

**Manual****Open Access****The CLIMIDSON Manual for Antimicrobial Stewardship Programmes in Nigerian Health Care Facilities**

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Executive Summary:

Antimicrobial stewardship (AMS) remains a cornerstone of efforts aimed at improving antimicrobial-related patient safety. It slows the development and spread of antimicrobial resistance (AMR), while helping clinicians to improve clinical outcomes and minimise harm by improving antimicrobial prescribing. AMS programmes (ASPs) are driven through various processes and people. An AMS structure comprises the core elements that should be in place to support the ASP including the AMS team, treatment guidelines, and surveillance of AMR and antimicrobial use (AMU). This manual aims to provide a practical guide to health care facilities in Nigeria and other low-and-middle-income countries, for establishing, implementing and sustaining ASPs, and is structured into 14 sections. Section 1 introduces the subject matter and gives background information on the current situation of AMS in Nigeria. It describes the efforts of the National Antimicrobial Stewardship Working Group (NASWOG), an arm of the Clinical Microbiology and Infectious Diseases Society of Nigeria (CLIMIDSON), in identifying the AMR issues in health care facilities in the country and providing evidence-based recommendations for ASPs. Section 2 describes the goals of AMS and core elements which must be in place for successful and sustainable ASPs. Section 3 presents how a health care facility could start an ASP depending on the size, highlighting the important role of point prevalence survey (PPS) in obtaining baseline data on AMU and prescribing practice in health care facilities, which is useful in developing an action plan. Although management support is key for a successful ASP, the governance of the programme rests with the AMS committee, which composition and size will depend on the level of health care facility. Section 4 describes AMS strategies, which include the core and supplemental strategies. Every hospital should aspire to do at least a core strategy, although it may be convenient to start with other stewardship activities and supplemental strategies. Section 5 describes the antibiotic policy and guidelines, which provide the framework for all AMS activities, and is an effective means of changing behaviour in antimicrobial prescribing. The guidelines should be written by a multidisciplinary team and due consideration must be given to the local antibiotic susceptibility data and the common infectious disease syndromes in the facility or region. Dissemination of the policy and guidelines should be given wide publicity. At the primary health care facilities, where there may be no doctors to prescribe, "standing orders" are used to guide antibiotic prescribing. Section 6 describes the critical importance of stakeholder engagement to a successful ASP. If stakeholders are more informed about AMR issues and ASP, they are better able to positively support the programme. AMS stakeholders will differ from facility to facility but generally include health care facility management, clinicians, pharmacists, nurses, infection prevention and control (IPC) practitioners, clinical microbiologists, other relevant laboratory staff, and patients. The importance of education and training to the successful implementation of AMS is presented in section 7. Health care facilities should provide induction and in-service training to all staff on AMS and IPC. Training objectives should be clear and targets of education and training should include AMS committee and team(s), clinicians, pharmacists, nurses and other health care staff, patients and caregivers, and advocacy and community campaigns. Sections 8 and 9 explain how monitoring and evaluation (M&E) of ASP, and feedback to stakeholders are conducted. Monitoring and evaluation are critical to identifying the impact of intervention measures and opportunities for improvement. This involves the evaluation of the structures, processes and outcomes of ASPs. Sections 10 and 11 delved into the roles of clinical microbiology laboratory support for AMS, and diagnostic stewardship as well as information and communication technology (ICT) in ASPs. The clinical microbiology laboratory should provide quality antibiotic susceptibility testing data, and standard antibiograms periodically to the AMS committee. Sections 12, 13 and 14 enumerated the core elements of outpatient ASP, institutional mentoring in AMS, and system building approach to sustainability of ASP. The recommendations for outpatient AMS in this document apply to either stand-alone clinics and casualties or those located in secondary or tertiary hospitals.

Keywords: Antimicrobial resistance; Antimicrobial stewardship; Implementation; Health care facility; Manual

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Le Manuel CLIMIDSON Pour les Programmes de Gestion des Antimicrobiens dans les Établissements de Santé Nigériens

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Résumé Exécutif:

La gestion des antimicrobiens (AMS) demeure la pierre angulaire des efforts visant à améliorer la sécurité des patients liée aux antimicrobiens. Il ralentit le développement et la propagation de la résistance aux antimicrobiens (RAM), tout en aidant les cliniciens à améliorer les résultats cliniques et à minimiser les dommages en améliorant la prescription des antimicrobiens. Les programmes AMS (ASP) sont pilotés par divers processus et personnes. Une structure AMS comprend les éléments de base qui devraient être en place pour soutenir l'ASP, y compris l'équipe AMS, les directives de traitement et la surveillance de la RAM et de l'utilisation d'antimicrobiens (AMU). Ce manuel vise à fournir un guide pratique aux établissements de soins de santé au Nigeria et dans d'autres pays à revenu faible ou intermédiaire, pour l'établissement, la mise en œuvre et le maintien des ASP, et est structuré en 14 sections. La section 1 présente le sujet et donne des informations générales sur la situation actuelle de l'AMS au Nigeria. Il décrit les efforts du Groupe de travail national sur la gestion des antimicrobiens (NASWOG), une branche de la Société de microbiologie clinique et des maladies infectieuses du Nigeria (CLIMIDSON), pour identifier les problèmes de résistance aux antimicrobiens dans les établissements de santé du pays et fournir des recommandations fondées sur des preuves pour ASP. La section 2 décrit les objectifs de l'AMS et les éléments de base qui doivent être en place pour des ASP réussies et durables. La section 3 présente comment un établissement de santé pourrait démarrer un ASP en fonction de la taille, soulignant le rôle important de l'enquête de prévalence ponctuelle (EPP) dans l'obtention de données de base sur l'UAM et les pratiques de prescription dans les établissements de santé, ce qui est utile pour élaborer un plan d'action. Bien que le soutien de la direction soit la clé du succès d'un ASP, la gouvernance du programme incombe au comité AMS, dont la composition et la taille dépendront du niveau de l'établissement de soins de santé. La section 4 décrit les stratégies AMS, qui comprennent les stratégies de base et supplémentaires. Chaque hôpital devrait aspirer à mettre en place au moins une stratégie de base, bien qu'il puisse être pratique de commencer par d'autres activités de gestion et des stratégies supplémentaires. La section 5 décrit la politique et les directives en matière d'antibiotiques, qui fournissent le cadre de toutes les activités de l'AMS et constituent un moyen efficace de modifier les comportements en matière de prescription d'antimicrobiens. Les lignes directrices doivent être rédigées par une équipe multidisciplinaire et une attention particulière doit être accordée aux données locales de sensibilité aux antibiotiques et aux syndromes de maladies infectieuses courants dans l'établissement ou la région. La diffusion de la politique et des lignes directrices devrait faire l'objet d'une large publicité. Dans les établissements de soins de santé primaires, où il se peut qu'il n'y ait pas de médecins à prescrire, des « ordonnances permanentes » sont utilisées pour guider la prescription d'antibiotiques. La section 6 décrit l'importance cruciale de l'engagement des parties prenantes pour la réussite d'un ASP. Si les parties prenantes sont mieux informées sur les problèmes de résistance aux antimicrobiens et sur l'ASP, elles sont mieux à même de soutenir positivement le programme. Les parties prenantes de l'AMS différeront d'un établissement à l'autre, mais comprennent généralement la direction de l'établissement de soins de santé, les cliniciens, les pharmaciens, les infirmières, les praticiens de la prévention et du contrôle des infections (IPC), les microbiologistes cliniques, d'autres membres du personnel de laboratoire concernés et les patients. L'importance de l'éducation et de la formation pour une mise en œuvre réussie de l'AMS est présentée dans la section 7. Les établissements de soins de santé doivent fournir à tout le personnel une formation initiale et continue sur l'AMS et l'IPC. Les objectifs de la formation doivent être clairs et les cibles de l'éducation et de la formation doivent inclure le comité et les équipes AMS, les cliniciens, les pharmaciens, les infirmières et autres personnels de santé, les patients et les soignants, ainsi que les campagnes de plaidoyer et communautaires. Les sections 8 et 9 expliquent comment le suivi et l'évaluation (S&E) de l'ASP et les retours d'information aux parties prenantes sont effectués. Le suivi et l'évaluation sont essentiels pour identifier l'impact des mesures d'intervention et les possibilités d'amélioration. Cela implique l'évaluation des structures, des processus et des résultats des ASP. Les sections 10 et 11 se sont penchées sur les rôles du soutien du laboratoire de microbiologie clinique pour l'AMS, et de la gestion du diagnostic ainsi que des technologies de l'information et de la communication (TIC) dans les ASP. Le laboratoire de microbiologie clinique doit fournir périodiquement au comité AMS des données de test de sensibilité aux antibiotiques de qualité et des antibiogrammes standard. Les sections 12, 13 et 14 énumèrent les éléments de base de l'ASP ambulatoire, le mentorat institutionnel dans l'AMS et l'approche de construction de système pour la durabilité de l'ASP. Les recommandations pour l'AMS ambulatoire dans ce document s'appliquent soit aux cliniques autonomes et aux blessés, soit à celles situées dans des hôpitaux secondaires ou tertiaires.

Mots clés: Résistance aux antimicrobiens; Gestion des antimicrobiens; Mise en œuvre; Programme; Manuel

Section 1: Introduction

1.1. Purpose, Objective and Scope

Purpose:

This document provides evidence-based support and guidance to promote the successful establishment, implementation and sustenance of AMS programmes (ASPs) across

Nigerian health care facilities as a strategy to optimise antimicrobial use (AMU) and combat antimicrobial resistance (AMR).

Objective:

To provide a practical guide to health care facilities for establishing, implementing and sustaining ASPs.

