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स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय एवं
महानिदेशक, आई सी एम आर

Prof. (Dr.) Balram Bhargava, Padma Shri
MD, DM, FRCP (Glasg.), FRCP (Edin.),
FACC, FAHA, FAMS, FNASc, FASc
Secretary to the Government of India
Department of Health Research
Ministry of Health & Family Welfare &
Director-General, ICMR

भारतीय आयुर्विज्ञान अनुसंधान परिषद
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स्वास्थ्य एवं परिवार कल्याण मंत्रालय
वी. रामलिंगस्वामी भवन, अंसारी नगर
नई दिल्ली – 110 029 (भारत)
Indian Council of Medical Research
Department of Health Research
Ministry of Health & Family Welfare
V. Ramalingaswami Bhawan, Ansari Nagar
New Delhi - 110 029 (INDIA)

Preface

Antimicrobial resistance (AMR) is a major public health challenge, which is recognized as high priority area by the Government of India. The increasing consumption of antibiotics is one of the key drivers of antimicrobial resistance seen in bugs of public health importance. Irrational prescription of broad-spectrum antibiotics, poor regulations around sale of antibiotics, self-medication, lack of education and awareness regarding responsible use of antibiotics have been identified as some of the key factors driving antimicrobial resistance in our country. The 'National Health Policy' (2017), addresses antimicrobial resistance as one of the key issues and prioritises development of guidelines regarding antibiotic use, limiting the over-the-counter use of antibiotics, restricting the use of antibiotics as growth promoters in livestock, and pharmaco-vigilance including prescription audit inclusive of antibiotic usage in the hospital and community.

Hospital based programs dedicated to improving antibiotic use, commonly referred to as Antimicrobial Stewardship Program (AMSP) have been found helpful in improving the quality of patient care and safety through increased infection cure rates, reducing treatment failures, and increasing the frequency of correct prescription for therapy and prophylaxis. Implementation of an effective AMSP requires a multidisciplinary approach involving a variety of experts. Unfortunately, most of hospitals in India lack structure and process of AMSP. Recognizing the importance to create AMSP structures in health care institutions in the country, ICMR has initiated AMSP activities by developing AMSP curriculum, conducting workshops and developing AMSP research projects. I am pleased that ICMR has developed AMSP guidelines, which will be of immense help to the hospitals to create their own AMS program. We are thankful to all the experts who contributed to the guidelines. We hope that this guideline will inform, encourage and support health care institutions to initiate the implementation of antimicrobial stewardship initiatives, as well as combating antimicrobial resistance.

Prof. Balram Bhargava
Secretary, Department of Health Research
Director General, Indian Council of Medical Research

CONTENTS

1. Introduction

Antimicrobial resistance (AMR) has emerged as a major public health problem all over the world. Infections caused by resistant microbes fail to respond to treatment because of limited therapeutic options resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, with increased numbers of infected people in the community. This in turn exposes the general population to the risk of contracting a resistant strain of microorganisms. As they become resistant to first-line antimicrobials, the forbidding high cost of the second-line drugs may result in failure to treat these diseases. Most alarming of all are the diseases caused by multidrug-resistant microbes, which are virtually non-treatable and thereby contributes to a "post-antibiotic era". Inappropriate antimicrobial use is associated with the emergence of resistance. In addition, the misuse of antibiotics contributes to the growing problem of antimicrobial resistance and is considered as a most serious threat to public health.

An effective antimicrobial stewardship program with appropriate

- drug selection
- dosing
- route of administration and
- duration of antimicrobial therapy

coupled with comprehensive infection control program has shown to limit the emergence and transmission of antimicrobial resistant pathogens. Patients who are exposed to inappropriate/unnecessary antibiotics are placed at risk for serious adverse events with no clinical benefit. Moreover, to restrict the misuse or unnecessary antibiotic prescription, the Policy Statement on Antimicrobial Stewardship by SHEA, IDSA, and PIDS strongly encourages healthcare institutions to develop stewardship programs. In 2015, the English surveillance programme on antimicrobial utilisation and resistance (ESPAUR) have published a report on prescribing patterns of antimicrobials in different healthcare settings between 2010 and 2014. This showed that i) the total consumption of antibiotics in primary and secondary care increased from 21.6 to 23.0 defined daily doses (DDD)/ 1,000 inhabitants/day between 2011 and 2014, ii) 11.7% of increased antibiotic prescription

in in-patient, iv) 8.5% of increased prescription in hospital outpatients settings. Overall, 6% of increased antibiotic prescription in both community and hospital was seen.

In 2006, CDC guideline "Management of multi-drug resistant organism in health care setting stated that emergence of multi-drug resistance can be controlled in paying great attention to judicious antimicrobial use. Similarly, in 2009, CDC launched "Get Smart for Healthcare Campaign" to promote improved use of antibiotic in in-patient settings. In 2015, the White House published the National Action Plan for Combating Antibiotic-Resistant Bacteria with five main goals to: 1) curb antibiotic resistance, 2) strengthen antimicrobial resistance surveillance, 3) advance development of rapid diagnostics, 4) accelerate research targeting novel therapeutics, and 5) collaborate with other countries to strengthen prevention, development, and surveillance efforts

Antimicrobial stewardship program (AMSP) helps clinicians to improve:

- The quality of patient care
- Patient safety
- Reduced treatment failures
- Increasing frequency of prescribing appropriate therapy and prophylaxis
- Reduces the CDI rates
- Reduces antimicrobial resistance
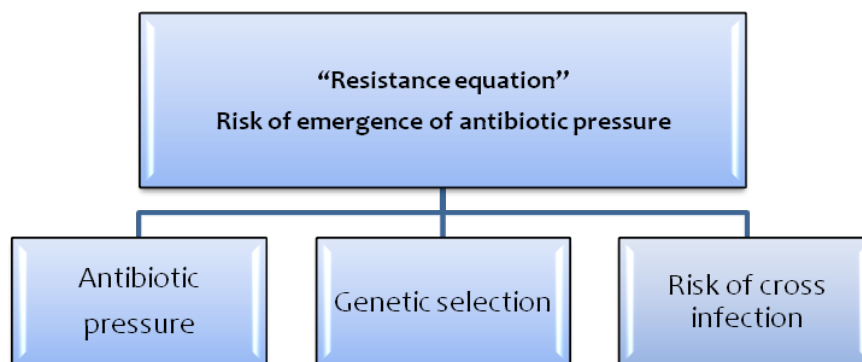
Figure 1: Emergence of resistance and hospital cross-infections

Table 1. Inappropriate use of antimicrobials leads to the following:

1. Causal associations between antimicrobial use and emergence of antimicrobial resistance
1. Changes in antimicrobial use are paralleled by the prevalence of resistance
2. Antimicrobial resistance: more prevalent in HA infection than CA infection
3. Health care–associated infections are more likely to be caused by resistant strains especially in those who have received prior antimicrobials
4. Hospitals that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use
5. Patient exposed to longer duration of antimicrobials have an increased risk of colonization with resistant organisms

2. Mortality rate correlates with the presence of multi drug resistant organisms
1. Association between development of antimicrobial resistance in *Staphylococus aureus,* Enterococci, gram negative bacilli and mortality
2. Enterococcal infections have been associated with mortality rates exceeding 30%
3. A Meta-analysis of published studies have found that patient with methicillin resistant *Staphylococcus aureus* (MRSA) bacteremia had a increased risk of mortality compared with methicillin susceptible *Staphylococcus aureus* (MSSA)

3. Stop killing the beneficial bacteria
1. Consensus about antibiotics focus on bacterial resistance but permanent changes to our protective flora have more serious consequences

4. Collateral damage
1. Average child receives 10-20 courses of antibiotics before 18 years of age
2. Antibiotic affect our resident microbiota and may not fully recover after a course of antibiotics
3. Over use of antibiotics may be contributing to obesity, DM, IBD, allergies and asthma

5.	**Why we need to improve antibiotic use**
1.	Antibiotics are the only drug where use in one patient can impact the effectiveness in another
2.	Improving antibiotic use improves patient outcome and saves money
3.	Antibiotic misuse adversely impact patient and society
4.	Antibiotics are misused across the continuum of care
5.	Inappropriate use of antibiotics in animals
6.	Improving antibiotic use is a public health imperative-WHO considers AMR an emerging threat to global health

6.	**What can the individual physicians do**
1.	Obtain appropriate cultures before starting antibiotic
2.	Review antibiotic use after 48 – 72 hours : does it need to be continued?
3.	Stop antibiotic in patient with alternative non-infectious diagnosis
4.	Optimize dosing and duration of antibiotic therapy
5.	Avoid unnecessary use, especially in viral upper respiratory tract infections (75 %)

Antimicrobial prescribing facts: The 30% Rule

- 30% of all hospitalised in-patient at any given time receive antibiotics
- Over 30% of antibiotics are prescribed inappropriately in the community
- Up to 30% of all surgical prophylaxis is inappropriate
- 30% of hospital pharmacy costs are due to antimicrobial use
- 10-30% of antimicrobial cost can be saved by antimicrobial stewardship programs

Antimicrobial resistance in health-care associated infections (HAI)

AMR is of great importance in health-care settings. Further, there is an association between the development of resistance and an increase in mortality, length of hospitalization and the cumulative cost of health care, which attributes to

inappropriate, inadequate or delayed therapy. In 2010, WHO recognized antimicrobial resistance as one of the three great threats to human health.

