR and unnecessary costs).

Accountable to (adapted to the national context)

1. National AMS TWG (or as applicable)
2. Health-care facility leadership/management

Responsibilities and activities

- Liaises closely with other existing committees, including the drug and therapeutics committee, IPC committee and patient safety committee.
- Reviews the health-care facility core elements checklist, undertakes a SWOT analysis.
- Develops, endorses and implements a stepwise facility plan of action for AMS that includes setting targets for optimized antimicrobial use.
- Ensures that an education and training plan on AMS is in place for clinical staff in the facility.
- Ensures allocation of financial and human resources for implementing an AMS programme in the facility.
- Formalizes a health-care facility AMS team that reports to the AMS committee.
- Endorses the implementation of systems to monitor AMC and/or use and resistance.
- Reviews, endorses and implements clinical guidelines for antimicrobial prescribing.
- Endorses the implementation of an education programme for appropriate prescribing and AMS, in liaison with clinical educators in the facility.
- Monitors and evaluates compliance with one or more of the specific interventions put in place by the AMS team and reports back to the AMS team and prescribers on a regular basis.
- Facilitates the development and dissemination of regular activity reports that include data on antibiotic use and describe the interventions implemented by the AMS team.
- Undertakes risk assessment and plans action to improve the effectiveness of the AMS programme.

Membership and roles (to be adapted based on the facility context)

The membership of the health-care facility AMS committee will consist of the following:

- health-care facility administrator (executive sponsor/chair)
- director medical services (deputy chair)
- infectious diseases physician and/or clinical microbiologist (AMS team clinical lead)
- AMS pharmacist or physician (secretary);
- directors of other departments
- patient safety and clinical quality manager
- nursing representative
- pharmacy representative
- medical staff representatives from the different wards
- microbiology representative
- IT representatives (if applicable)
- drug and therapeutics committee representative (if the AMS committee is not embedded in the drug and therapeutics committee)
- IPC committee representative (if the AMS committee is not embedded in the IPC committee)
- Patient safety committee representative (if the AMS committee is not embedded in the patient safety committee).

Other personnel may be co-opted as required to assist the work of the committee.

Frequency of meetings

The meetings should be held on a regular basis, ideally monthly, with a minimum of quarterly. It is advised that regular meetings also be held either with other relevant groups (e.g. drug and therapeutics committee, IPC) or that members from those other groups be invited to participate in the AMS committee meeting as needed.

Agenda preparation and circulation of minutes

Papers for the committee will be prepared by the AMS committee secretary and circulated 1 week prior to the meeting date. The agenda will be determined by the AMS committee chair prior to meetings. Minutes will be distributed to members within 2 weeks of the meeting date by the AMS committee secretary.

In addition to committee members, minutes will be made available to:

- the drug and therapeutics committee;
- the IPC committee;
- the patient safety committee; and
- others as needed.

Annex III: Sample terms of reference – health-care facility AMS team

Purpose

- To implement the health-care facility AMS action plan and to facilitate optimized use of antimicrobials in the departments and wards.

Accountable to

1. Health-care facility AMS committee

Responsibilities and activities

- Delineates the roles and responsibilities of each team member in the AMS team.
- Implements day-to-day AMS activities, including conducting regular ward rounds and other AMS interventions in select facility departments identified in the health-care facility AMS action plan.
- Undertakes audits or PPSs to assess the appropriateness of infection management and antibiotic prescription according to policy/guidance.
- In collaboration with the facility pharmacy, monitors, analyses and interprets the quantity and types of antibiotic use at the unit and/or facility-wide level.
- Monitors antibiotic susceptibility and resistance rates for a range of key indicator bacteria at the facility-wide level or uses the data from existing groups that are monitoring this information.
- Facilitates education and training on AMS in the facility.

Membership (to be adapted based on the country context)

Option 1: >2 health-care professionals constituting a multidisciplinary team (e.g. tertiary hospitals). The multidisciplinary team should comprise a physician, a pharmacist or clinical pharmacologist, a nurse with expertise in infections or IPC, and in facilities with a microbiology laboratory, a microbiologist or laboratory technician.