Scope:

This manual covers practical steps and guidance on establishing ASPs in primary, secondary and tertiary health care facilities, particularly concerning the promotion of appropriate prescribing and use of antibiotics in health care facilities.

1.2. Background information on AMR and AMS

Antimicrobial agents remain valuable in humanity's fight against infections, and this value is reducing and under grave threat, mainly due to the growing menace of AMR. The large number of such antimicrobial agents discovered in the early twentieth century heralded the golden age of modern medicine (1). These agents have the ability to inhibit or kill microorganisms, hence the concept of AMR connotes the ability of such microorganisms to defeat the actions of antimicrobial agents (2). This translates into a reduction in the efficacy of the agents and a corresponding decrease in positive patient outcomes (2). Aside from increasing mortality, AMR also adds to economic losses, estimated at 100 trillion US dollars in gross domestic products (GDP) globally by 2050 (3) as well as psychosocial stress in treating or controlling infections in patients, caregivers and the health system (4).

Antimicrobial resistance is a naturally occurring phenomenon that is a survival mechanism for wild type bacterial strains. The rate and variety of mechanisms, and the number of resistant microorganisms has increased exponentially in the last couple of decades beyond that which can be wholly ascribed to nature (4). This has been occurring in tandem with a decrease in the discovery, development and adoption of novel antimicrobials (2). The grave implications this has for health care, a world where no effective agents are left to manage even the simplest of infections, was recognised by the WHO in its 2015 action plan to tackle AMR (5,6).

Since the early recognition of penicillin resistance among *Staphylococcus aureus* and the emergence of more resistant types such as methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *S. aureus* (VRSA), other resistance types have been discovered and reported to cause high mortality in patients infected with multidrug resistant (MDR) organisms (1,7). Other clinically significant resistant organisms and mechanisms include extended spectrum beta-lactamase (ESBL)-producing *Enterobacteriales*, carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem resistant *Pseudomonas aeruginosa* (CRPA), carbapenem-resistant *Enterobacteriales* (CRE), vancomycin-resistant *Enterococcus faecium* (VRE), fluoroquinolone-resistant *Campylobac-*

ter (FRC) spp, fluoroquinolone-resistant *Salmonella* (FRS) spp, and cephalosporin-resistant *Neisseria gonorrhoeae* (CRNG) (7,8,9). Additionally, about 4.1% of newly diagnosed infections are caused by multidrug-resistant organisms (MDROs), which are reported to be spreading globally due to increased travels (10).

A recent systematic analysis suggests that in sub-Saharan Africa, AMR contributes up to 27.3 deaths per 100,000 population, and 250,000 deaths were directly attributed to AMR in 2019 alone (7). Nigeria has not been spared the increase in AMR among clinical isolates. Available data show that MRSA rates in clinical infections have reached 50% while resistance to third-generation cephalosporins exceeds 70% among clinical *Escherichia coli*, *Klebsiella* spp and *Pseudomonas aeruginosa* isolates (11,12). While the increased emergence of AMR has multifaceted roots, human activity is by far the most significant factor (13). This activity is in the form of antibiotic misuse, the emergence and effects of which were predicted by Sir Alexander Fleming, who discovered penicillin, as far back as 1945 (14). Animal husbandry and pisciculture comprise the bulk of antibiotic use and may be the major source of resistant bacteria entering the human population. However, a more direct association has been reported between inappropriate prescribing and poor dispensing practices and antimicrobial resistance (4,10,15). These are particularly applicable in low-and-middle-income-countries (LMICs) with limited resources and poor drug regulatory mechanisms (10,13,16). Data have shown that the levels of antibiotic prescribing in Nigeria are high, and vary from one region to another, ranging from 62.4% to 83.5% (17-21). These high prescribing rates are associated with low rates of appropriate prescribing practice (17).

Antimicrobial stewardship (AMS) is defined as the coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration, thus preventing harm to the patients and preserving drugs for future patients. This was first applied as a term by McGown and Gerding (22), and has been demonstrated as an effective tool to reduce the high levels of inappropriate antimicrobial use, and by extension reverse AMR emergence (6,16, 23). However, the level of awareness of AMS in Nigeria is low, ranging between 28.2% and 40.6% among physicians (24,25), and implementation rate is even lower, with only 10% of health care institutions surveyed having some form of AMS activity (12). The reasons for these include low utilization of microbiology laboratory services by physicians, poor knowledge and awareness among

key stakeholders, and institutional resistance to AMS due to poor knowledge and lack of understanding of AMS strategies (26,27).

The current poor state of AMS practice in our health care facilities emphasises the need for strategies to encourage the adoption of AMS in all aspects of human health care services (16). A sustained engagement of relevant stakeholders is needed to enable AMS programmes to have any chance of success (2,6). One way of engaging effectively is by acquiring data on antibiotic prescribing and utilization within individual health care facilities using acceptable scientific methods such as point prevalence surveys (6,27). In light of this dire need for quality and patient safety in our health care environment, the Clinical Microbiology and Infectious Diseases Society of Nigeria (CLIMIDSON), through its National Antimicrobial Stewardship Working Group (NASWOG), undertook to drive the process of raising awareness and knowledge base aimed at encouraging our health care facilities to embrace AMS practices and make them routine in their daily practice. This manual is one of the tools designed to achieve this purpose. We emphasise that this manual is not exhaustive, but we believe it will help resource-constrained health care facilities to initiate, establish and sustain effective and efficient ASPs.

1.3. National Antimicrobial Stewardship Working Group (NASWOG)

1.3.1. Role of NASWOG:

The National Antimicrobial Stewardship Working Group (NASWOG) is an arm of the Clinical Microbiology and Infectious Diseases Society of Nigeria (an Incorporated Trustee with the Corporate Affairs Commission of Nigeria), charged with the responsibility of promoting AMS in Nigeria. It is a research-led group of health care professionals with experience and zeal for quality health care, who aim to promote antimicrobial stewardship and related practices via mutual understanding, collaborative activities and interdisciplinary health care education. The objectives of NASWOG are to foster an understanding of AMS, enhance knowledge, provide templates for guidelines, educate policy makers and influence national policy.

The group was formally inaugurated in Owerri, Imo State, Nigeria, in August 2018. The inauguration paved way for the first workshop in Owerri, and a communique was published thereafter (28). The membership of NASWOG was drawn mainly from hospitals conducting the Global Point Prevalence Survey (Global-PPS) of AMU and AMR in their hospitals. In attendance were health care workers from various specialities and different parts of the country.

1.3.2. Vision of NASWOG:

To have every health care facility and practitioner in Nigeria practice AMS.

1.3.3. Mission of NASWOG:

To halt and reverse the rising incidence of AMR in Nigeria's health care facilities especially at the tertiary and secondary levels.

1.3.4. Goals of NASWOG:

- Development of national relevant working documents such as antibiotic guidelines, antibiotic policies, and AMS manual.
- Sensitisation and education of stakeholders
- Working with other stakeholders on monitoring antimicrobial consumption in Nigeria
- Establishing and sustaining AMS in Nigerian health care facilities
- Sensitisation of the Nigerian public to the danger of misuse and abuse of antimicrobials

Section 2: Goals and core elements of AMS

2.1. Goals of AMS:

The overarching goals of AMS are;

- Optimise antimicrobial prescribing by ensuring that only those who need antibiotics receive the right drug promptly in the appropriate dose and duration.
- Prevent antimicrobial overuse, misuse and abuse, and development of antimicrobial resistance by ensuring that antibiotic prescribing is evidence-based and indicated. This ensures that those who do not need antibiotics do not have them, and that those who need them do not use them indiscriminately.
- Reduce antibiotic-related adverse effects by ensuring that patients are not given drugs to which they are allergic. Also, that the antibiotic prescribing is evidence-based and as much as possible limited to non-toxic drugs and for an appropriate duration
- Decrease mortality, morbidity and length of hospital stay: When patients are placed on antibiotics without laboratory evidence, it increases the chance of inappropriate therapy, and this in turn increases the likelihood of prolonged illness, extended stay in the hospital, and death.
- Reduce healthcare-associated costs: Very often patients are prescribed ex-

pensive antibiotics without any laboratory evidence supporting that, whereas equally effective and much less expensive alternatives would have been identified for use had there been a laboratory culture. Again, when patients spend more time in the hospital receiving excessive drugs, some of which are unnecessary, they incur more costs.

2.2. Core Elements of AMS:

The core elements of AMS according to the Centers for Disease Control and Prevention (29) are:

- **Leadership commitment:** Requires the hospital Management recognising the importance of AMS and making a documented commitment, providing resources and taking other actions to support and promote AMS in their facilities.
- **Accountability:** Requires that ASP needs a leader that is passionate and knowledgeable in AMS issues, who should be responsible for the programme management and outcomes.
- **Pharmacy expertise:** Requires a passionate clinical pharmacist, preferably one with expertise in infectious diseases.
- **Action:** Refers to specific interventions taken to address the deficits in practice that promote AMR.
- **Tracking:** Every action/intervention leads to an outcome, which needs to be measured to determine its impact. This is the monitoring and evaluation component of ASP.
- **Reporting:** Data from AMS actions need to be shared with all stakeholders. This encourages further participation, cooperation and support
- **Education:** Necessary education needs to be provided to stakeholders to enable them play their roles effectively in AMS.

Section 3: How to Start an AMS programme (ASP)

In order to start an effective ASP, it is important to obtain baseline information on antimicrobial prescribing and use in health care facilities. This can be done with a simple and objective method, the Point Prevalence Survey (PPS), which can readily be conducted using the Global-PPS method.