About 50% of antimicrobial use has been found to be inappropriate (WHO). Hence, strategies to prevent the emergence and spread of health-care associated antimicrobial-resistant organisms are essential. Implementation of an effective strategy need to include components of:

- Effective clinical antimicrobial stewardship
- Meticulous hand hygiene
- Surveillance and monitoring of antimicrobial resistance, especially MDR organisms

Antimicrobial stewardship must include the evidence based education of physicians about appropriate drug, dose, dosing interval and duration. De-escalation and optimization campaigns should also be undertaken to educate and inform the public about the specific indications for antibiotic use, origin and spread of antimicrobial resistance and what needs to be done to control it.

Availability of new antimicrobials

The situation in the development and approval of newer antimicrobial agent is not encouraging. The solution to the current approaches to antimicrobial resistance is to preserve the effectiveness of the drugs which are presently available by antibiotic stewardship and to maximize hospital infection-control practices to limit the spread of resistance.

"Drug resistance follows the drug like a faithful shadow"

- Paul Erhlich 1854-1915

2. Definition of antimicrobial stewardship

Coordinated intervention is designed to improve and measure the appropriate use of antimicrobial agents, by promoting the selection of optimal antimicrobial drug regimen including dosing, duration of therapy and route of administration (SHEA, IDSA, PIDS – April 2012).
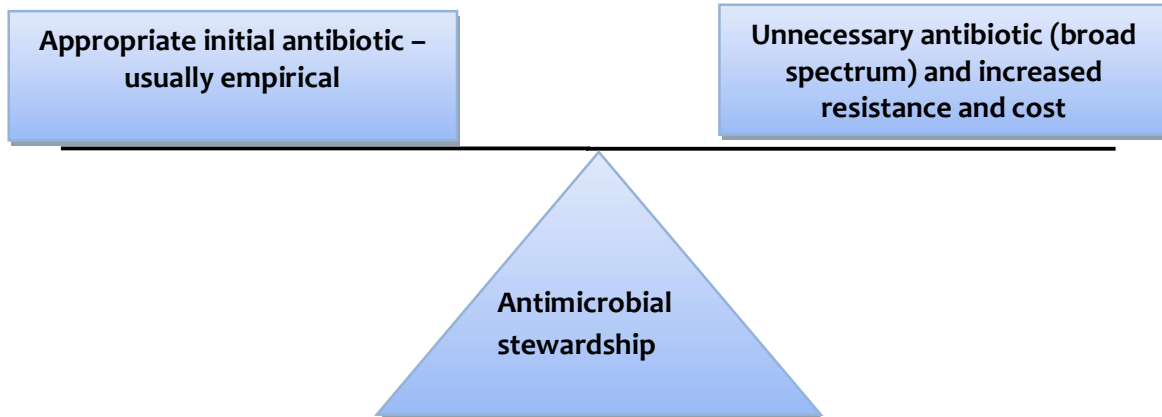
A Balancing ACT

Figure 2: Balancing act of antimicrobial stewardship program in healthcare settings.

3. Purpose of antimicrobial stewardship program

3.1 Primary goal

To optimize safe and appropriate use of antibiotics to improve clinical outcomes and minimize adverse effects of antibiotics.

3.2 Secondary goal

- To reduce health care costs without adversely impacting quality of patient care

- To reduce the incidence of antibiotic induced collateral damage

4. Strategic approaches to antimicrobial stewardship

1. Appropriate antimicrobial therapy.
2. Optimizing antimicrobial prophylaxis for operative procedures.
3. Developing and implementing ~~an~~ antibiotic policies and standard treatment guidelines (STG).
4. Prospective auditing and providing feedback and timely intervention in streamlining the antibiotic prescriptions.
5. Formulary restriction/ pre-authorisation.
6. Improving antimicrobial prescribing by educational and administrative means.

To achieve these, a comprehensive approach through a hospital policy on the rational use of antibiotics is essential.

5. Essential elements of antimicrobial stewardship

5.1 Active strategy

5.2 Supplemental strategy

5.3 Other strategies

5.3.1. Information technology

5.3.2. Role of Microbiology laboratory

5.3.3. Monitoring of process and outcome measurement

5.3.4 Comprehensive multidisciplinary antimicrobial management program

The overall essential components of antimicrobial stewardship are given in fig. 3.

5.1. Active strategies

5.1.1. Prospective audit with feedback intervention

This intervention improves antibiotic use and is a core component of stewardship program. This is done by optimizing drug selection, dose, duration & route of therapy. It also involves concurrent review of patients who receive antimicrobials. This is a process which involves active review of a patient on antibiotics, by an ID physician. Cochrane database of systematic review decreased DOT by use of this intervention.

In a study, the prospective audit with intervention and feedback resulted in 22% decrease in the use of parental broad spectrum antimicrobial despite increase in patient acuity over a seven year period. They also demonstrated decrease in rate of *Clostridium difficile* infections, nosocomial infections caused by drug resistant Enterobacteriaceae. A Cochrane review analysed 14 RCTs and reported high certainty evidence by using this intervention in antibiotic prescription. This systematic review and meta-analysis showed reduction in the duration of antibiotic treatment from 11 days to 1.9 days.
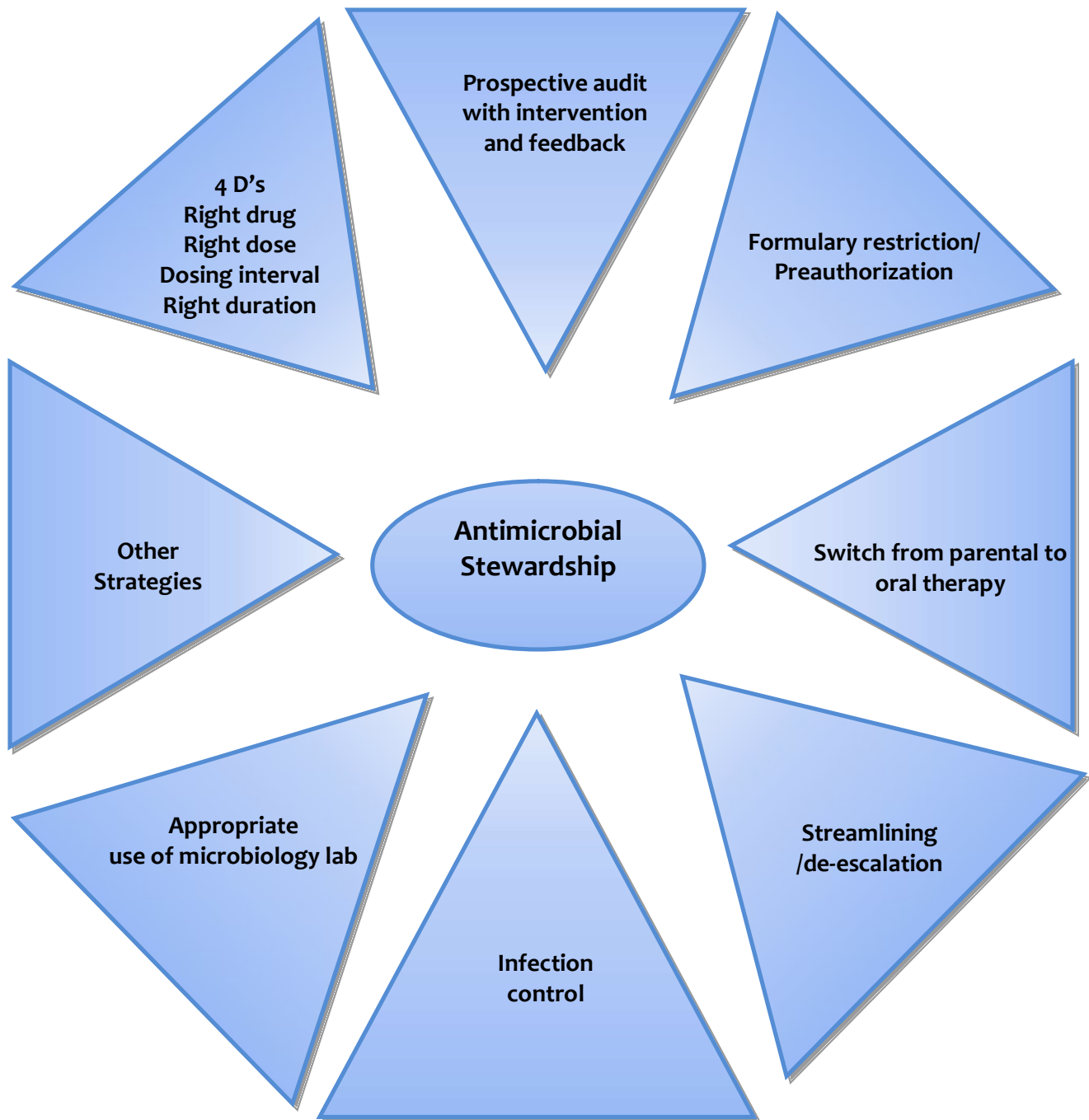
Figure 3. Components of antimicrobial stewardship. However the highest quality of evidence in prospective audit with intervention and feedback and formulary restriction/pre-authorization.

