

# Significance of antimicrobial stewardship programme

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**Abstract** Antimicrobial resistance is an increasing threat in hospitalised patients and many of those are multidrug-resistant organisms. Antimicrobial Stewardship Programme (AMSP) has become a critical responsibility for all health-care institutions and antimicrobial prescribers. This aims mainly to optimise the antimicrobial use among patients to reduce antibiotic resistance, improve patient outcomes, safety and provide cost-effective therapy. This review describes the significance of AMSP, goals, strategies and key essentials for AMSP.

**Keywords:** Antibiotic policy, antimicrobial resistance, antimicrobial stewardship programme

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## INTRODUCTION

Antimicrobial resistance (AMR) is a rising threat in hospitalised patients and inappropriate therapy with antimicrobials is known to adversely affect the outcomes. With the emergence of AMR, several organisations have identified antimicrobial stewardship programme (AMSP) as a critical responsibility in today's health care environment.<sup>[1,2]</sup>

Problems associated with excessive use of antibiotics were recognised shortly after their introduction in the 1940s. Further introduction of new antibiotics during the next decades saw an increasing and often inappropriate usage of these agents. Approximately, 60% of hospitalised patients receive at least one dose of an antibiotic drug during their hospital stay. Of this, nearly 50% of it is inappropriate or unnecessary.

These programmes definitely minimise the inappropriate usage of antibiotics, improve the outcome of the patients,

provide cost-effective therapy and curtail emergence of AMR. Antimicrobial stewardship has become a critical responsibility for all health-care institutions and antimicrobial prescribers.

Implementation of antimicrobial stewardship is very crucial as AMR is a rising threat globally. There is a dramatic increase in the AMR in the recent days and many of those are multidrug-resistant. The multi-drug resistance organisms are prevalent in each and every country though the extent and the severity of the problem vary.

## DEFINITION OF ANTIMICROBIAL STEWARDSHIP

The Infectious Diseases Society of America (IDSA) broadly defines antimicrobial stewardship as a 'rational, systematic approach to the use of antimicrobial agents to achieve optimal outcomes'.<sup>[1]</sup> It is primarily to optimise antimicrobial use and reduces the emergence of antibiotic resistance, improve patient outcomes, and provide

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cost-effective therapy. Education is an important feature of these programmes, and it is considered essential to teaching the knowledge which is necessary for effective stewardship programme.<sup>[1-3]</sup> Several educational interventions have been shown to improve antimicrobial prescribing practices and infection control.<sup>[4-7]</sup>

The Centers for Disease Control (CDC) has defined 'Antimicrobial stewardship' as shown in Table 1.<sup>[8]</sup> At health care facility level, antibiotic stewardship has to provide the importance of AMSP and challenges while implementing the programme in the hospital and their solutions and also provides the necessary recommendations to the clinicians in health care settings to improve the quality of antibiotic prescribing reduce the emergence of AMR and improve the patient outcomes. Antimicrobial stewardship also includes implementation of an AMSP and continuous monitoring and analysis of antibiotic utilisation to track changes in antibiotic resistance and to monitor the effects of containment strategies. The intent of this review is to throw limelight on the factors that are essential for creating an effective AMSP in a health care facility.

### Goals of antimicrobial stewardship programmes

Four main goals of AMSP are restriction of antibiotics, improvement of patient outcome and safety and finally to ensure cost-effective antimicrobial therapy. The first goal being restriction of antibiotics both at the individual patient level and at the community level results in the reduction of antibiotic pressure which, in turn, prevents the development of AMR. Restriction of antibiotics can reduce colonisation or infection with resistant bacteria. Improvement in patient outcome can be achieved by improving infection cure rates, reducing surgical infection rates and reducing mortality and morbidity.

To improve patient safety can be attained by reduction in antimicrobial utilisation, without increasing mortality, morbidity or infection-related readmissions. Moreover, also by restricting the use of 'high-risk' antibiotics,<sup>[9]</sup> colonization or infection with *Clostridium difficile* can be controlled. The final goal of antibiotic stewardship is to ensure cost-effective antimicrobial therapy, without compromising the quality of care.