In low-and-middle-income-countries (LMICs) such as Nigeria, AMS strategies may be cumbersome in resource-limited settings

especially those without good laboratories. Global-PPS provides an easy tool to obtain background data on antimicrobial prescribing, which are necessary for health care facilities to begin their ASP. It also allows the identification of antimicrobial prescribing problems, highlights peculiar issues, and enables monitoring and evaluation of the ASP. AMS programme can be initiated by the appointment of an AMS committee or team (by the hospital management), which is led by a health care practitioner with high level training, interest and passion for AMS/AMR.

3.1. Starting AMS Programme using Global-PPS

The Global-PPS is a simple, standardised, freely available web-based surveillance method (available free at <https://www.global-pps.com/>) which enables assessment of the quality of antibiotic use and identification of targets for quality improvement. It provides an objective snapshot of the antimicrobial situation at the health care facility at a precise time. The method collects documented data from the medical records on:

- Drug name and dosage of antimicrobials prescribed for the patient
- Diagnosis
- Indications for prescribing antimicrobials
- Route of administration of antimicrobials
- Stop/review date of antimicrobials
- Targeted or empirical therapy
- Availability and compliance with antibiotic guidelines
- Duration of surgical antibiotic prophylaxis
- Healthcare-associated infections
- Presence of invasive devices

3.1.1. Procedures for conducting Global-PPS:

- Register the health care facility (HCF) on the Global-PPS website. This should be done by the AMS committee or team lead.
- Assess the HCF to know the following:
 - Number of wards
 - Number of beds
 - Number of patients on admission in each ward
 - Hospital work schedule (clinic, theatre and ward round days)
- Plan on how to carry out the Global-PPS based on the above information
- Identify and engage key stakeholders (department/unit/ward heads) to facilitate the Global-PPS
- Download the information-guiding tools from the Global-PPS website such as

the Global-PPS protocol, data collection forms, and gather other materials such as pencils and erasers needed for the work.

- Assign duties/roles (data collection, validation and entry) to members of the Global-PPS team and train them on the Global-PPS method.
- Collect the data based on the Global-PPS method as detailed on the forms.
- Ensure the data forms are securely kept and available for validation.
- Validate the data by cross-checking for errors and omissions.
- Upload the data onto the web-based Global-PPS analysis tool through the facility portal
- Download analysed data
- Interpret the data and identify key areas for intervention.

3.1.2. Dissemination of Global-PPS data:

The Global-PPS data should be disseminated locally, and probably, nationally and internationally.

- Communicate findings from the Global-PPS to the stakeholders with emphasis on gaps/challenges determined from the Global-PPS data
- When disseminating the data, consider the proposed audience and present the data in a way that enables them to reflect on their practice and change their behaviour.
- Avenues for dissemination of information include;
 - Multi-disciplinary meetings – Grand rounds
 - Department/ward/unit meetings
 - Clinical meetings
 - Presentations at professional meetings and conferences
 - Scientific journals, newsletters and similar publications

3.2. Writing up an AMS action plan:

The AMS action plan (see template at www.climidson.org.ng) should be created based on the findings of the health care facility strength, weakness, opportunity and threat (SWOT) analysis using the CLIMIDSON Assessment checklist (www.climidson.org.ng), which covers the AMS core elements as thematic areas;

- HCF/Leadership/Management
- Commitment
- Accountability
- Pharmacy/Drug Expertise
- Action
- Tracking
- Reporting
- Education

3.3. Advocacy for health facility leadership/management support for AMS

The results of SWOT analysis and Global-PPS data should be used to engage management to; identify AMS as a top priority, provide financial support and dedicated time for health care workers involved in AMS activity, and include AMS responsibilities in job descriptions and appraisal of relevant staff.

3.4. Setting up an Antimicrobial Stewardship Committee and Team(s) with Clear Terms of Reference

3.4.1. Setting up an AMS Committee:

Antimicrobial stewardship programmes (ASPs) require appropriate oversight and governance to ensure proper implementation, monitoring and sustainability. Planning and implementing an effective AMS programme requires the involvement of key players such as facility leadership (management and executives), medical doctors, nurses, pharmacists, microbiologists, and other relevant staff.

The AMS committee should be constituted and inaugurated by the hospital management to coordinate the implementation and review of the AMS programme at the hospital or facility. The AMS committee will bring together key players and involve them in the programmes' decision making from planning to delivery of its initiatives.

3.4.2. Membership of AMS Committee

The membership of the Committee may include;

- A representative from top management
- Clinical microbiologist
- Infectious diseases physician
- Pharmacist
- Nursing representative(s)
- Medical staff representatives from different wards/departments/units (Medicine, Surgery, Obstetrics and Gynaecology, Paediatrics, Oncology, Emergency, Intensive Care, Community Medicine, General Outpatients, Dentistry)
- Drug and Therapeutics Committee representative
- Infection Prevention Control Committee representative
- Clinical microbiology laboratory representative
- Information and Technology (IT) representative (for example, a system analyst)
- Patient Safety and Clinical Quality

- Manager
- Consumer representative (optional, if available)
- Medication Safety Committee representative (optional, if available)
- Other personnel may be co-opted as required to assist the work of the Committee.

Membership at secondary and primary health care facilities will depend on available human resources.

3.4.3. AMS Committee Chairman:

The Chairman of the AMS Committee should be a physician with interest, knowledge, passion and expertise in the field of AMS and AMR, usually a Clinical Microbiologist or Infectious Disease Physician (29,30). In their absence, a Clinical Pharmacist or Nurse with the above attributes may play this role.

The key functions of the Chairman are to; directly oversee the activities of the AMS Committee, convene meetings quarterly or more frequently if needed, report on the committee's activities to the management, and represent the committee at meetings amongst others.

3.4.4. Terms of reference of the AMS Committee:

The Committee should have clearly defined Terms of Reference including but not limited to:

- Roles and responsibilities
- Reporting lines
- Review of membership and terms of reference as needed
- Evaluation and identification of Key Performance Indicators (KPI)

3.4.4.1. Roles and Responsibilities

- Reviewing hospital AMS core elements checklist and undertaking SWOT analyses
- Implementing the restriction of selected antimicrobial agents in liaison with the hospital Drug and Therapeutics Committee
- Developing, endorsing and planning implementation of;
 - Systems to review antimicrobial prescribing and feedback results to prescribers
 - Systems to monitor antimicrobial usage and resistance
 - Clinical guidelines for antimicrobial prescribing
 - An education program for good antimicrobial prescribing practice and AMR, in liaison

with clinical educators in the hospital

- Resources to support point-of-care interventions
- Liaising with clinical microbiology services in hospital to ensure selective reporting of susceptibility testing results is in place and aligns with the antimicrobial formulary and guidelines
- Monitoring the effectiveness of strategies used in the ASP at the hospital, including the review of relevant reports and key performance indicators
- Performing AMR surveillance
- Planning action to improve the effectiveness of the ASP at the hospital
- Provide an action plan for the ASP and review it periodically

3.4.4.2. Reporting lines:

The AMS Committee should meet at least quarterly to generate a report of its activities to be presented to the management of the health care facility on a regular basis. The committee can meet as often as it may deem fit in case of emergency. The report should be prepared to outline:

- AMS strategies implemented and progress made, following gap analyses and risk assessments.
- Reports reviewed by the committee relevant to the ASP for example, AMS Team reports, antibiograms, Global-PPS reports

The AMS Team(s) should report to the AMS Committee

3.4.4.3. Evaluation and Key Performance Indicators (KPI):

- The AMS Committee should develop KPIs for the hospital based on the content of the AMS action plan.
 - Process measures from Global-PPS and audit data, for example, the prevalence of AMU.
 - Outcome measures, for example, AMR rate, length of hospital stay and mortality rate.
- Monitoring hospital AMS action plan and its performance.
- Publication and distribution of hospital AMS Committee reports.
- Meeting frequency and attendance in accordance with the terms of reference

3.4.5. AMS Team:

The AMS Team should consist of staff

with daily duties to support the ASP, implement the hospital AMS action plan and facilitate optimised use of antimicrobials in the departments and wards. Depending on the size of the hospital, there can be one AMS Team for the whole hospital (Central AMS Team) and/or an AMS Team for each department/unit.

3.4.5.1. Membership of AMS Team(s):

At the minimum, the Central AMS Team should be led by a physician with an interest in infections or antimicrobial use, and should include a pharmacist and a nurse. At the departmental level, a clinician in that department, preferably the representative of the department in the AMS Committee, should lead the AMS Team.

The departmental AMS Team should comprise mainly doctors and nurses in the department with support from the Central AMS Team and AMS Committee. The AMS Team should be accountable to the hospital AMS Committee.

3.4.5.2. Roles and responsibilities of AMS Team:

- Development, use and review of local antimicrobial guidelines and audit tools
- Promotion of AMS core and supplemental strategies
- Conduct AMS rounds in wards
- Perform monitoring and evaluation of AMS interventions
- In collaboration with the hospital pharmacy, monitor, analyse and interpret the quantity and types of antibiotic use at the unit and/or facility-wide level (antimicrobial consumption data)
- In collaboration with microbiology laboratory, monitor antibiotic susceptibility and resistance rates for a range of key indicator bacteria at the facility-wide level
- Facilitate the required education and training on AMS in the hospital and/or departments.
- Should meet on a regular basis at a frequency that enables them to carry out their responsibilities.

The AMS Team should work in close synergy with IPC and other relevant committees in the facility.

Section 4: Antimicrobial Stewardship Interventions

Antimicrobial stewardship (AMS) interventions comprise actions (or strategies) designed to achieve the objective/goals of the programme. These are divided into two main groups, namely the core and supplemental strategies.

The strategies are normally practised as a bundle of interventions, however, if properly practised, each of these interventions will result in optimising antibiotic use and reducing health care expenditures without compromising clinical outcomes.