Stewardship program can decide to include one strategy or a combination of both strategies based on the availability of the facility specific resources for consistent implementation. Advantages of this strategy include the ability to provide education at the point of intervention and customization of the intervention to any patient group, drug, or syndrome. For example, all patients treated with broad spectrum therapy based on the customized recommendations for streamlining or discontinuation. This intervention did not change the hospital antibiogram but resulted in a 28% decrease in the use of broad-spectrum agents in that particular institution. At another centre, a multidisciplinary team made customized antibiotic recommendations and calculated a cost savings of $2602 per intervention. A disadvantage of audit and feedback is increased time and clinical expertise compared to other interventions.

5.1.2 Formulary restriction/preauthorization

Formulary restriction/ preauthorization are an effective method to control antibiotic use and cost. It could also help in decreasing the antimicrobial resistance. It also utilizes the pharmacist and therapeutic committee or equivalent group. Both of these strategies are evidenced based on the strategies which substantially reduce antibiotic utilization. Similarly, a Cochrane review has reported reduced antibiotic prescription and reduced antimicrobial resistance in in-patients with the use of this intervention.

A survey of 22 institutions found that those that implemented a program of carbapenem restriction experienced a statistically significant reduction in both carbapenem use and *Pseudomonas aeruginosa* resistance to carbapenems compared to those institutions that allowed unrestricted use of carbapenems. Restrictions have also been effective in prevention of *Clostridium difficile* infection (CDI). The major risk event for CDI is the disruption of normal enteric flora by antimicrobial agents. A study has demonstrated that the use of a bundled set of interventions including pre-authorization resulted in 41% reduced targeted antibiotic use and 71% reduced incidence of nosocomial CDI over 5 years. Similarly, an outbreak of severe CDI was controlled, after restrictions of high-risk antimicrobials.

The major drawback to strategies centered on antibiotic restriction and pre-authorization is that antibiotic use is driven to other agents that select for resistance. For example, Rahal and colleagues decreased cephalosporins use to 80% through using restrictions and noted a 44% decrease in ESBL-producing *Klebsiella*. Likewise, increased imipenem use is associated with the high incidence of 69% imipenem-resistant *P. aeruginosa*. The phenomenon of restriction driving use to another agent has been described as 'squeezing the balloon' and may mitigate some or all of the benefits of a restrictive strategy. Another disadvantage of these strategies is that they may not be well accepted and ordering physicians may attempt to circumvent them.

5.2 Supplemental strategies

5.2.1. Didactic education

Education is the most frequently employed intervention and is considered to be an essential element of any program designed to influence prescribing behavior. Education effects include conference presentations, student and house staff teaching sessions, provision of written guidelines or e-mail alert. However, education alone, without incorporation of active intervention is only marginally effective and has not demonstrated a sustained impact.

Passive educational activities such as lectures or informational pamphlets should be used to complement stewardship activities. Academic medical centers and teaching hospitals should integrate education on fundamental antibiotic stewardship principles into their pre-clinical and clinical curricula. During the period of active intervention, 25% of antimicrobial orders were modified, which improves compliance resulting in a significant increase in microbiologically based prescribing.

Antibiotic stewardship programs should provide regular update on antibiotic prescribing, antibiotic resistance and infectious diseases management that addresses both national and local issues. Sharing facility specific information on antibiotic use is a tool to motivate improved antibiotic prescribing practices. There are many options for providing education on antibiotic use including presentations, posters and flyers, newsletter or electronic communication to staff. A variety of web based education

resources are available, that can help to facilitate education, development of AMSP programs.

5.2.2. Facility specific clinical practice guidelines for common infectious diseases syndrome

Facility specific clinical practice guidelines and algorithms can be an effective way to standardize prescribing practices based on the local epidemiology. Most published studies of clinical practice guidelines have involved pneumonia including community acquired pneumonia in adults, children and health care associated pneumonia. Several of these studies recommended interdisciplinary guidelines along with the multi-faceted dissemination and implementation strategies to increase awareness. Such strategies included guideline dissemination in electronic or hard copy formats, provided education, audit and feedback of prescribing practices, checklist and incorporation of recommendations into electronic order sets.

Implementation of facility specific guidelines have included statistically significant increases in likelihood of adequate initial therapy, use of narrow spectrum antibiotic regimen, earlier switch from iv to oral therapy and shorter duration of therapy without any adverse effect on other clinical outcomes. Interventions to maintain guideline adherence overtime may be necessary and intended outcome should be monitored.

5.2.3. Patient specific clinical practice guidelines for common infectious diseases syndrome

AMSP intervention for patient with specific infectious diseases syndrome can be an effective way to improve prescribing activities. To reduce the use of broad spectrum therapy and shorten the duration of treatment with uncomplicated SSTIs in adults, intervention was developed to include dissemination of treatment algorithm, electronic order sets and quarterly feedback to providers of compliance with the guidelines.

A study including 169 adults demonstrated 3 day reduction in the length of therapy, 30% reduction in broad spectrum antibiotic prescribing and 0.3 % reduction in clinical failure by using this intervention. Another study included patients with CAP have increased the proportion of patient receiving appropriate therapy from 59.4 % to 93.4 %.

5.2.4. Guidelines and clinical pathways

The development of standard treatment guidelines (STG) should be based on cumulative antibiogram of organisms, antimicrobial policy, surveillance on antimicrobial resistance, antibiotic consumption data and hospital acquired infection (HAI). These STG should contain disease/ condition specific intervention based on evaluation, diagnostic studies, treatment/prevention. Treatment of infectious disease should be based on evidence based electronic data (published studies) and level of recommended evidence (Table 2).

Clinical practice guidelines are being produced with increasing frequency, with the goal of ensuring high-quality care. Antimicrobial stewardship programs can facilitate multidisciplinary development of evidence-based practice guidelines that incorporate local microbiology and resistance patterns. Based on the level of evidence, IDSA/SHEA recommendations are given in Table 3.