There are two major strategies to antimicrobial stewardship which include front and back strategies. Most successful programmes generally implement a combination of both.

The key requirements of implementation of AMSP – the six steps of AMSP are depicted in Table 2.

**Table 1: CDC definition of antimicrobial stewardship**

The right antibiotic
For the right patient
At the right time
With the right dose, and
The right route causing
The least harm to the patient and future patients

CDC=Centers for Disease Control

**Table 2: Key steps for implementing an antimicrobial stewardship programme**

1. Administrative support (leadership)
2. Assess the situation
  - Supporting infrastructure
  - Supporting workforce
3. Set up AMS team
4. Frame antimicrobial policy - Hand book with system-wise indications
5. Implement AMS strategies
  - Front-end strategies - formulary restrictions
  - Back-end strategies - antimicrobial review methods (prospective audits and pharmacy driven AMSP)
6. Educate and train

AMS=Antimicrobial stewardship; AMSP=AMS Programme

#### *Step 1: Administrative support (leadership)*

The most important prerequisite for implementing AMSP is strong administrative support. Role of ID physicians, microbiologists or infection control specialist to establish AMSP is likely to be unsuccessful without active involvement by hospital leadership. Hospital administrator should play a front role and show leadership quality while implementing AMSP and publicly committed to the programme. Regarding programme funding, adequate support form hospital leadership must be there for effective programme, since these programmes do not generate revenue although they may result in significant cost savings. In addition, hospital administrators should provide the liberty, freedom and power to the members of antimicrobial stewardship team to execute the policy.

#### *Step 2: Assess the situation*

Availability of tools like rapid microbiology diagnostic tools (automation-Culture by BACTEC or BacT/Alert), identification by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), antibiotic susceptibility testing and biomarkers (C-reactive protein, procalcitonin and interleukin-6) as diagnostic support is recognised as a key interventions in implementation of antimicrobial stewardship in hospitals. Monitoring of serum antibiotic level by high-performance liquid chromatography (HPLC) and monitoring antibiotic quality by HPLC, etc., is performed to assess the availability of pharmacodynamics support. Next, workforce support availability has to be assessed. AMSP team must include ID physician (dedicated), fully functional hospital infection control (HIC) committee, designated infection control

officer, stewardship nurses and clinical pharmacists. 24/7 reporting facility for culture and sensitivity by the Department of Microbiology must be accessible. In addition, hospital information system, computerised order-entry and decision support systems must be available.

*Step 3: Set up antimicrobial stewardship team*

Antimicrobial stewardship team (AMS team) is a multidisciplinary committee who will be involved in executing the interventions (both front- and back-end strategy as described later) and evaluating the adherence to AMSP. The members of AMS team include ID physician, stewardship nurses, HIC officer and nurses, microbiologist trained in clinical aspects, pharmacist with expertise in infection, quality improvement/patient safety managers and pharmacy department.

*Step 4: Frame antimicrobial policy*

Every hospital should frame their own hospital antibiotic policy in the form of an 'Antimicrobial stewardship guide'. Common consensus has to be made after preparing the treatment regimen; the major departments involved for each system should initiate discussion among intraunit, intra and interdepartmental to arrive at a common consensus. The AMS team members should coordinate via mail, personal and subgroup meetings with various departments to arrive at the common consensus. Every stakeholder's opinion and consensus should be taken and hence that once the AMS guide is implemented, maximum adherence can be obtained.

*Step 5: Implement antimicrobial stewardship strategies*

Front-end strategies comprise formulary restrictions and antibiotic cycling.<sup>[10]</sup>

Formulary restriction is an implementable front-end strategy. A list of restricted antimicrobial agents has to be determined and criteria for their use which is monitored regularly through audit and feedback to the clinicians.