4.1. Core strategies:

These are the two-core evidence-based strategies for hospital ASPs. They both require that antibiotic guidelines are obeyed and personnel are available to ensure this. These core strategies enable health care facilities to take direct control over antimicrobial prescribing at the facilities and have the advantage of providing education to prescribers when enquiries are made. The major challenge is that prescribers may perceive a loss of autonomy, especially with pre-authorisation, although this may be overcome with education.

4.1.1. Prospective audit with intervention and feedback:

This is an audit of antibiotic prescribing based on antibiotic guidelines and the hospital antibiotic policy. Recommendations (feedback) are made to the clinicians in real time when the antimicrobial prescribing is considered inappropriate. Recommendations may include changing antibiotics, adjusting doses, duration, and de-escalation based on antibiotic policy and guidelines.

The AMS Team will give feedback to the clinicians, and then check for the level of compliance to the recommendations, and also find out why some may not have complied with the recommendations. The feedback could be during ward rounds, face-to-face meeting, phone conversations, or any other appropriate and effective means. Audit data are obtained from case notes, drug prescription charts or relevant section in the electronic medical record (EMR) where this is used.

4.1.2. Pre-authorisation with formulary restriction:

Under formulary restriction and pre-authorisation, specified antimicrobials will only be dispensed based on approval of prescription by recognised personnel. The choice of restriction to antibiotics may be guided by the WHO AWaRe classification of antimicrobials (31), and this should be clearly specified in the locally formulated antibiotic guidelines.

4.2. Supplemental strategies

4.2.1. Education of health care professionals:

The health care professionals to be

educated should include the AMS Committee, AMS Team(s), clinicians, pharmacists, nurses, IPC practitioners and all other health care workers.

Education has been shown to be impactful in improving antimicrobial prescribing and use (32,33). The goal of education is to achieve behavioural change with respect to antimicrobial prescribing, dispensing, procurement and distribution. Appropriate and standardised content and curricula for health care workers education and training on AMR/AMS have been developed and published (34). The content should create awareness of:

- The impact and drivers of AMR
- Principles and practice of AMS
- Rational or appropriate AMU
- Diagnostic stewardship/surveillance of AMR
- Infection prevention and control

4.2.2. Guidelines and clinical pathways:

Clinical pathways are a common component of improvement initiatives. They aim to organise and standardise care processes, thus maximising patient outcomes and improving organisation efficiency. They may be developed as paper-based forms or charts or algorithm, or electronic documents, and should be based on local protocols (Fig 1, Table 1).

4.2.3. Intravenous (IV) to oral switch therapy:

In many instances there is no advantage of IV antimicrobials over oral formulations except when a high serum concentration is urgently required as in life-threatening conditions such as sepsis and meningitis. There-

fore, whenever a patient is able to tolerate orally, an IV or parenteral antimicrobial should be changed to oral, provided there is an oral formulation. This reduces the length of hospital stay so that patients can complete oral antibiotics at home where necessary, and reduces cost and complications associated with the administration of IV antibiotics. There should be a section in the policy and guidelines for IV to oral switch.

4.2.4. Dose optimisation:

Optimised antimicrobial dose should be based on patients' age, weight, organ dysfunction and tissue penetration and other factors such as obesity or critical illness, site of infection (for example central nervous system and blood) and pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of the drug, for example, concentration or time dependent activity. For instance, in critically-ill patients, extended-infusion administration of beta-lactams is required for dose optimisation.

Prescribers need to do a review of patient's antimicrobial prescription(s), to determine the need or otherwise to continue the antimicrobial or modify as necessitated by the microbiology laboratory report. The review is usually done after 48-72 hours of administration of empirical therapy, when the laboratory report would have been received.

4.2.5. Automatic stop orders:

This is used to ensure that the administration of specific and prescribed antimicrobials does not exceed a predetermined duration, for example, a maximum of 48 hours for vancomycin where MRSA infection is suspected until confirmed by the laboratory. The

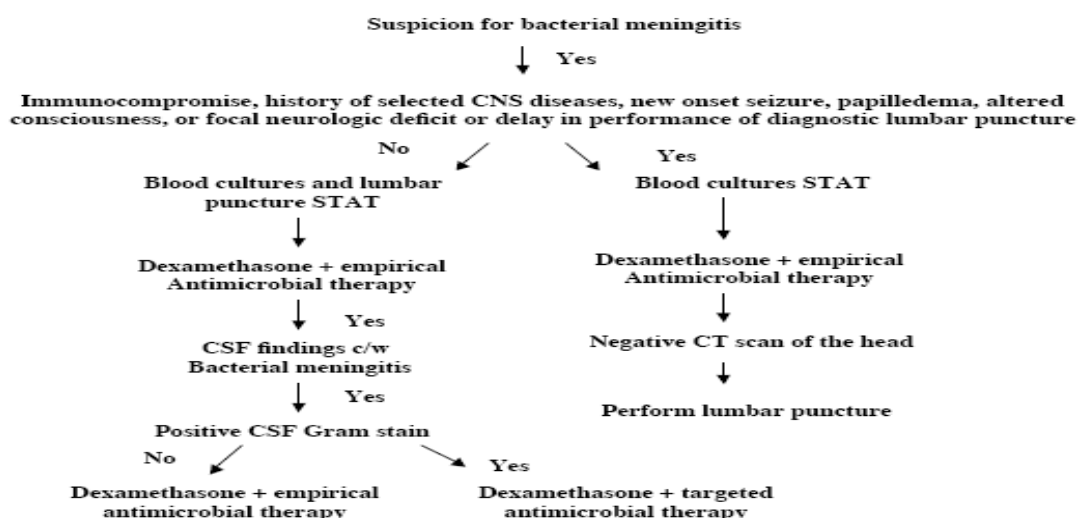


Fig 1: Management algorithm/clinical pathway for bacterial meningitis

Table 1: Template for empirical treatment guideline for bacterial meningitis

Infection syndrome (e. g. Bacterial meningitis)	First line antibiotics (dose/duration)	Alternative antibiotics* (dose/duration)
Age		
0-4 weeks		
1-3 months		
3 months – 50 years		
> 50 years		
Impaired cellular immunity		
Head trauma, neurosurgery		

*May be required for patients with allergies, recent antibiotic therapy or risk factors for specific microorganism

pharmacist stops further dispensing until laboratory evidence is provided confirming the infection requiring the antibiotics. It has the advantage of ensuring that patient safety is not compromised.

4.2.6. De-escalation or escalation:

This refers to the process of changing a prescription from a broad-spectrum antibiotic to a narrower spectrum antibiotic that targets specific microorganisms. Sometimes, escalation to an active antibiotic may be indicated if the identified organism is resistant to the antibiotic in use. Both escalation and de-escalation depend on result of antimicrobial susceptibility test (AST), the type and site of infection.

4.2.7. Microbiology strategy:

4.2.7.1. Comments in Clinical Microbiology Reports:

The clinical microbiologist should provide guidance to prescribers on the interpretation and use of microbiology reports as a routine practice, for example, to know which pathogens might represent colonisation or contamination.

4.2.7.2. Antibiotic testing policy:

- Microbiology laboratories should have a testing policy based on hospital antibiotic guidelines or the WHO AWaRe classification (31). This will ensure doctors do not prescribe antibiotics outside of the hospital formulary.
- Every Clinical Microbiology laboratory should choose antibiotics to test against particular bacteria from clinical samples. This should be in accordance with the facility's antibiotic guidelines and patients' clinical information. This will further guide prescribers in making rational choice of antibiotics.

Section 5: Writing Antibiotic Policy and Guidelines

Antimicrobial stewardship interventions rely on policies and guidelines which provide the basis/framework for all activities. An AMS programme requires the development and use of certain documents which include antibiotic policy and guidelines. These documents should outline how the health care facility would ensure appropriate use of antibiotics and monitor compliance.

Using antibiotic policy and guidelines has been shown to improve patient outcomes, enhance cost savings by reducing the cost of patient care, improve quality of care, reflect local patterns of resistance, and is an effective means of changing behaviour in antimicrobial prescribing.

Antibiotic policy contains the principles that guide rational and prudent antimicrobial prescribing while antibiotic guidelines are recommendations for prescribing antimicrobials for specific indications.

5.1. Objectives of Antibiotic Policy and Guidelines

- To promote appropriate use of antimicrobials.
- To provide a simple approach for treating common infections.
- To curb the emergence of AMR in the health care facility.
- To recommend antimicrobials with consideration of local antibiotic susceptibility patterns.

5.2. Writing the Policy and Antibiotic Guidelines

The flow chart of the process of writing antibiotic policy and guidelines is shown in Fig 2 (35).