Table 3: Benchmarking in expectations and recommendations from Joint commission and IDSA/SHEA guidelines

Recommendations	Joint commission (IDSA/SHEA)	IDSA/SHEA
Pre-authorization	√	√
IV to oral conversion	√	√
Care of patients with C .diffcile	√	√
Formulary restriction	√	√
Assess appropriateness of antibiotic use in specific indication (CABP, ABSSSI, UTI)	√	√
PK monitoring services – aminoglycoside and vancomycin	-	√
Minimise treatment duration	-	√

IDSA/SHEA (2016) Recommendations (Any Level of Evidence)

- Provider led antibiotic review
- Computerised decision support
- Alternative dosing strategies for beta-lactams
- Rapid viral testing for respiratory pathogens
- Penicillin skin testing
- Stratified antibiogram
- Rapid diagnostic blood cultures
- Procalcitonin in ICU

The greatest challenges in implementing antimicrobial stewardship in hospitals settings includes i) clinician unaware of STG, ii) clinician aware of STG, but unfamiliar with specific intervention, iii) not agree with specific recommendation, iv) guidelines not convenient for clinical or other AMPs team to use, v) unable to reconcile guidelines with patient preferences, vi) clinician may not have control over some changes, vii) Clinician doubts about performance according STG, viii) Clinicians believe recommendation is unsuccessful, ix) Clinician unmotivated to change previous practices

5.2.5. Antibiotic cycling

"Antimicrobial cycling" refers to the scheduled removal and substitution of a specific antimicrobial or antimicrobial class to prevent or reverse the development of antimicrobial resistance. Cycling is an attempt at controlled heterogeneity of antimicrobial use to minimize antimicrobial selection pressures. Studies of true antimicrobial cycling are limited and vary in terms of antimicrobial class selection, duration of cycling, therapeutic options offered during cycling periods, and cycling by time period versus by patient. Concerns about allergies, adverse drug events, and conflicts with national guidelines have led to 10%–50% of patients in cycling programs to receive "off-cycle" antimicrobials, resulting in poor implementation and decreased effectiveness.

5.2.6. Antimicrobial order forms

Antimicrobial order forms decrease antimicrobial consumption through the use of automatic stop orders and the requirement of physician justification. They aid in the utilization of developed guidelines. Defining the optimal timing and duration of perioperative antimicrobial prophylaxis, use of perioperative prophylactic order forms with automatic discontinuation at two days resulted in a decrease in the mean duration of antimicrobial prophylaxis. Automatic stop orders should not replace clinical judgment, and renewal requirements must be clearly communicated to providers to avoid inappropriate treatment interruptions.

5.2.7. Antibiotic use measures

Periodic assessment of antibiotic use for treatment of infection should be performed to determine the quality of antibiotics use. Antibiotic use can be optimized by using accurate diagnostic criteria for infection, prescribing recommended agents for particular indication, planned duration of antibiotic therapy, obtained blood culture prior to antibiotic therapy. Drug use evaluation can be performed by using antibiotic audit forms.

Antibiotic use can be measured by two strategies, days of therapy (DOT) or defined daily dose (DDD). DOT is an aggregate sum of days for which any amount of an specific antimicrobial agent is administered or dispensed to a particular patient divided by a standardized denominator (patient days). DDD metric estimates antibiotic use in hospitals by aggregating the total number of grams of each antibiotic purchased, dispensed or administered during a period of interest divided by WHO assigned DDD. Compared to DOT, DDD estimates are not appropriate for children and those with reduced drug excretion such as renal impairment.

5.2.8. Combination therapy

The rationale for combination antimicrobial therapy includes broad-spectrum empirical therapy for serious infections, improved clinical outcomes and the prevention of resistance. However, the available data are insufficient to recommend the routine use

of combination therapy to prevent resistance. However, in many situations, combination therapy is redundant and unnecessary.

5.2.9. Dose optimization

Dose optimization takes several factors into account. This includes, PK/PD – characteristics, patient characteristics, causative organism and site of infection. PK monitoring and adjustment program can reduce cost and decrease adverse effects. It is recommended to implement PK monitoring for aminoglycosides and vancomycin. This dose optimization strategy reduces nephrotoxicity, length of hospital stay and mortality.

5.2.10. Duration optimization

While duration optimization helps to avoid automatic 10-14 day course of therapy, following is the new evidence of duration of therapy.

Table 4: There are evidence where the recommended duration is proved to be sufficient compared with the earlier recommendation

Infections	Duration of therapy
Uncomplicated UTI	5 days
Community acquired pneumonia	7 days
Ventilator associated pneumonia	8 days
CR-BSI Coagulase negative staphylococci	7 days
Acute Hemosteomyelitis in children	21 days
Meningococcal meningitis	7 days
Uncomplicated secondary peritonitis with source control	7 days
Uncomplicated SSTI	5 days

5.2.11. Streamlining/de-escalation

Excessively broad spectrum therapy contributes to the selection of antimicrobial resistant pathogens. This conflict can be resolved when culture results become available

which in turn promote judicious use of antibiotics by streamlining or de-escalating empiric therapy to more targeted therapy that decreases antimicrobial exposure and contains cost.

Based on the diagnostic information, hospitalized patients are often empirically treated with antibiotics. However, prescribers often do not revisit the selection of antibiotics after microbiological data become available. An antibiotic time out promotes the reassessment of continuation, choice of antibiotic or change to targeted therapy. All clinicians should perform a review of antibiotics 48 hours after prescription. The following key questions should be checked from the available clinical and laboratory data.

- Has the patient with an infection responded to the given antibiotic?
- If so, can the patient on right antibiotic choice, dose, route of administration change the therapy to targeted antibiotic choice (deescalate) to treat the infection
- Calculate the duration of antibiotic therapy

Some health care facilities restrict the use of certain antibiotics based on the spectrum of activity caused or adverse events and to ensure that the use must be discussed with an antibiotic expert before initiation of therapy. This intervention requires an expertise in antibiotic use and infectious disease and authorization to modify the antibiotic use in a timely manner.

A Cochrane systematic review and meta-analysis on de-escalation of antimicrobial treatment described that there is no adequate direct evidences to whether de-escalation of antimicrobial is effective and safe for adults with sepsis, severe sepsis or septic shock.

5.2.12. Switch from parenteral to oral therapy

Antimicrobial therapy for patients with serious infections requiring hospitalization is generally initiated with parenteral therapy. Enhanced oral bioavailability among certain antimicrobials—such as fluoroquinolones, oxazolidinones, metronidazole, clindamycin, trimethoprim-sulfamethoxazole, fluconazole, and voriconazole—allows conversion to oral therapy once a patient meets defined clinical criteria. This can decrease length of

hospital stay and health care costs. It may be facilitated by the development of clinical criteria and guidelines allowing conversion. There may be some exception to this especially when dealing with endovascular infections, osteomyelitis, etc. where a longer duration of iv antibiotics is required.

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┌──────────────────────────────────────────┐
│  Conversion from intravenous to oral       │
│             antimicrobials                  │
│          (Switch criteria)                  │
└──────────────────────────────────────────┘
                    │
┌──────────────────────────────────────────┐
│  1. Clinical stability                      │
│     Downward fever trend                    │
│     Downward WBC trend                      │
│     Stable vital signs                      │
│  2. Ability to tolerate oral intake         │
│     On oral diet/medication/enteral feeds   │
│     No vomiting/diarrhoea                    │
│     No malabsorption problem                 │
└──────────────────────────────────────────┘
          │                        │
      ┌───────┐                ┌───────┐
      │  Yes  │                │  No   │
      └───────┘                └───────┘
          │                        │
 ┌─────────────────┐    ┌─────────────────┐
 │ Convert to oral* │    │  Continue with   │
 │                  │    │   intravenous    │
 └─────────────────┘    └─────────────────┘
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*Unless
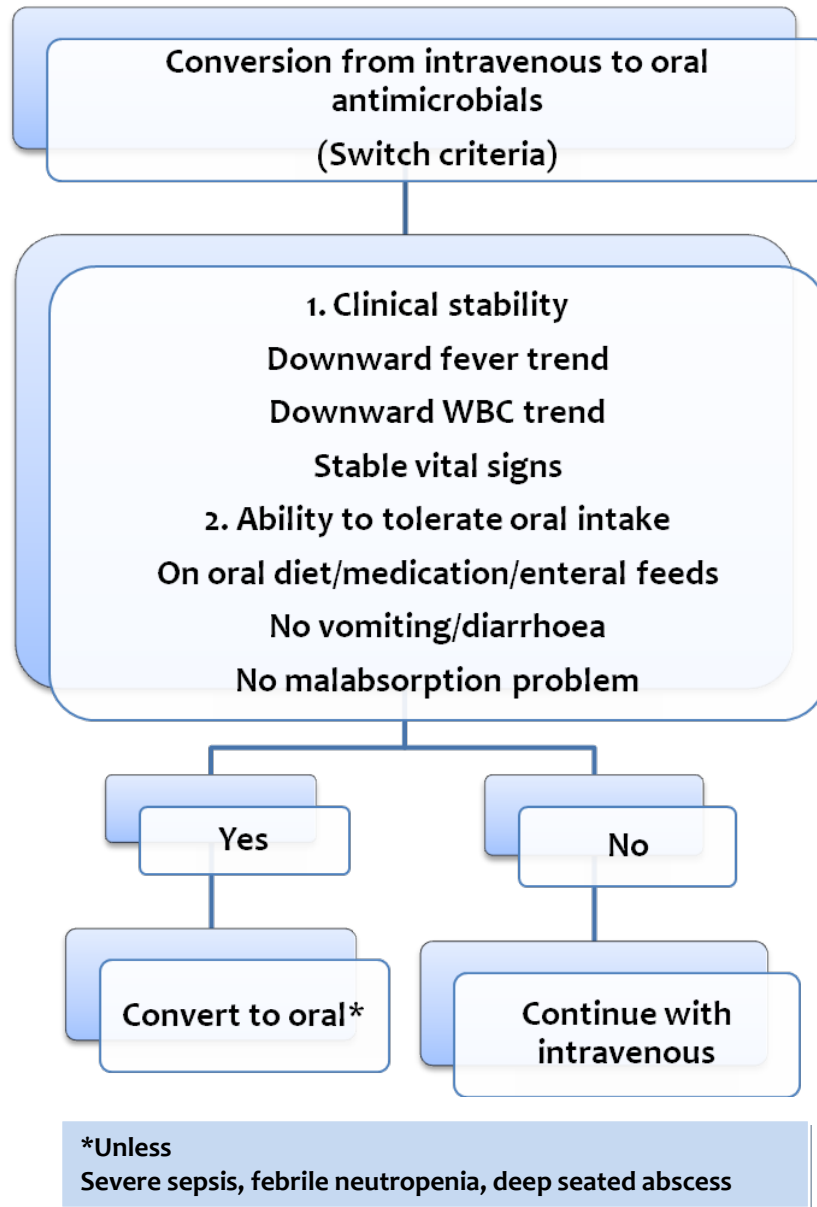Severe sepsis, febrile neutropenia, deep seated abscess