Option 2: a physician and a nurse or pharmacist, with access to expert advice (e.g. secondary or small facilities).

Option 3: a nurse or pharmacist leading the stewardship programme, with access to expert advice (e.g. secondary or small facilities with limited resources).

Frequency of meetings

- Weekly to two times a month

Annex IV: Sample AMS review form

Patient information		
Date:	Department:	Ward:
Patient name:	Age:	Sex: Male ☐ or Female ☐

Antibiotic prescriptions				
Antibiotics prescribed	Dose	Route	Interval	Start date

Indication for antibiotic treatment				
Prophylaxis ☐	Urinary tract infection ☐	Pneumonia ☐	Gastrointestinal infection ☐	Bloodstream infection ☐
CNS ☐	Skin infection ☐	Bone infection ☐	Other:	

Initial review of antibiotic treatment		
Is indication for antibiotic treatment documented? Yes ☐ No ☐	Is antibiotic treatment prescribed according to guideline? Yes ☐ No ☐ Why not? Comment →	Comments
Correct dose? Yes ☐ No ☐	Appropriate route? Yes ☐ No ☐	Treatment duration or review date stated? Yes ☐ No ☐

48-hour review of antibiotic treatment				
Is antibiotic treatment reviewed? Yes ☐ No ☐			If yes, what action?	
Escalate ☐	Continue ☐	De-escalate ☐	Stop ☐	IV-oral switch ☐
Why is antibiotic treatment being continued?				
Continuing clinical signs of infection ☐	Confirmed infection ☐	Other (comment):		
Microbiology specimens collected? ☐ Date:	Microbiology results received? ☐ Date:	Microbiology results acted upon? ☐ Comment:		

General comments: Date:_____ Name/signature (reviewer) _____

Annex V: Sample pre-authorization/restricted prescribing form

Date:_____

Patient information		
Patient name:	Department:	Ward:
Age:	Sex: Male □ Female □	Allergies:

Indication for antibiotic treatment

Request for pre-authorized/restricted antibiotics				
Antibiotic(s) requested	Dose and duration	Administration route	Interval	Reason for request

Are microbiology test results with sensitivity testing available? Yes □ No □
If yes, provide details:

Date	Specimen	Pathogen identified and susceptibility results

Has the patient already received antibiotic(s)? Yes □ No □ If yes, what?				
Antibiotic(s) prescribed	Dose and duration	Administration route	Interval	Why is the treatment not adequate?

Requesting physician's name/contact number:_____

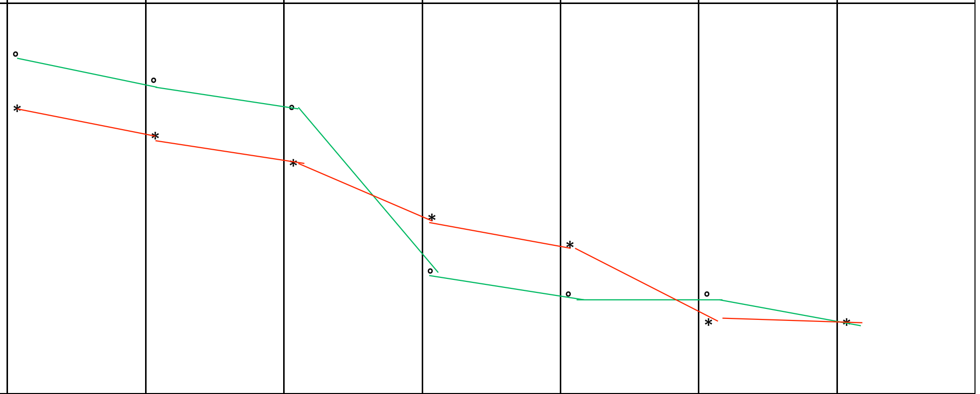
Comments from the AMS team/Drug and therapeutics committee/Pharmacy department