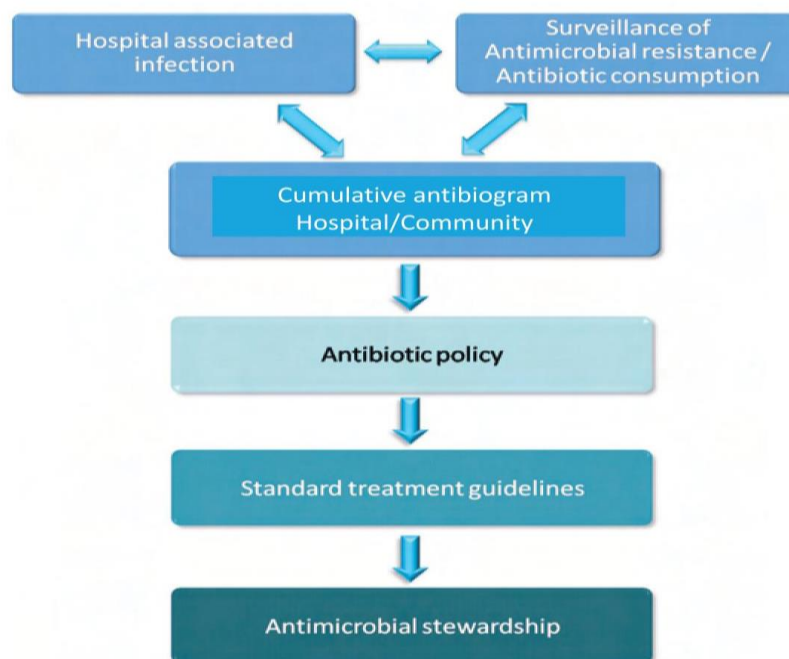


Fig 2: Flow chart of the process for writing antibiotic policy and guideline (35)

5.2.1. Human Resources

- Clinicians, clinical microbiologists, nurses, pharmacists, and IPC practitioners should form a team to write the antibiotic policy and guidelines
- At the primary health care facilities, where these health care workers are not available, “standing order” is used for antibiotic prescribing (usually of antibiotics in the Access group of WHO AWaRe classification). The “standing order” should be reviewed periodically based on an applicable antimicrobial susceptibility test report. The “standing order” may be available from the Primary Health Care Development Agency (PHCDA).
- The AMS Team may identify available evidence-based policies and guidelines (national or international) and adapt appropriately to fit local situations and write the first draft.
- The Team must have information on the local antibiotic formulary of the hospital or country and the antibiotics that are available locally.
- Local antibiotic susceptibility data should be provided by the clinical microbiology laboratory.
- A list of common infectious disease syndromes or infections based on the result of the Global-PPS should be provided.

5.2.2. Scope of Hospital Antibiotic Policy

Each hospital should design an antibiotic policy to govern prophylactic, empirical and targeted antibiotic therapy. In particular, there should be a policy on surgical antibiotic prophylaxis, antibiotic time-outs, use of the clinical laboratory to guide targeted therapy, and access to restricted or reserved antimicrobials. The guideline must align with the policy.

5.2.3. Content of Hospital Antibiotic Policy

- Contains a list of antibiotics for general use, reserved and restricted antibiotics
- Recommendations for principles of AMS
- Guidance for IV to oral switch
- AWaRe classification of antibiotics
- Policies for good antibiotic prescribing

5.2.4. Getting started with Guideline

- Choose your indications (common infections) in the health care facility based on the point prevalence survey of antibiotic use
- Look for available national and international guidelines, or guidelines from agencies, professional societies or ministries of health on antibiotic use, which may be adopted for your facility
- The AMS Team and stakeholders write the first draft of the guideline taking

into consideration the local antimicrobial susceptibility data. This can be done in each clinical department in a tertiary health care facility.

- This is disseminated to all stakeholders including resident doctors, medical officers, pharmacists among others for input.
- Based on the input from all stakeholders, a second draft is prepared.
- Do a pilot testing of the second draft in a section of the health care facility.
- Monitor and review the guideline based on the pilot testing.
- Write the final version of the guideline which will be approved by the antimicrobial stewardship committee.
- It is very important that antibiotic guideline is written by those who will use it so that they can take ownership and responsibility for implementation.

5.2.5. Contents of Guidelines

The following factors should be included in the contents of the guideline;

- Should be syndrome/disease based such as urinary tract infection (UTI), skin and soft tissue infection (SSTI), pneumonia
- Type of clinical setting: outpatient clinics, inpatient units, ICU setting
- When to switch from parenteral to oral route
- Clinical criteria for the diagnosis of infection/syndrome.
- Severity of illness
- Suggestion for diagnostic testing of disease condition(s)
- When to discharge
- Choice of antibiotics for empirical therapy, dose, route and duration of administration.

5.2.6. Selection of Antibiotics

In the selection of antibiotics, the following factors should be taken into consideration;

- Appropriate choice, dosage, route of administration, and duration of antibiotics
- Alternatives for allergy to first-line agents
- Adjusted dosage for patients with impaired liver or renal function including special needs of individual patient groups, for example, critically ill, pregnancy and obesity
- Severity of infection
- Site of infection
- Spectrum of antibiotic activity

- Pharmacokinetics/pharmacodynamics
- Adverse effects
- Potential to select resistance
- Cost of antibiotics, administration and monitoring microbiological causative microorganisms

5.2.7. Antibiotics Prophylaxis

- The duration of the prophylaxis should be specified
- Antibiotics dedicated for prophylaxis should not be used as first line or for empirical therapy except indicated by the results of AST.

5.3. Dissemination of the Antibiotic Policy and Guidelines

- Electronic copies sent to WhatsApp and e-mails of prescribers
- Print copies to be placed in the wards
- Pocket book copies that can be given to all prescribers
- Intranet within an electronic medical record
- Mobile applications

5.4. Audit of compliance to the Antibiotic Policy and Guidelines

- The periodic audit of antibiotic policy should focus on;
 - Documentation of the indication for antibiotic use
 - Stop/review date
 - IV-to-oral switch
- The periodic audit of antibiotic guideline should focus on compliance with current;
 - Clinical treatment guidelines
 - Guidelines for surgical prophylaxis
- Feedback of audit results to prescribers and health care facility management and other stakeholders is essential.

Note that:

- It is important that clinicians, pharmacists, nurses and other stakeholders are educated on the policy and guidelines and given an opportunity for feedback.
- Dissemination of the policy and guidelines should be given wide publicity
- It should be the responsibility of the AMS Committee/Team to assess and ensure the compliance of clinicians and other health care workers with their antibiotic policy and guidelines.
- Policy and guidelines are living docu-

ments, therefore, they should be reviewed at periodic intervals based on current medical knowledge, clinical practice and local circumstances.

Section 6: Engaging Stakeholders on Antimicrobial Resistance and Stewardship

Stakeholder engagement is critical to a successful ASP. Stakeholders become more informed about issues and are able to positively support such programmes. A good engagement clarifies the purpose of the activity; why it is important; clarifies the context; and sets a clear direction of action. Engagement is a means to an end.

For effective stakeholder engagement, the following factors should be taken into consideration;

- Identifying who the stakeholders are
- Understanding who has the most influence on the issue
- Sharing and delivering on expectations
- Showing an understanding of the stakeholders' concerns

AMS stakeholders include health care facility management, clinicians, pharmacists, nurses, IPC practitioners, clinical microbiologists, other relevant laboratory staff, patients, etc. The stakeholders should be engaged in the following areas; AMR awareness, appropriate antibiotic prescribing, IPC, diagnostic stewardship and surveillance.

6.1. Goals, Processes and Tools for AMS stakeholders' engagement

- **Goal 1:** To inform and inspire stakeholders

This is usually a one-way communication to stakeholders to inform them about a health issue or policy matter. Tools/processes for this include handbills, fact sheets or meetings solely for information, for example 24-hour surgical prophylaxis compliance rates from Global-PPS results.

- **Goal 2:** To consult and listen to stakeholders

Here, the stakeholders are given the opportunity to make input or suggestions to proposals but debates for or against these proposals are usually not done at this level. The tools/processes for this includes meetings, submissions, focal group discussions, surveys, for example determination of reasons for non-compliance

with 24-hour surgical prophylaxis, and suggestions for improvement.

- **Goal 3:** To involve the stakeholders

Stakeholders receive new information on the issues under consideration, deliberate on them and then come to an agreement and/or make recommendations to inform the decisions. The tools/processes for this include workshops, and committees, for example, form a group to review the information available on non-compliance with surgical prophylaxis, and proffer solutions.

- **Goal 4:** To collaborate with stakeholders

Committees/sub-committees should be created from members who have some decision-making authority. The tools/processes to achieve this include participatory decision-making strategies, for example, a meeting of authorities involved in ensuring compliance with antibiotic guidelines at the highest level, such as meeting with the head of department and consultants in surgery

- **Goal 5:** To empower the stakeholders

In this case, a committee is set up to undertake the responsibility entirely and tasked with addressing a public problem over an extended period of time. The tools/processes for this include a committee for implementation, for example, a committee to implement and monitor compliance with 24-hour surgical prophylaxis, such as the AMS Committee.

Note that each level of engagement deepens the involvement of the stakeholders.

6.2. Strategies for successful stakeholder engagement

- The reason or goal for engagement must be clear.
- Share the identified purpose with the stakeholders very early.
- Adopt the appropriate process; the type of engagement needs to be tailored to the purpose (see goals 1 to 5 above).
- Usually, stakeholders' engagement is most effective when it stretches to collaborative and empowerment levels.
- Stakeholders are not a uniform group, therefore, engagement needs to focus on a specific issue or topic and invo-

ives interaction with the groups most relevant to the issue.

6.3. Platforms for stakeholders engagement on AMS

- Hospital meetings/Grand rounds
- Focus group discussions
- Surveys
- Web-based engagements
- Print and electronic media
- Billboards, Posters, Handbills
- Social media
- Relevant committees and professional bodies/Associations
- Conferences and Workshops

6.4. Categories of stakeholders

The knowledge and attitude of stakeholders on particular issues vary, and must be considered during engagements (36).

- **The unaware:** These are not aware of the issues (for example AMR, AMS) and their potential impact such as high mortality and morbidity
- **The resistant:** These are aware of the issues and potential impacts, but are resistant to change
- **The neutral:** These are aware of the issues, but are neither supportive nor are resistant to change
- **The supportive:** These are aware of the issues and potential impacts, and are supportive of change
- **The leading:** These are aware of the issues and potential impacts, and are actively engaged in ensuring the programme is a success

The overarching target is to make all stakeholders become supportive towards the programme.

Section 7: Education and Training

Training and education are paramount to the successful implementation of interventions in ASPs (37). However, it is most effective when paired with interventions and measurement of outcomes (29). The health care facility should provide training to all staff on AMS, during new staff orientation programmes and provide continuous in-service training or continuous professional development on AMS and IPC (38).