Figure 4: A systemic plan for parenteral to oral conversion of antimicrobials with excellent bioavailability, when the patient's condition allows, can decrease length of hospital stay and health care costs (A-I)

The switch of IV to oral decreases the risk of IV associated complications like thrombophlebitis, catheter related infections and improves the outcome of the patient. It also promotes earlier discharge and saves the health care costs. Antibiotics suitable for IV to oral conversion with highest bioavailability (~90%) includes, ciprofloxacin (70-80%), levofloxacin (>90%), moxifloxacin (~90%), metronidazole (>95%), co-trimoxazole (>90%), fluconazole (>90%), linezolid (>90%), clindamycin (>87%).

Important criteria for switching comprises i) good oral absorption, ii) temperature less than 38°C for 24 to 48 hours, iii) no signs of sepsis, iv) appropriate oral antibiotic is available, v) Increase the tissue penetration of antibiotic. The switching should be considered when there is a gram negative bacteraemia, hospital acquired infections, intra-abdominal infections, pneumonia, skin and soft tissue infections and urinary tract infections.

The individual physician can obtain appropriate culture before starting antibiotics and review antibiotic use after 48-72 hours. The physician can stop antibiotic in patients with alternative non-infectious diagnosis and optimize dosing and duration of antibiotic therapy. Unnecessary use of antibiotics especially in viral URIs [75%] can be avoided.

Table 5: A few suggested conversion regimen - antibiotic for dosing in specific indications

IV		ORAL	
Antimicrobial	Usual dose	Antimicrobial	Usual dose
Ampicillin	1-2 g IV QID	Ampicillin	500 mg – 1 g oral TDS
Azithromycin	500 mg IV daily	Azithromycin	300 mg oral daily
Benzyl penicillin	1.2 g IV QID	Benzyl penicillin	500 mg oral QID
Cephazolin	1 g IV TDS	Cephazolin	500 mg oral QID
Ciprofloxacin	200-400 mg IV BD	Ciprofloxacin	250-500 mg oral BD
Flucloxacillin	1g IV QID	Flucloxacillin	500 mg oral QID

Lincomycin	600-900 mg IV TDS	Lincomycin	300-600 mg oral TDS
Fluconazole	200-400 mg IV daily	Fluconazole	200-400 mg oral daily
Metronidazole	500 mg IV BD	Metronidazole	400 mg oral TDS

5.3. Other strategies

5.3.1. Information technology

Computer surveillance and decision support

Traditionally, AMS programs relied on manual methods combined with clinical oversight and intervention. However, the advent of improved modern health care information technology has offered the opportunity to expand the breadth, depth, and efficiency of AMS programs. Point-of-care access to current medical information is easily available to the practitioner through the use of smart phones, iPads, and other personal digital assistants. In addition, mobile health has enormous scope within AMS to both assist patients with antibiotic reminders, and to assist busy clinicians with antimicrobial information, clinical prescribing support and efficient collection of antimicrobial data.

Expert computer clinical decision support systems have been a very promising information technology advance. A seven-year study conducted in Salt Lake City, Utah, implemented computer-assisted decision support programs using local clinician-derived practice guidelines. They demonstrated that such decision support could improve antibiotic use, reduce associated costs, and stabilize the emergence of antibiotic-resistant pathogens in their institution. A computerized antimicrobial approval system developed in Australia has also shown effectiveness in reducing the use of both 3rd and 4th generation cephalosporins, fluoroquinolones, glycopeptides and carbapenems with a favourable influence on local antibiograms. Electronic clinical decision support via hand-held devices has been shown to significantly reduce patient length of stay and antibiotic prescribing in a critical care unit and to improve the appropriateness of antimicrobial selection for acute respiratory tract infections in a rural primary care setting. In addition,

a meta-analysis of studies found that clinicians with decision support were 1.6 times more likely to order recommended treatments than providers without such a system.

Electronic health records are widely used in the United States, but many of these do not meet criteria for "meaningful use". Only a small number of institutions have been able to demonstrate an improvement in safety, quality and efficiency as a result of such electronic systems. In addition, an evaluation of a computerized decision support system in Nebraska, which triggered prospective alerts regarding both the patient's condition and the antimicrobial therapy, revealed that over 8,000 alerts were received over a 5-month period. Only 30% of these alerts were actionable and the labour intensity of reviewing these alerts was substantial at approximately 5 hours per day.

Computer physician order entry (CPOE) and electronic medical records is considered as 1 of the 3 most important "leaps" that organizations can take to substantially improve patient safety. Computer surveillance program presents epidemiological information with detailed recommendations and warnings regarding antimicrobial regimens and courses of therapy. Even if a physician overrides the recommendation for the antimicrobial and selects his or her own treatment plan, the computer still automatically reviews the patient's allergies and potential drug-drug interactions, recommending a dosage and interval based on the patient's renal and hepatic functions.

In addition to improving antimicrobial use and care of the individual patient, their system has facilitated the electronic surveillance of hospital-acquired infections and adverse drug events. CPOE with complex clinical management that can be subjective, interpretive, and reactive has been a challenge at other institutions. Computer surveillance programs help us to merge hospital pharmacy and microbiology databases, to identify antimicrobial interventions.

Incorporation of computerized clinical decision supports at the time of prescribing into AMSP. However, computerized decision support systems are designed to improve antibiotic use by providing treatment recommendations to clinicians at the time of prescribing. Implementation of this system for prescriber has been associated with reduced use of broad spectrum antibiotics, improved antibiotic dosing, reduced

antibiotic resistance, more appropriate antibiotic selection, fewer prescribing errors, reduced adverse events and antibiotic cost, reduced length of stay and mortality.

Integration of IT into the clinical data presentation and decision making for antibiotic use will expand with increased update and capabilities of electronic health record. The dissemination of well-constructed electronic decision support systems has not been brought to date, likely due to issues of cost, the requirement for compatibility with existing electronic systems, and the fact that such systems cannot stand-alone and be effective. Such technology to assist prescribing must be part of a broader framework of AMS with an engaged AMS team in order to have an impact.

5.3.2. Role of microbiology laboratory

The clinical microbiology laboratory plays a critical role in the timely identification of microbial pathogens and the performance of susceptibility testing. Susceptibility testing can aid in the prudent use of antimicrobials and direct appropriate therapy based on local guidelines. Molecular diagnostics allows the identification of difficult-to-culture pathogens, potentially avoiding the need for extended courses of broad-spectrum empirical therapy. Clinical microbiology laboratory should be actively involved in resistance surveillance. Role of rapid diagnostics and biomarkers in antimicrobial stewardship is recognized as a key recommendation by the IDSA.