Approver	
☐ APPROVED	☐ NOT APPROVED
Remarks: Name/signature of specialist:_____ Date:_____	

Annex VI: Sample medical chart

Name of the ward Date admitted: 19/09/2018	Patient name, address, telephone no.: Date of birth: 10/08/1948	Weight: 70 kg Height: 168 cm	Dates:
Diagnosis: Pneumonia-Ca	Allergies: None		
Co morbidities			

P*	T*	19/09/2018	20/09/2018	21/09/2018	22/09/2018	23/09/2018	24/09/2018	30/09/2018
130	40							
110	39							
90	38							
70	37							
50	36							



Date of prescription	Name of the medicines	Dosage	Adm. route	Dose interval 00-06- 06-12-	 12-18- 18-24-	Dr. initials	BP: RR: 00-06- 06-12-	 12-18- 18-24-	BP: RR: 00-06- 06-12-	 12-18- 18-24-	BP: RR: 00-06- 06-12-	 12-18- 18-24-	BP: RR: 00-06- 06-12-	 12-18- 18-24-	BP: RR: 00-06- 06-12-	 12-18- 18-24-	BP: RR: 00-06- 06-12-	 12-18- 18-24-	BP: RR: 00-06- 06-12-	 12-18- 18-24-
19/09/	Amoxicillin	500mg	iv	1 1	1	IS	1 1	1	1 1	1	1 1	1	1 1	1	/ IS					
19/09/	Gentamicin	350 mg	iv	 1		IS	1		1	/ IS**										
23/09/	Amoxicillin	500mg	po	1 1	1	IS									1 1	1	1 1	1	/ IS ***	

*: Temperature and pulse measured in the morning. Enter as a dot and a triangle or star; and draw lines between the dots and the triangles, respectively; during the week.
**: /IS the doctor's initials who stopped the medication
***: On discharge the patient may receive a prescription.

Annex VII: Sample bug-drug chart

Site of Infection		Skin and soft tissue			Respiratory	Gastrointestinal / Urinary							Gut anaerobes
"Common pathogens"		MRSA	MSSA	*Beta-hemolytic streptococci*	*Streptococcus pneumoniae*	*Enterococcus faecalis*	*Enterococcus faecium*	*E. coli*	*Klebsiella*	Resistant Gram-negatives			
										Pseudomonas	ESCAPPM	ESBLs	
Penicillins	Penicillin			+									
	Amoxicillin / Ampicillin			+	+	+							
	Cloxacillin		+	+	+/-								
Cephalosporins	Cephalexin / Cefazolin		+	+				+/-	+/-				
	Ceftriaxone / Cefotaxime			+	+			+	+				
	Ceftazidime							+	+	+			
Beta-lactam / beta-lactamase inhibitors	Co-amoxiclav		+	+	+	+		+	+				+
	Piperacillin-tazobactam		+	+	+	+		+	+	+			+
Carbapenems	Ertapenem		+	+	+			+	+		+	+	+
	Meropenem / Imipenem		+	+	+			+	+	+	+	+	+
Glycopeptides	Vancomycin	+	+	+	+	+	+						
Miscellaneous	Doxycycline	+	+		+/-			+/-	+/-		+/-	+/-	
	Trimethoprim-sulfamethoxazole	+	+					+/-	+/-		+/-	+/-	
	Moxifloxacin		+	+	+	+		+	+				+/-
	Ciprofloxacin	+/-	+/-					+/-	+/-	+/-	+/-	+/-	
	Aminoglycosides							+	+	+	+	+/-	
	Daptomycin / Linezolid	+	+	+	+	+	+						
	Clindamycin	+/-	+/-	+/-									+/-
	Polymyxin / Colistin*							+	+	+	+/-	+	
	Metronidazole												+

* Serratia, Proteus, Providencia, Morganella, B. cepacia are intrinsically resistant to polymyxin/colistin.