7.1. Training objectives should be to:

- Create awareness of AMR, AMS and their relationship

- Provide knowledge on the drivers and impact of AMR
- Impart detailed knowledge of ASPs
- Promote behavioural change in antimicrobial prescribing, use, procurement, dispensing and disposal
- Educate new or rotating staff and students
- Emphasise and promote the need for appropriate use of the clinical microbiology laboratory
- Update and reinforce previous knowledge
- Encourage continuous quality improvement

7.2. Targets of Education & Training

Activities should target various audiences using behavioural change communication strategies. These targets should include:

7.2.1. Antimicrobial Stewardship Committee and Team(s)

The members of the AMS Committee (AMSC) should be adequately trained on AMS and the ASP including principles/actions required for its establishment and implementation, antimicrobial policy and guidelines, and IPC. This should be done at the inception of the Committee and reinforced periodically. Training should be practical and specific to the roles of each member. Award of certificates of participation would be a motivation and an added advantage.

Administrative heads of health care institutions should support AMSC and AMS Team(s) (AMSTs) by facilitating opportunities for training and retraining, to reinforce previous training as well as updating their knowledge. They should also provide funding and foster collaboration with partners, nationally and globally to support their ASPs (29). Resources on practical guidance for implementing an ASP should be made available and accessible when required.

Hospital AMS campaigns should be publicised. This is necessary to gain support for successful interventions in identified priority areas. Critical stakeholders such as clinicians and other health care providers should be educated on the proposed activities around the priority area. AMS champions in the specialty(ies) in focus should lead publicity efforts in their units. Heads of health care facilities and key opinion leaders may be made ambassadors to successfully drive the programme.

7.2.2. Clinicians, Pharmacists, Nurses, and other health care staff

This should be an ongoing process with trainings repeated as much as feasible.

Education should cover the fundamentals of AMR, AMS, the importance of proper and optimised diagnosis, and promote adherence to antimicrobial policy and guidelines. Structured training relevant to specific AMS interventions is essential.

Opportunities for training include orientation programmes for new staff, grand rounds, clinical meetings and undergraduate medical education by including it in the curriculum. Information, education and communication (IEC) materials (posters, fliers, banners, text messages, social media posts) shared physically, via telephone and on social media, could be used to promote ASP activities. Telemedicine could provide AMS support for prescribers such as mobile Apps for AMS and antimicrobial guidelines (38). A health care worker guide has been published by the Public Health England and the WHO with details on the training of various health care workers (34).

7.2.3. Patients and Caregivers

These stakeholders should be educated on the inappropriate use of antimicrobials, negative consequences of inappropriate antimicrobials use, including sharing, use of leftovers, inappropriate disposal and demand for antibiotics. Fora such as the antenatal clinic (ANC), immunisation clinics and waiting areas in consulting clinics should be utilised to drive the health education.

They should know what antibiotics they are receiving, and for what reason(s), and about their adverse effects (signs and symptoms to identify these) including those that may occur after discharge or stopping antibiotics. They should be encouraged to be antimicrobial guardians. Engaging patients and caregivers in the development and review of educational (IEC) materials is beneficial (29).

7.2.4. Community

This includes teachers and educators, journalists and communication experts, social media influencers, religious leaders, and the general community including children and young persons. To support AMS at the community level, they should be educated regularly on antimicrobial resistance, ills of self-medication and the responsible use of antibiotics. This can be routinely done by trained public health, ASP ambassadors and advocates, and family medicine practitioners (39).

7.2.5. Advocacy and community campaigns

Regular engagement and awareness creation campaigns on the threat of antimicrobial resistant infections and measures to

contain them, should be carried out by AMS practitioners using data generated locally. Highly visible and regular national advocacy activities, among policy-makers and the general public (such as during World Antimicrobial Awareness Week) are beneficial, to raise the political and public profile of AMS and to get their "buy-in" to AMS programmes (39).

Section 8: Monitoring and Evaluation

Monitoring and evaluation (M & E) are critical to identifying opportunities for improvement and the overall impact of intervention measures. M & E involves the evaluation of structures, processes and outcomes of ASPs.

8.1. Monitoring

Monitoring is a systematic and routine collection of data to enable implementers to determine whether the objectives of the programme are being achieved. The attainments are compared to set targets during evaluation and actions taken to address gaps or deficits. Data acquired through monitoring is used for evaluation.

8.2. Evaluation

Evaluation involves assessment of a programme as systematically and objectively as possible, at defined time points. It appraises data and information that inform strategic decisions and helps to draw conclusions about the relevance, effectiveness, efficiency, impact, and sustainability of the intervention. It is an integral concept in every project or programme design.

8.3. Approach to Monitoring and Evaluation in AMS

For convenience and ease of understanding, monitoring and evaluation in AMS could be grouped into structure, processes, and outcomes.

8.3.1. Structure:

This should cover aspects that include the composition, terms of reference and governance structure of the AMS Committee and Team(s). Membership and composition of the Committee/Teams are as highlighted in Section 3.4 of this document. The CLIMIDSON AMS checklist (www.climidson.org.ng) can be used as a tool for measurement.

8.3.2. Processes:

The processes in this context include quality indicators in the application and implementation of AMS which can best be evaluated

using the Global-PPS and audit of specific antimicrobials. Some of the process measures/indicators based on Global-PPS include documented indication for antibiotic use, stop/review date, compliance with current clinical treatment guidelines, de-escalation, and IV-to-oral switch. Others include prevalence of antibiotic consumption measured as defined daily doses (DDD) or day of therapy (DOT), prevalence of antimicrobial prescribing, and surgical antibiotic prophylaxis (SAP) not beyond 24 hours.

8.3.3. Outcomes:

Outcomes of AMS represent the intended benefits which include AMR rates, mortality rates and length of hospital stay. Outcome indicators should be defined at the planning stage of the ASP and monitored while implementing the programme.

Section 9: Feedback of Data from Surveillance and M&E

This entails the distribution of results and outcome of AMS interventions and surveillance activities to those who need to know and act. This is essentially communicating the outcome to relevant stakeholders, including but not limited to hospital management and prescribers. This can be done using appropriate media and platforms such as presentations at clinical meetings/grand rounds, advocacy, fliers, posters and scientific publications.

During dissemination, opportunities should be created for responses from the stakeholders to the feedbacks. Such responses can then be used to improve the AMS action plan. These include feedback to prescribers, AMS Committee and Teams, and health care facility management on:

- Global-PPS data
- Antibiotic consumption data
- AMS interventions and actions
- AMR surveillance and antibiogram

Section 10: Clinical Microbiology Laboratory Support and Diagnostic Stewardship

10.1. Strengthening Laboratory Capacity for Hospital ASPs

The clinical microbiology laboratory plays a key role in ensuring the success of the antimicrobial stewardship programme. In order to provide quality services and reliable data, clinical laboratories should ensure the followings:

10.1.1. Provide guidance to laboratory users

The laboratory should provide documents (laboratory handbook, periodic advisories) with details of the policies and operations of the laboratory including; hours of operation, proper collection and transport of laboratory specimens, appropriate use of laboratory services and other relevant information (29). These documents should be made accessible and available to the laboratory users. It should also provide interpretation of laboratory results and reports.

10.1.2. Provide quality laboratory services including Antibiotic Susceptibility Testing (AST)

The laboratory should perform the right test requested at a minimal turn-around-time (TAT), release laboratory reports to health care providers in a timely manner to guide physician decisions on treatment and optimise communication of critical test result values and alert systems (40,41). With respect to AST, the laboratory should:

- Ensure quality-assured AST data are available
- Adhere to standardised protocols with appropriate quality controls
- Be involved in proficiency testing (PT)
- Test supplementary antimicrobial agents in the event of resistance
- Promptly report unusual patterns of AMR
- Provide advice to the physician on therapy for such patients.
- Update methods for susceptibility testing periodically

The use of automated or semi-automated testing systems is encouraged where possible, especially when dealing with severe life-threatening infections. The use of single antibiotic disc for AST offers the staff the opportunity to choose specific antibiotics for testing against specific organisms.

10.1.3. Promote Diagnostic Stewardship

Diagnostic stewardship (DS) is the coordinated guidance and interventions to improve the appropriate use of microbiological diagnostics to guide therapeutic decisions (42). It refers to the appropriate use of laboratory testing, including use of biomarkers, to guide patient management, in order to optimise clinical outcomes and limit the unnecessary use of antibiotics and spread of AMR.

This requires synergy between clinical laboratories and physicians so that appropriate tests are requested, and laboratory reports are translated into appropriate antimicrobial management (43). DS aims to promote appropriate and timely test request/ordering, specimen collection, specimen processing and reporting. The process of implementing DS is summarised in Fig 3 (44).

10.1.4. Continuous laboratory quality improvement

The laboratory should upgrade diagnostic capacity to:

- Perform standardised tests, which include microscopy, culture, identification (ID) and AST.
- Use rapid diagnostic technologies for targeted critical specimen types and detection of AMR
- Test for biomarkers of infection including non-culture-based fungal markers.
- Promote appropriate use of point-of-care microbiological tests, when available (41).

10.2. Antimicrobial resistance surveillance

Antimicrobial resistance surveillance involves tracking changes in microbial populations for early detection of resistant strains of clinical and public health importance, and reporting on trends in resistance on a periodic basis. Clinical laboratories should collaborate with the institution's AMS committee, using information from the analysis of AST, to determine priority pathogens, syndromes, patient populations, antimicrobials and provide target

for stewardship interventions. Thus, AMR surveillance data are needed to;

- inform clinical therapy decisions
- guide policy recommendations and treatment guidelines development
- assess the impact of ASP interventions to contain AMR

At the facility level, regular analyses of AMR data should be provided to groups with responsibility for antimicrobial guidelines (i. e. AMSC/AMST, DTC) to inform empirical therapy recommendations and formulary management.