Local antibiogram with pathogen-specific susceptibility data should be updated at least annually, to optimize expert-based recommendations for empirical therapy. Computerized surveillance can facilitate more-frequent monitoring of antimicrobial resistance trends. The laboratory is an important partner with infection control in the identification and molecular epidemiologic investigation of local outbreaks of infection. The development of resistance organisms which allow the implementation of infection control measures to prevent secondary spread. Clonal characterization of resistant strains through molecular typing can help focus appropriate interventions, leading to a reduction in nosocomial infections with associated cost savings.

- Appropriate culture should be obtained before starting antimicrobial therapy. Prior therapy may interfere with bacterial growth

- Promote optimal usage of diagnostic services such as ensuring the specimens are appropriate, clinically relevant and timely
- Undertake selective antimicrobial susceptibility testing especially those that are listed in formulary
- Clinical interpretations to laboratory reports
- With hold the susceptibility reports when clinical information is inadequate. Failure to do will result inexperienced prescriber to assume that the results have been interpreted by the laboratory and are clinically significant and to initiate antibiotics inappropriately.
- Selective reporting of only relevant/first line drugs alone
- Undertake rapid identification and susceptibility testing
- Collect and collate surveillance data and report trends and susceptibility profiles to guide empirical therapy.

5.3.3. Monitoring of process

Useful and determining programs must establish process and outcome measures to determine the impact of antimicrobial stewardship on antimicrobial use and resistance patterns. The "process goal" is often to change use of a specific antimicrobial or class of antimicrobials. The related "process measure" for this goal would determine the degree to which the intervention to change the use of an antimicrobial or class of antimicrobials has been successfully implemented, compared with baseline levels.

The "outcome goal" of these process changes is to reduce or prevent resistance or other unintended consequences of antimicrobial use. "Outcome measurements" define the degree to which these outcomes are achieved, such as reduced antimicrobial resistance, adverse drug events, and cost, as well as unintended consequences. Drug use data can be standardized using the defined daily dose, calculated as the total number of grams of an antimicrobial agent used divided by the number of grams in an average adult daily dose of the agent. The World Health Organization publishes defined daily dose values for nearly all antimicrobials (http://www.whocc.no/atcddd/).

Clinical outcomes should be tracked to measure the impact of interventions to improve antibiotic use. Improving antibiotic use has significant impact on a reduction in

antimicrobial resistance and infectious diseases. The impact of stewardship interventions on resistance is best assessed by the measurement focused on the pathogens that are recovered from the patients after admission (screening).

5.3.4. Antimicrobial consumption outcome measures

ASPs mainly focus on accomplishing changes in broad spectrum IV prescriptions, because broad spectrum antimicrobials are more likely to promote resistance development and IV treatment is more likely to cause secondary infections/complications. An IV-to-oral switch program is one of the most frequently implemented interventions. To measure the effect on therapy, different outcome measures can be used. Often it is chosen to quantify the antimicrobial therapy as defined daily doses (DDDs, as defined by the WHO), with a denominator correcting for clinical activity such as bed days or admissions (http://www.whocc.no/atc_ ddd_index). This can be done either by looking at dispensing data or at purchasing data, which are strongly correlated with each other.

The use of defined daily doses is recommended to compare antimicrobial use with other hospitals, recognizing the challenges of inter-hospital comparisons and the potential need for "risk adjustment." Populations with renal compromise and for drugs that require renal dose adjustment, the DDD may be less accurate than measures of antimicrobial-days of therapy. Investments in data systems allow for evaluation as a routine measure of quality improvement. The antimicrobial consumption (AMC) tool, consumption data provided as numbers of packages into numbers of DDD using the ATC/DDD index. AMC Tool uses the ATC/DDD index developed by the WHO collaborating centre for drug statistics methodology.

The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America advocate DDDs/1000 patient days as universal outcome measure for ASP programs. With respect to pediatric populations, these outcomes are far from optimal, because they are based on adult dosages. This should be taken into account, although it is unclear which measure should preferably be used alternative to DDDs. Personalized therapy measures such as prescribed daily doses (PDDs) or recommended daily doses (RDD) are a more patient-specific approach to quantify

antimicrobial treatment and might give more suitable results. Furthermore, the length of the therapy (in days) can be evaluated as duration of therapy [DOT]. A discrepancy when compared to DDDs is known to occur because of the difference between administered dose and the WHO DDD values. In particular, an ASP focuses on optimizing therapy, often by promoting narrow spectrum oral medication; it can be worthwhile evaluating effects of these interventions specifically. Pareto charts are useful to provide an overview of antimicrobial usage at ward level and helps in identifying the ward that have high total usage or high use of restricted antimicrobials.

5.3.5. Human resources required for antimicrobial stewardship activities:

The composite index is used to assess the proper use of antibiotics in French healthcare facilities includes a target number for full-time equivalents (FTE) related to the antibiotic/infectious disease lead supervisor's activities. The target number is based on the number of hospital beds. In 2015, the French ministry of Health set up a task force on antibiotic resistance (antimicrobial stewardship group), conducted a study to evaluate the human resources needed to implement all the required activities of the multidisciplinary antimicrobial stewardship teams and estimated that 3.6 FTE/1000 beds for ID specialist, 2.5 FTE/1000 beds for pharmacist and 0.6 FTE/1000 beds for microbiologist. This clearly shows that dedicated and sustainable funding for AMPs is urgently needed to implement comprehensive and functional AMPs programs in all healthcare facilities.

6. Importance of Standard Treatment Guidelines (STG)

Effective standard treatment guidelines (STG) improve patient care while enhancing cost savings. The STG also reflect data on resistance, recognizing that local patterns of resistance often differ across geographical regions. The use of the STG can be an effective means of changing behaviour; hence the STG should be readily adaptable for local implementation.

Prerequisites of STG

- Should be based on local antibiograms
- Should be syndrome/disease based

- Should specify type of clinical setting – outpatient clinics, inpatient units ICU setting

- Should specify rationale of guidelines

- Should provide evidence based strength of recommendations

- Should involve treating physicians to bring ownership to the guidelines

Validation of STG

STG validation should be done by the internal peer review process. STG needs to be submitted to selected reviewers and changes recommended by the individual reviewers should be discussed by the STG developing group and incorporated into the final document. The STG is then reviewed by an eminent peer who was not part of the STG panel but who is an expert in that particular speciality.

7. Implement Policies and Interventions to Improve Antibiotic Use

Implement policies that support optimal antibiotic use. Utilization of specific interventions that can be divided into three categories: broad, pharmacy driven and infection and syndrome specific. Avoid implementing too many policies and interventions simultaneously; always prioritize interventions based on the needs of the hospital as defined by measures of overall use and other tracking and reporting metrics. Restricted reporting of reserved drugs would prevent unnecessary inappropriate antibiotic dosage. Restricted reporting encourage prudent and appropriate use of antibiotics, pathogen-specific antibiotic therapy (when culture and susceptibility report available). The most preferred practice and recommendation is to with-hold the susceptibility report of broad spectrum antibiotics, when the narrow spectrum antibiotics are susceptible. Empiric therapy has to be changed to targeted therapy when AST result available within 72 hours. In particular, treating ICU patients recommendations from infectious disease expertise would be more preferable to de-escalate or change therapy. A classification of antibiotics based upon the local AMR profile should be used to promote antimicrobial stewardship. Infections should be treated and not contaminants to preserve antibiotic and prevent antimicrobial resistance.

7.1 Policies that support optimal antibiotic use

Documentation of dose, duration, and indication helps to specify the dose, duration and indication for all courses of antibiotics so they are readily identifiable. Making this information accessible helps ensure that antibiotics are modified as needed and/or discontinued in a timely manner.

7.2 Develop and implement facility specific treatment recommendations.

Facility-specific treatment recommendations, based on national guidelines and local susceptibilities and formulary options can optimize antibiotic selection and duration, particularly for common indications for antibiotic use like community-acquired pneumonia, urinary tract infection, intra-abdominal infections, skin and soft tissue infections and surgical prophylaxis

8. Rational use of antimicrobials in Dental, ENT, Dermatology, prophylaxis in surgery

International and national campaigns draw attention worldwide to the rational use of the available antibiotics. This has been stimulated by the high prevalence rates of drug-resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), a threatening spread of development of resistance in Gram-negative rod-shaped bacteria and the selection of *Clostridium difficile* with a simultaneous clear reduction in the development of new antibiotics. The implementation of antibiotic stewardship programs aims to maintain their effectiveness by a rational use of the available antibiotics.