Annex VIII: Sample cumulative antibiogram for gram-negative bacteria

Gram-negative Bacteria	Isolates	β-Lactams											Aminoglycosides			FQ		Other	
		Penicillins			Cephalosporins					Carbapenems									
	(N)	AMP	AMC	TZP	CZO	CXM	CTX	CAZ	FEP	IPM	MEM	ETP	AMK	GEN	TOB	CIP	ATM	SXT	NIT
Gram-negative bacteria (all)	34 932	28	69	89	59	63	73	-	83	91	95	96	95	880	85	68	69	68	76
Haemophilus influenzae	900	85	93	-	-	96	-	-	-	-	-	-	-	-	-	96	-	92	-
Moraxella catarrhalis	211	-	95	-	-	100	-	-	-	-	-	-	-	-	-	95	-	99	-
Enterobacteriaceae	27 972	28	70	92	60	-	75	-	84	95	99	98	98	89	87	67	79	68	-
Citrobacter koseri (diversus)	550	R	95	98	90	80	95	-	98	98	99	99	100	99	99	96	91	98	87
Enterobacter cloacae	802	R	R	86	R	51	79	-	92	91	98	94	99	93	93	86	86	89	48
Enterobacter aerogenes	543	R	R	85	R	R	82	-	95	65	98	98	100	95	94	85	88	92	25
Escherichia coli	16 810	36	74	93	59	66	71	-	81	99	99	99	99	89	86	62	76	60	94
Klebsiella pneumoniae	5 713	R	79	87	60	70	76	-	85	97	97	97	98	91	86	73	80	77	32
Klebsiella oxytoca	236	R	90	93	-	75	88	-	91	98	98	99	98	95	88	83	83	88	86
Morganella morganii	305	R	R	96	R	R	68	-	92	53	99	99	100	79	79	44	77	61	R
Proteus mirabilis	878	66	93	99	84	92	92	-	94	22	98	96	98	82	87	65	91	62	R
Providencia spp.	111	R	R	95	R	-	92	-	97	59	95	90	100	79	71	68	-	84	R
Salmonella spp. (non-typhoid)	566	86	92	99	-	-	97	-	99	-	-	-	-	-	-	-	-	96	-
Salmonella Typhi/Paratyphi	267	73	81	92	-	-	81	-	71	-	-	-	-	-	-	-	-	73	-
Serratia marcescens	652	R	R	95	R	R	91	-	97	71	98	98	100	97	89	87	98	98	R
Shigella spp.	79	37	72	98	-	-	65	-	78	-	-	-	-	-	-	52	-	48	91
Non-fermenting gram-neg rods	5 638	R	R	77	-	-	-	82	80	76	76	R	82	82	80	73	56	72	-
Acinetobacter baumannii	750	R	R	72	-	-	-	70	70	78	76	R	89	77	77	73	R	82	-
Pseudomonas aeruginosa	3 728	R	R	91	-	R	R	87	90	84	83	R	95	91	95	82	68	R	R
Stenotrophomonas maltophilia	479	R	R	R	-	-	R	66	-	R	R	R	R	R	R	-	R	87	-

FQ = fluoroquinolones, N = number, spp. = species, R = intrinsically resistant, (-) = no data available, or small number of isolates tested (N<30), or antimicrobial agent is not indicated, or not effective clinically.
Interpretation standard: CLSI M100 ED29:2019. Presentation standard: CLSI M39-A4:2014.
AMC = Amoxicillin/Clavulanic acid, **AMK** = Amikacin, **AMP** = Ampicillin, **ATM** = Aztreonam, **CAZ** = Ceftazidime, **CIP** = Ciprofloxacin, **CTX** = Cefotaxime, **CXM** = Cefuroxime, **CZO** = Cefazolin, **ETP** = Ertapenem, **FEP** = Cefepime, **GEN** = Gentamicin, **IPM** = Imipenem, **MEM** = Meropenem, **NIT** = Nitrofurantoin, **SXT** = Trimethoprim/Sulfamethoxazole, /Clavulanic acid, **TOB** = Tobramycin, **TZP** = Piperacillin/Tazobactam.

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