A specification for health care facility cumulative antibiogram is an essential step towards achieving detailed, accurate and efficient AMR surveillance. To achieve this, health care facilities should ensure that;

- A standard technical specification of a facility cumulative antibiogram is developed using the appropriate CLSI document (45)
- There is ongoing maintenance and revision of the cumulative antibiogram specification.
- Clinical microbiology laboratory should report signal resistances from antibiogram data for the health care facility's ASP annually.

10.3. Antibiogram

An antibiogram is an overall profile of antimicrobial susceptibility testing results of a specific microorganism to a battery of antimicrobial drugs within a defined period (45). This is produced periodically, usually annually, to provide information on common pathogens

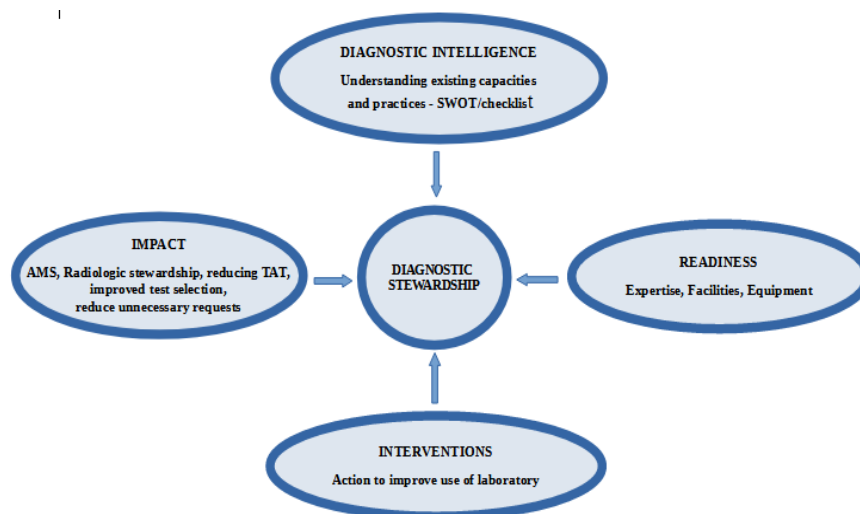


Fig 3: Implementation of Diagnostic Stewardship (adapted from 44)

and their antibiotic susceptibility patterns to guide the choice of empirical antibiotics.

Antibiogram should be derived from records of culture and antibiotic susceptibility testing carried out during the period under consideration.

10.3.1. Uses of an antibiogram

- Helps in guiding the clinicians and AMS team in the selection of best empirical antimicrobials treatment in the event of pending microbiology culture and susceptibility results. It should be the basis for facility and national guidelines development.
- Useful tools for detecting and monitoring trends in AMR, which can then be investigated.

10.3.2. Specifications for antibiogram

- Cumulative antibiograms should be produced differently, for urine, non-urine and blood culture isolates.
- For statistical significance, there should be at least 30 isolates at the species level. However, if this is not possible, the isolates can be grouped by genus or family.
- In smaller laboratories, cumulative antibiograms may be produced for all isolates combined irrespective of specimen type but should be categorized into Gram-negative and Gram-positive bacteria (Tables 2a and 2b).
- When the antibiotic data from less than 30 isolates is presented, it is recommended that a footnote should state that the results may not have attained a statistically significant measure of susceptibility in that microbial population
- Each cumulative antibiogram should consist of data for one calendar year and be published early in the following year.
- Only the antibiotic susceptibility data from the first isolate of a bacterial species from an individual patient should be included to eliminate duplicates. If the same bacteria species is isolated from urine, a non-urine site or blood from an individual, then the susceptibility data from the first isolate from each site should be included in their respective antibiogram.
- Only validated antibiotic susceptibility test results from clinical isolates submitted for diagnostic purposes should be included.
- For each genus, species or other groupings, the number of isolates (deno-

minator) used in determining the percentage should be noted on the antibiogram report.

- Limitations of the antibiogram should be listed in the footnote.

10.4. Signal Resistance

Certain combinations of microorganisms and antibiotic resistance should be reported in a specialised antibiogram to draw attention to multi-drug resistant organisms (MDROs) and resistant mechanisms (Tables 3a and 3b). With automated ID and AST methods, these are more readily detectable and characterised. The frequency of these should be reported including zero occurrences. Signal Resistances may include:

- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-intermediate and vancomycin-resistant *Staphylococcus aureus* (VISA, VRSA). The method used for identifying VRSAs should be reported.
- Vancomycin-resistant Enterococci
- *Enterobacterales* resistant to third or later generation cephalosporins. Where the genetic mechanism for this resistance has been determined such as with ESBL, the method should be reported
- Carbapenem-resistant *Enterobacterales* (CRE) and other plasmid mediated carbapenemase producing Gram-negative bacteria such as *Acinetobacter* spp and *Pseudomonas aeruginosa*.
- *Streptococcus pneumoniae* with a penicillin MIC ≥ 0.06 $\mu\text{g/ml}$. These should be categorised as intermediate (MIC 0.12 – 1 $\mu\text{g/ml}$) and resistant (MIC > 2 $\mu\text{g/ml}$) referring in the commentary to the fact that breakpoints for meningitis differ.

Section 11: Role of Information and Communication Technology (ICT) in the AMS Programme

The following are areas where ICT can be of benefit to AMS (46,47);

- Electronic medical records/hospital information system. This can be used for interventions such as audit, and for monitoring and evaluation.
- Database on procurement and ward dispensing at the facility pharmacy level. This can be used in calculating antimicrobial consumption and establish trend over time.
- Database of AMR surveillance in different units/departments

Table 2: Template for presenting cumulative antibiogram

[Health care facility Logo]

(a): Cumulative antibiogram for all hospital isolates (Gram-Negative Bacteria) (Jan – December)

Bacterial Pathogen	No of Isolates Tested	Percent Susceptible																			
		Ampicillin	Ampicillin/ Sulbactam	Piperacillin/ Tazobactam	Cefazolin	Cefepime	Cefoxitin	Ceftazidime	Ceftriaxone	Cefuroxime	Aztreonam	Ertapenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Levofloxacin	Trimethoprim/ Sulfa	Nitrofurantoin*	Tetracycline
<i>Escherichia coli</i>																					
<i>Klebsiella pneumoniae</i>																					
<i>Proteus mirabilis</i>																					
<i>Pseudomonas aeruginosa</i>																					

Antibiogram with <30 isolates are of questionable statistical significance; interpret data with caution
 * = Nitrofurantoin is reported for urine sources only; Antibiogram with <30 isolates are of questionable statistical significance; interpret data with caution
 NB: The antibiogram should report antibiotic susceptibilities for the antibiotics in actual clinical use, not the susceptibility to any surrogate antibiotic used in the laboratory e. g. for a laboratory using CLSI method, the antibiogram should report as percentage susceptible to flucloxacillin and not percentage susceptible to cefoxitin for *Staphylococcus aureus*.
 If the 'breakpoint' for any antimicrobial-organism pair has changed since the last publication of a cumulative antibiogram for an institution, then the date the change was implemented should be indicated in a footnote to the table.

(b): Cumulative antibiogram for all hospital isolates (Gram-Positive Bacteria) (Jan – December)

Pathogen	No of Isolates Tested	Percent Susceptible													
		Penicillin	Ampicillin	Oxacillin ¹	Gentamicin	Ciprofloxacin ²	Levofloxacin ²	Moxifloxacin	Trimethoprim/ Sulfa	Clindamycin ³	Daptomycin ⁴	Nitrofurantoin ⁵	Linezolid	Vancomycin	Tetracycline ²
<i>Staphylococcus aureus (MSSA)</i>															
<i>Staphylococcus aureus (MRSA)</i>															
<i>Enterococcus faecalis</i>															
<i>Enterococcus faecium</i>															
<i>Viridian streptococci</i>															
<i>Coagulase negative staphylococcus⁶</i>															

1. Oxacillin predicts susceptibility to most cephalosporins, carbapenems, and beta-lactam/beta-lactamase inhibitors; 2. For *E faecalis*: ciprofloxacin, levofloxacin, tetracycline is reported for urine sources only
 3. For *Staphylococcus* species: clindamycin is reported for non-urine sources only; 4. For *Staphylococcus* species: daptomycin is reported for non-respiratory sources only; 5. Nitrofurantoin is reported for urine sources only
 6. Only clinically significant isolate should be reported

Table 3: Template for signal resistance reporting [Health care facility logo]

(a): Multidrug resistant bacteria isolated from non-urine (January – December)

Extended Spectrum Beta-Lactamase Producing Enterobacterales (ESBL)			
Bacteria	Total No of isolates Tested	No ESBL Positive	% ESBL positive
<i>Escherichia coli</i>			
<i>Klebsiella spp</i>			
<i>Enterobacter spp</i>			
<i>Citrobacter spp</i>			
Carbapenem-Resistant Enterobacterales (CRE)			
Bacteria	Total No of Isolates Tested	No CRE Positive	% CRE positive
<i>Escherichia coli</i>			
<i>Klebsiella spp</i>			
<i>Enterobacter spp</i>			
<i>Citrobacter spp</i>			
Vancomycin Resistant Enterococci (VRE)			
Bacteria	Type	No VRE Positive	% VRE positive
<i>Enterococcus spp</i> total			
	<i>Enterococcus faecalis</i>		
	<i>Enterococcus faecium</i>		
Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA)			
Bacteria	Type	No MRSA positive	% MRSA positive
<i>S. aureus</i> total			
	<i>S. aureus</i> (non-multi-resistant)		
	<i>S. aureus</i> (multi-resistant hospital-associated)		
<i>Streptococcus pneumoniae</i> Penicillin Susceptibility*			
<i>S. pneumoniae</i> (Oral Penicillin V Breakpoint)	MIC category	No of Isolate	% Isolate
	Sensitive ($\leq 0.06 \mu\text{g/ml}$)		
	Intermediate ($0.12 - 1 \mu\text{g/ml}$)		
	Resistant ($\geq 2 \mu\text{g/ml}$)		
*Breakpoint for non-meningitis isolate IV treatment ($R \geq 8 \mu\text{g/ml}$), meningitis isolate IV treatment ($R \geq 2 \mu\text{g/ml}$)			
Viridians Streptococcus Group Penicillin Susceptibility			
Viridian streptococci	MIC category	No of Isolate	% Isolate
	Sensitive ($\leq 0.12 \mu\text{g/ml}$)		
	Intermediate ($0.25 - 2 \mu\text{g/ml}$)		
	Resistant ($\geq 4 \mu\text{g/ml}$)		