Overuse of antibiotics is a common dental practice for conditions like caries, gingivitis, pulpitis and chronic apical inflammation which could be managed by dental procedures, suggesting irrational antibiotic use in dentistry. Globally, dentists were reported to prescribe up to 11.3 % of all antibiotics. Dentists tend to prescribe broad-spectrum antibiotics empirically either to give prophylaxis or to manage oral/dental infections.

Diseases of the ear, nose and throat (ENT) affect adults and children, with significant impairment in daily life. Upper respiratory tract infections including rhino

pharyngitis, pharyngitis, tonsillitis and otitis media are the most common reasons for which patients seek treatment in ENT OP. The most common cause of acute upper respiratory tract infections (URTIs) are due to viruses and do not need antimicrobial agent. Acute respiratory infections are the reasons for the 75% of the antibiotic prescriptions each year and is the most frequent reason for seeking medical attention. This occurs despite the fact that in most cases of URTIs, antibiotic confers little or no benefit.

Dermatologists prescribing potent steroid–antibacterial–antifungal topical combinations to treat superficial fungal infections or advising mometasone-containing modified Kligman's regimen for application on women's face for an extended duration are not rare examples. With reference to topical corticosteroids that peer pressure, rapid 'feel good' effect and ignorance about harmful effects lead to continuation of treatment beyond the prescribed duration. It is much easier to prescribe a systemic immunosuppressive than prescribe, educate and motivate a patient to use topical steroids in such a condition as localized or mild bullous pemphigoid, though there is good quality evidence to use the latter as first-line therapy in this scenario. The problem is compounded by the fact that, everyone can prescribe dermatological medications, particularly the topical applications. Dermatologists' prescriptions account for a minor proportion of sales of topical medications – other specialists (pediatricians, internists etc), general practitioners, over-the-counter sales, pharmacists and self-prescription account for the major percentage of procurement of these products.

Surgical site infections are the second most common cause of nosocomial infections. Up to 2% - 5% patients undergoing clean extra-abdominal operations and up to 20% undergoing intra-abdominal operations will develop an SSI. Administration of prophylactic antibiotics in certain surgical procedures can decrease post-operative infections, decrease the length of hospital stay and reduce the overall cost of care. The use of pre and peri-operative antibiotics has become an essential component of the standard of care in virtually all surgical procedures and has resulted in a reduced risk of post-operative infection when sound and appropriate principles of prophylaxis are applied. But inappropriate and excessive use of antibiotics for this purpose leads to increase in hospital costs, ineffectiveness and/or a decline in susceptibility of bacteria.

The essential target of therapy with antibiotics is successful treatment of individual patients with bacterial infections. The optimal clinical treatment results can only be achieved when the toxicity, selection of pathogens and development of resistance are minimized.

9. AMSP in primary care to tertiary care hospitals, corporate hospital

Primary care is the first level of care in the whole healthcare system and family doctors are the main providers. They play a pivotal role in tackling AMR problem by reducing unnecessary antibiotic use. In connection to this, Centre of Health Protection of the Department of Health rolled out the "Antibiotic Stewardship Programme in Primary Care", aiming to optimize the use of antibiotics by providing evidence-based antibiotic prescription guidance for common infections in community for doctors and healthcare professionals as reference. The guidance notes will be kept updating based on local epidemiology and international best practice.

Post-prescription feedback would be more helpful to stop, modify and continue antibiotic and to assess the appropriateness of therapy.

Methods to start AMSP

1. Timely and Appropriate Initiation of Antibiotics
    a. Promptly identify patients who require antibiotics
    b. Obtain cultures before starting antibiotics
    c. Determine and verify antibiotic allergies and tailor therapy accordingly
    d. Consider local susceptibility patterns in selecting therapy
    e. Start treatment promptly
    f. Specify expected duration of therapy based on evidence and national and hospital guidelines
2. Appropriate Administration and De-escalation
    a. Make antibiotics patient is receiving and start dates visible at point of care and in health records
    b. Give antibiotics at the right dose and interval

    c. Stop or de-escalate therapy promptly based on the culture and sensitivity results

    d. Reconcile and adjust antibiotics at all transitions and changes in patient's condition

    e. Monitor for toxicity reliably and adjust agent and dose promptly

3. Monitoring, Transparency, Infrastructure

    a. Monitor, feedback and make visible data

        i. Antibiotic utilization

        ii. Antibiotic resistance

        iii. Cost

        iv. Adherence recommended culturing and prescribing practices

4. Expertise at Point of Care

    a. Develop and make available expertise in antibiotic use

        i. Cultivate local expertise among staff

        ii. Develop a process for antibiotic formulary management

    b. Ensure expertise is available to clinicians at the point of care

5. The outcome of the AMSP will be based on Days of therapy/1000 patient days which includes the proportion of antibiotic prescription, de-escalation, intervention rate and acceptance rate.

10. Antimicrobial Self-assessment Toolkit

The Antimicrobial Self-assessment Toolkit (ASAT v15a) was developed by a pharmacist reference group of an Advisory Non-Departmental Public Body on Antimicrobial Resistance and Healthcare Associated Infections (ARHAI), in conjunction with the Department of Health (DH). This version of the ASAT can be accessed via http://www.researchdirectorate.org.uk/uhsm/asat/asat.asp. In England, AMS toolkits are freely and openly available to assist organizations to fulfil their obligations with regard to national guidance and regulations. These toolkits are Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) for primary care, and Start Smart Then Focus (SSTF) for secondary healthcare settings.

Antimicrobial stewardship in community settings is required to help out health care practioners which are often compelled to treat empirically and to prevent use of unregulated drugs approved in the community and to prevent self medication and antibiotics on over the counter.The core elements of outpatients AMSP recommended by CDC includes i) accountability for optimising antibiotic prescription ii) use evidence based diagnostic criteria and treatment recommendation iii) self-evaluate antibiotic prescribing practices iv) use effec.tive communication strategy to educate patients.

The most frequent diagnosis leading to antibiotic prescription includes sinusitis, acute otitis media, pharyngitis, cold and bronchtitis, UTI and pneumonia. The most concerned antibiotic use in community where fluroquinolones and macrolides to which more than 70% of resistance was prevailing in Indian settings. The key providers for the establishment of outpatient AMS includes adult and paediatric primary care, emergency care, dentist and physician assistance.

10.1 Antimicrobial Self-assessment Toolkit (ASAT)

The ASAT is an evidence-based toolkit which contains organisational methods of implementing hospital-based ASPs (Table 6). The primary purpose of the ASAT is to identify and to assess the organisational methods of implementation utilised by NHS Trusts to promote AMS within their respective organisations. It embodies the relevant guidelines produced relating to AMS and also published research studies translating them into a single workable document. Consensus expert opinion from the members of ARHAI which was based on experiential knowledge in antimicrobial management and prescribing was used to inform some of the content of the toolkit. In particular, the ASAT focuses on strategies for implementing antimicrobial stewardship in hospitals. However, the ASAT does not measure or quantify actual antimicrobial prescribing such as antimicrobial consumption.

10.2 TARGET

The TARGET toolkit is launched by PHE and the Royal College of General Practitioners in November 2012. TARGET resources include guidance (local or national antibiotic treatment recommendations), educational materials and tools that general

practitioners (GPs) can share with patients during consultations (including information on expected duration of infection, self-care and back-up prescriptions) and suggested antibiotic practice audits. The TARGET materials were updated in 2013 following user testing and evaluations.