Although sounds more attractive and appears to be the most ideal way to achieve antimicrobial stewardship practically implementing formulary restrictions is not that easy. It creates a lot of confusion as it directly impacts the clinician's freedom to choose antimicrobials. More so availability of the concerned authority to give approval all the time further complicates the problem, especially in emergency situations. Hence, instead of surveillance on the usage of all antibiotics, monitoring higher-end antibiotics is a more practical and implementable strategy. Antimicrobials can be classified into restricted, limited access and unrestricted groups [Table 3].<sup>[11]</sup> All antimicrobial prescriptions must be countersigned in duplicates by the consultants or faculty in charge of the unit, not by the post-graduate students or residents. The pharmacy will keep one prescription for its record purpose and will hand over the second prescription to the AMS team. The AMS team will review the antibiotic prescription and give a second opinion by countersigning on it. Further continuation of the antimicrobial use will depend on the approval from the AMS team. The duration to obtain the approval from AMS team can vary depending on the class of antimicrobials.

Antibiotic cycling or antibiotic rotation refers to the development of strategies using scheduled rotation of antimicrobials to minimise the emergence of bacterial resistance. Theoretically, when an antimicrobial is out of rotation (i.e, off the cycle) during the periods and its use is minimal, antibiotic pressure will be removed; as a result resistance to particular antibiotic will decrease. These programmes typically target Gram-negative resistance and are limited to the intensive care unit setup. Antibiotic cycling or antibiotic rotation has poor compliance.

Back-end strategies include antimicrobial review methods and providing timely feedback. Antimicrobial review methods comprise pre-authorisation or prospective audit and feedback. Pre-authorisation is required for targeted

**Table 3: Proposed formulary restriction<sup>[10]</sup>**

Restricted antimicrobials	Limited access antimicrobials	Unrestricted antimicrobials
Colistin Carbapenem Tigecycline	Teicoplanin Vancomycin Daptomycin Linezolid Third- and fourth-generation cephalosporins	First- and second-generation cephalosporins Co-trimoxazole Azithromycin Clarithromycin Fluoroquinolones
Pharmacy supply of >1 day requires prior approval by AMS team (for second opinion) pharmacy supply in duplicate before dispensing. Pharmacy will send the prescription for a compulsory second opinion from AMS team within 24 h	Pharmacy supply of >3 days requires prior approval by AMS team (for the second opinion) Pharmacy supply need a prescription in duplicate before dispensing. Pharmacy will send the prescription for compulsory second opinion from AMS team within 72 h	Pharmacy supply does not require AMS team approval. However, retrospective review of antimicrobial use will be done by AMS team from time-to-time

AMS=Antimicrobial stewardship

antimicrobials which are used to treat multidrug resistance bacterial infections, which means clinician requires prior approval before they are prescribed. Prospective audit and feedback or combined with pre-authorisation can be an alternate strategy. The prospective audit allows the engagement of the prescribing clinicians to optimise antimicrobial treatment. Both methods can decrease antibiotic misuse and minimises the emergence of resistance. Hospitals should choose one or both of these methods as part of their programme based on their local resources and expertise.<sup>[12]</sup> Although difficult to perform, it is the most effective strategy to implement AMSP. This is done at two stages. First, during the clinical rounds, an exhaustive and thorough intra unit review of various aspects of antimicrobial use can be carried out. This should be further reviewed (for a second opinion) during stewardship rounds which should be carried out by AMS team members. Various aspects of antimicrobial use which can be reviewed are indication for antibiotic and compliance with policy, appropriate choice of antibiotic, dose, route and duration, duplicative therapy (potential overlapping spectra), revision of therapy based on microscopy or other rapid tests (polymerase chain reaction), timely de-escalation or escalation based on antimicrobial sensitivity report, potential for conversion from Intravenous (IV) to oral route, requirement for therapeutic drug monitoring, adverse events related to antibiotic usage, any potential drug interactions, drug allergy if any, requirement for renal adjustment and need for extended infusion.