(b): Multidrug resistant bacteria isolated from urine (January – December)

Extended Spectrum Beta-Lactamase Producing Enterobacterales (ESBL)			
Bacteria	Total No of isolates Tested	No ESBL Positive	% ESBL Positive
<i>Escherichia coli</i>			
<i>Klebsiella spp</i>			
<i>Enterobacter spp</i>			
<i>Citrobacter spp</i>			
Carbapenem-Resistant Enterobacterales (CRE)			
Bacteria	Total No of Isolates Tested	No CRE Positive	% CRE Positive
Enterobacterales (total non-duplicates reported)			
Vancomycin Resistant Enterococci (VRE)			
Organism	Types	No VRE Positive	% VRE Positive
<i>Enterococcus spp</i> total			
	<i>Enterococcus faecalis</i>		
	<i>Enterococcus faecium</i>		
Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA)			
Organism	Types	No MRSA Positive	% MRSA Positive
<i>S. aureus</i> total			
	<i>S. aureus</i> (non-multi-resistant)		
	<i>S. aureus</i> (multi-resistant hospital-associated)		

- Alerts on specific antibiotic use can be generated and used to check the AMS process especially when restricted antibiotics are prescribed
- Time-sensitive automatic stop orders
- Electronic guidelines (via electronic mailings to prescribers, intranet)
- Adapted for mobile applications for antibiotic guidelines and other relevant documents.
- Point-of-care access to microbiological results from all units
- Clinical decision-support system

Section 12: Outpatient Antimicrobial Stewardship (OPAS)

Although the principles of AMS in the in-patient and out-patient sections of the health care facility are essentially the same, the approach to implementation may vary depending on the facility and the resources available to it. This manual is focused mainly on in-patients, but it was considered necessary to accommodate some principles and recommendations for out-patient AMS. The recommendations here may therefore apply to stand-alone clinics and casualties or those located in secondary or tertiary hospitals.

The outpatient AMS may be based on the 4 core elements of the CDC outpatient stewardship checklist for both clinician and facility (48).

12.1. Commitment

12.1.1. Leadership:

Health care facility leadership will create a multidisciplinary AMS team to collaborate on AMS activities, including representatives from clinicians, nursing, pharmacy, information technology, electronic health records, infection prevention, and quality improvement. AMS activities include;

- Regular meetings (monthly or quarterly)
- Provision of AMS guidelines, protocols, and defined prescribing standards and recommendations
- Tracking and reporting at least one aspect of antibiotic prescribing
- Making an AMS action plan and reviewing annually as needed
- Receiving feedback from clinicians about current AMS interventions.
- Reviewing the AMS plan document annually and revising as needed.
- Communicating prescribing standards to staff and providers.

The same facility AMS set up for in-patient programme can also serve the out-

patient section. There is no need for a dual AMS committee

12.1.2. Accountability:

Health care facility leadership will identify one physician leader to be responsible for AMS oversight and promotion. He/she will lead the AMS team. AMS responsibilities will be included in job description or performance review criteria.

12.1.3. A written commitment statement in support of AMS will be posted in the facility, visible to patients, families, and all staff.

12.1.4. AMS team will regularly communicate with all clinic staff to manage patients' expectations.

12.2. Action for Policy and Practice

These are intended to support appropriate prescribing practices by individual prescribers and to inform all staff about the importance of AMS. The actions should include;

- Evidence-based diagnostic criteria and Antibiotic policy and treatment guideline
- Policy to document the indication for antimicrobial prescription in the patient's case notes including the dose, duration, route of administration and frequency.
- Delayed prescribing and watchful waiting. This involves the supply of antibiotic prescription to a patient with clear instructions about when to commence the treatment in relation to their symptoms. It is useful for conditions that usually resolve without treatment but which can benefit from antibiotics if the condition does not improve.
 - Patient communication required when initiating a watchful waiting period include; diagnosis, suggestions for symptom relief (including any non-antibiotic medications), and instructions for follow-up.
- Provide communication skills training for clinicians through;
 - Annual communication skills training to enhance their ability to address patient concerns about prognosis, benefits and harms of antibiotics and management of self-limiting conditions,
 - To address clinician concerns about managing patient expectations for antibiotics.

12.3. Tracking and Reporting

- Track and report antibiotic prescribing for one or more high-priority conditions such as upper respiratory tract infection, acute bronchitis, sinusitis, pharyngitis and acute watery diarrhoea.
- Track and report the percentage of all visits leading to antibiotic prescriptions. This can be done as a point prevalence survey using the out-patient Global-PPS.
- Assess documentation of indication for antibiotic prescription in the patients' case note.
- List of staff who have completed communications skills training.
- Feedback on tracking of antibiotic prescribing for high priority conditions
- Monthly or quarterly AMS reports to the health care workers and health care facility leadership
- Antibigram

12.4. Education and Expertise

- Use effective communications strategies to educate patients and families about when antibiotics are and are not needed.
- Educate patients and families about the potential harms of inappropriate antibiotic treatment
- Provide patient education materials
- Provide continuing education activities for clinicians
 - Annual in-service training
 - Induction or orientation training for new staff

Section 13: Mentorship in AMS

Antimicrobial stewardship mentorship will contribute to capacity building and support towards the implementation of the ASP. The aim of the AMS mentorship is to improve knowledge, performance and skills of the AMSC and AMSTs in carrying out an effective ASP in various institutions.

The mentorship programme requires clear goals and objectives, as well as an agreement on the method and frequency of communication. Mentorship could be between individuals or between institutions/organisations or institutions/organizations and individuals. The mentor will be an expert in antimicrobial resistance and stewardship or an institution that is advanced in AMR/AMS practices (49).

The roles of a mentor are to motivate and;

- Advise and support the facility to develop multidisciplinary AMSC/AMST
- Increase the knowledge of the facility AMSC/AMST on AMR and AMS and develop action plan.
- Train the facility AMSC/AMST on the principles of rational AMU and AMS
- Train facility AMSC/AMST on how to monitor and evaluate AMS interventions using Global-PPS and other methods
- Assist facility AMSC/AMST in developing AMS policies and guidelines including antibiotic guidelines
- Support the health care facility in strengthening diagnostic stewardship or assisting in the analysis of microbiological investigations as the case may be.
- Advise facility AMSC/AMST on how to carry out communication and awareness programmes amongst staff
- Advise and guide facility AMSC/AMST on grant applications in order to promote researches on AMR and AMS

It is also essential to establish KPIs that should be used to measure the impact of the mentorship programme. Collection of both qualitative and quantitative data is important in the assessment of the impact of the mentorship. The key indicators that should be focused on are as follows;

- Engagement indicator: This will cover data collection on mentoring sessions, mentoring hours and actions taken
- Process indicator: This will include collecting data on the number of goals established and achieved, and personal satisfaction scores

AMS mentorship initiatives can be conducted following a step-wise pattern;

- Application by mentee institution to AMS mentor, for example CLIMIDSON, NASWOG
- Complete a pre-visit survey (for example with CLIMIDSON AMS checklist) including information about the facility's current ASP. This information will be critical to a successful onsite visit.
- Mentoring onsite visit: The mentor will work with the AMS Team leader and other members of the AMS Team by phone in advance of and following the onsite visit.

- The onsite visit will feature an in-depth evaluation of the facility's AMS programme, practices, challenges and opportunities for improvement, and proposed activities to enhance patient care. Presentations can be made during the visit and specific activities during the visit will vary according to mentee institution goals and needs but may include meeting with the AMS Team and other teams (such as IPC and quality improvement teams), as well as reviewing protocols, policies and procedures.
- Following the site visits, the mentor will provide a customised report of proposed interventions to improve the facility ASP.
- Report outcomes: Following a visit, the facility (mentee) is expected to implement AMS improvement project and report key outcomes approximately 6 months after the onsite visit.

Section 14: System Building and Sustainability Plan in AMS

The sustainability plan in AMS for health care facility requires that important factors that can influence programme implementation and sustainability be identified (50). It is important to recognise ASP as a behaviour change programme, and that changing prescribing habit cannot occur over-night (51). Implementing and sustaining ASPs in health care facilities will be facilitated by;

- Having an ASP sustainability plan
- Continuous support of the management in terms of human, material and financial resources.
- Facility management need to recognise AMS as a quality improvement programme and include it in their annual performance indicators.
- Having leaders who are passionate and knowledgeable on the issues of AMR/AMS.
- Regular and periodic performance of Global-PPS as integral part of M & E to measure progress and success.
- Prioritising interventions that are easier to perform such as supplemental strategies like education, guideline development, IV-to-PO switch, de-escalation, dose optimisation, and microbiology strategies. Start small and then scale up the interventions.
- Ensuring ongoing education training with feedback of relevant personnel.
- Should be all inclusive: All stakeholders should be involved.
- Provision should be made for both

internal and external mentorship

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