Back-end strategies, although more labour-intensive, are extensively practicable, well approved by clinicians. These strategies contribute a good tool for educating and training health-care professionals. These probably improve and sustain the overall quality of antimicrobial prescribing.<sup>[13]</sup>

*Step 6: Educate and train*

Similar to any other health-care programme, AMSP also needs continuous training, motivation and assessment of the health-care providers. Developing antimicrobial

stewardship is a behavioural change within the person. Hence, adequate motivational education must bring in such change. Persons who should receive education in hospitals are stake holders, medical practitioners (physicians and surgeons), pharmacists and nurses. AMSP should be brought in as a part of undergraduate, internship and post-graduate curriculum. Educating patients and the general public are also essential and it may reinforce hospital education training. The aspects should be addressed in training are general hygiene, hazards of antibiotic use without prescription and mainly discouraging over the counter sale.

The content of education includes primary knowledge of infection control and prevention, microbiology, significance of quality prescribing to tackle AMR and best practices to support safe and effective prescribing. Training should be delivered by the AMSP team members. However, the administrators should take part active role and address the audience from time to time to increase the seriousness of the training.

The evaluation process is very crucial in the education and training programme. Without assessment, no educational training can be effective. Various assessment tools such as attendance forms, completion certificates, questionnaires and case scenario-based test can be used for the competency assessment of the trainee from time to time.

**NEW GUIDELINES AT A GLANCE<sup>[14-17]</sup>**

Pre-authorisation and prospective audit and feedback should form the base of an AMSP as shown in Table 4. The expert panel behind the guidelines included the following components to establish the development and implementation of an effective programme depicted in Table 5.

**Evaluation of antimicrobial steward programme**

Monitoring of prescribing is a key component to evaluate the impact of stewardship intervention on clinical practice. It is said that ‘If you cannot measure it, you cannot improve

**Table 4: Comparison of pre-authorisation and prospective audit and feedback strategies for antimicrobial stewardship**

	Advantages	Disadvantages
Preauthorization	Decreases the initiation of inappropriate or unnecessary antimicrobials Prompt review of prior cultures and the clinical data at the time of treatment initiation	May delay the treatment Perceived loss of prescriber autonomy May increase the use of and resistance to an alternative agent
Prospective audit and feedback	Reduces cost due to high-cost antimicrobials Education for clinicians Provides more clinical data for recommendations Maintains prescriber autonomy	The effectiveness depends on the approver’s skill Labour intensive May be difficult to identify patients with inappropriate therapy Success will depend on how feedback is delivered to the prescribers

**Table 5: New guidelines at a glance**

1. Pre-authorisation or prospective audit and feedback (strong recommendation, moderate-quality evidence) [Table 4]
2. Syndrome-specific interventions (weak recommendation, low-quality evidence)
3. Rapid diagnostic testing  
Respiratory specimens (weak recommendation, low-quality evidence)  
Blood cultures (weak recommendation, moderate-quality evidence)
4. Restricted usage of antibiotics that have a high risk of *C difficile* infections (strong recommendation, moderate-quality evidence)
5. Antibiotic time-outs or other strategies to motivate clinicians to review antibiotic regimens routinely (weak recommendation, low-quality evidence)
6. Embodiment of computerised systems, at the time of prescribing that are integrated into the electronic health record to improve antibiotic prescribing (weak recommendation, moderate-quality evidence)

**Table 6: Methods for evaluation of antimicrobial stewardship programme**

1. Policy adherence indicator (process indicator)  
AMS audit
2. Antibiotic usage-outcome indicator  
Antibiotic usage surveillance DDDs and DOTs
3. Antimicrobial resistance - outcome indicator  
AMR surveillance - Manual and WHONET application
4. Clinical outcome indicators-  
morbidity and mortality
5. Financial outcome indicators

DDD=Daily defined doses; DOTs=Daily observed therapy;  
AMS=Antimicrobial stewardship; AMR=Antimicrobial resistance

it'. There are various ways the impact of AMSP is evaluated in Table 6.

To conclude, prior intimation of using broad-spectrum antibiotics and review after 2 or 3 days of treatment shall form the keystone of AMSP's to provide the right drug is prescribed at the right time for the right diagnosis. The ultimate goal is to reduce the emergence of AMR and preserve current and future antibiotics, although improving patient safety and reducing health-care costs are important concurrent aims.

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### Conflicts of interest

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