Table 6: Descriptions of the Domains of ASAT v.15a

Domains	Description
Antimicrobial management with the Trust	Patients, Carers and the Public
Antimicrobial management with the Trust	Examines the types of control documents such as antimicrobial guidelines
Antimicrobial management with the Trust	Examines patient safety principles that should be undertaken when prescribing antimicrobials
Clinical governance assurance	Examines patient safety principles that should be undertaken when prescribing antimicrobials
Education and Training	Examines the education, training needs and training packages available to antimicrobial prescribers
Antimicrobial Pharmacist	Examines the role of the antimicrobial pharmacist to optimise their role in antimicrobial stewardship
Patients and the Public	Information given to the public such as consent for antimicrobial therapy

10.3 Start Smart Then Focus (SSTF)

In 2011, Antimicrobial stewardship: Start Smart - then Focus was published by ARHAI. The aim of this publication is to provide NHS hospitals with an outline for

evidence-based AMS. Proof of adherence to SSTF AMS principles helps organizations to demonstrate compliance with The Health and Social Care Act 2008: Code of Practice on the Prevention and Control of Infections and Related Guidance (updated in 2015). The Code of Practice states that registered providers should demonstrate 'Systems to manage and monitor the prevention and control of infection' and 'Ensure appropriate antimicrobial use to optimise patient outcomes and to reduce the risk of adverse events and antimicrobial resistance. This report is accompanied with a suite of resource tools so that hospitals can routinely audit their prescribing behaviour. These guidelines have been categorised into two sections and these are as follows:

START SMART:

- do not start antibiotics in the absence of clinical evidence of bacterial infection
- if there is evidence/suspicion of bacterial infection, use local guidelines to initiate prompt effective antibiotic treatment
- document on drug chart and in medical notes: clinical indication, duration or review date, route and dose
- obtain cultures first
- prescribe single dose antibiotics for surgical prophylaxis; where antibiotics have been shown to be effective

THEN FOCUS:

- review the clinical diagnosis and the continuing need for antibiotics by 48 hours and make a clear plan of action - the 'Antimicrobial Prescribing Decision'
- the five Antimicrobial Prescribing Decision options are: Stop, Switch IV to Oral, Change, Continue and Outpatient Parenteral Antibiotic Therapy (OPAT).
- it is essential that the review and subsequent decision is clearly documented in the medical notes

The publication 'START SMART and then FOCUS' include a suite of tools which could be used to evaluate or audit antimicrobial prescribing. Some examples of these tools include the Hospital Antimicrobial Prudent Prescribing Indicators (HAPPI) audit tool and the Antibiotic Review Bundle. These guidelines focus primarily on the prescribing

decision. Also, the National Institute for Health and Clinical Excellence (NICE) in conjunction with the Health Protection Agency (HPA) have produced a quality improvement guide for the prevention and control of HCAIs. This guide is not mandatory for hospitals however it is suggested that it is used as quality standards for tracking HCAIs.

11. Antimicrobial stewardship measures:

Structural measures:

- Antibiotic order form
- Availability of expert advice
- Guidelines
- Computerised decision support system
- Rapid diagnostic test

Educative measures:

- Restrictive prescribing
- Review of prescription
- Systematic expert advice

Monitoring:

- Antibiotic use and restriction
- Feedback and benchmarking

No unnecessary prescription:

- Better diagnosis

No inappropriate prescription:

- Dose
- Route of administration
- Duration

12. Comprehensive Multidisciplinary Antimicrobial Management Programs

The core members of a comprehensive antimicrobial management program include an infectious diseases physician and a clinical pharmacist with infectious diseases training, with the inclusion of infection control professionals, the hospital epidemiologist, a clinical microbiologist, and an information system specialist. The core elements of hospital stewardship programs are as follows

- Leadership Commitment: Dedicating necessary human, financial and information technology resources
- Accountability: Appointing a single leader responsible for program outcomes
- Drug Expertise: Appointing a single pharmacist leader to improve antibiotic use
- Action: Systemic evaluation of ongoing treatment
- Tracking: Monitoring antibiotic prescribing/resistance patterns
- Reporting: Regular reporting information on antibiotic use/ resistance to doctors, nurses and relevant staff
- Education: Educating clinicians (resistance/optimal prescribing)

Hospital administrative support is essential for effective implementation of antimicrobial stewardship program. Consensus building with the support of administration and local providers is essential, with the focus on collaborating in the safety and care of their patients rather than a policing role.

12.1 Antimicrobial stewardship team

Medical directors- Prescriber of antibiotics should be fully engaged in prescribing antiibiotics. They should provide supportive efforts to improve antibiotic use in hospitalsthrough assessing, monitoring and communicating the changes by setting standard antibiotic prescribing practices.

Pharmacist - They have a responsibility to take prominent role in antimicrobial stewardship program and participate in the infection prevention and control program of health systems -American Society of Health Systems Pharmacists, 2010. Responsibilities of pharmacist includes: avoid the dispersing of drugs over the counter without

prescription, emphasizing the correct drug, dose, duration and educating the patient on the antimicrobial use and quality assurance activities.

Microbiologist – can guide accurate and reliable diagnostic test for infectous disease. They can suggest empirical therpy derived from cumulative antibiotic resistant report available in hospitals. Clinical Microbiologist plays a crucial role in sending alerts of multi-drug resistant pathogens and educate about the rapid diagnostic tests available in healthcare settings.

Infection prevention control committe–They should monitor and prevent the spread of health care associated infections through auditing, analyzing and reporting data. They track antibiotic use in hospitals, adherence to evidence-based published criteria and review antibiotic resistance patterns in the healthcare facility. They educate staff on the importance of appropirate antibiotic use and implement antibiotic stewardhip strategies to optimize antibiotic use.
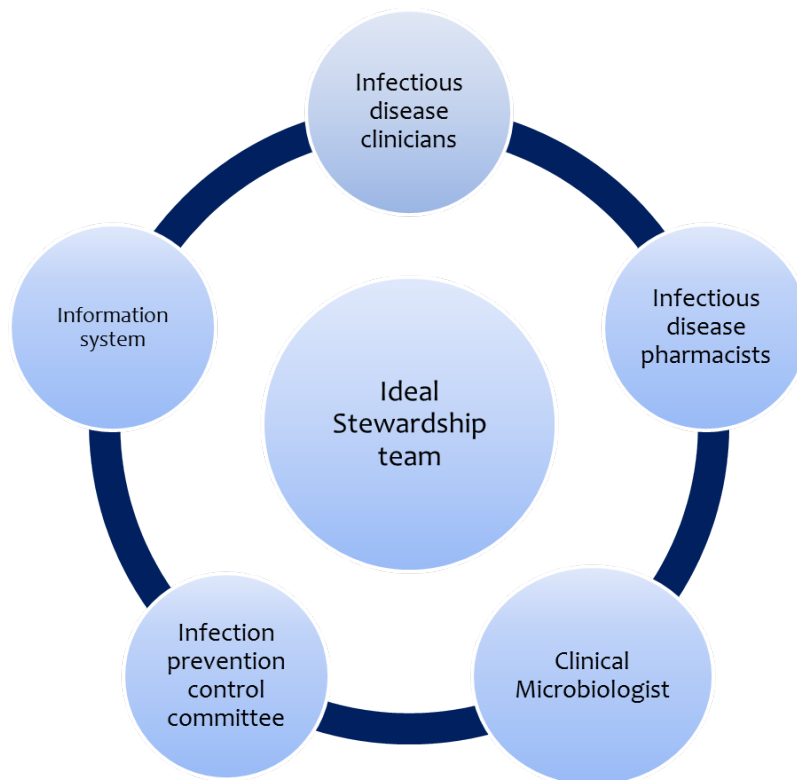
Fig 6: Antimicrobial stewardship team

13. Integrated stewardship model: antimicrobial, infection prevention and diagnostic (AID)

AID stewardship model is the combination of Antimicrobial Stewardship Programs (ASPs), Infection Prevention Stewardship Programs (ISP) as well as Diagnostic Stewardship Programs (DSP). This combined model aims at optimizing (laboratory) diagnostics, interpreting results and initiating correct and appropriate antimicrobial therapy (Fig 7). Furthermore, they act at the network level, aiding in taking the right infection control measures in order to provide a safe environment for patients and healthcare workers. Ultimately, this should also lead to more cost-effective healthcare in the mid-to-long term.

Integration of infection control and prevention measures into AID model improves overall infection management. Without the proper infection prevention measures, other interventions such as ASPs and DSPs will not yield the optimal effect. Within the AID stewardship model, infection prevention stewardship entails early detection and close surveillance of MDROs, as well as an adequate rapid reaction to every possible transmission. The success story of the containment of MRSA within The Netherlands by a search-and-destroy strategy is an example of the substantial positive effect of close cooperation between clinical microbiology and infection prevention specialists.

Diagnostic stewardship is state-of-the-art right diagnostics which are performed timely, for right patient before initiating antimicrobial therapy (table 7 and table 8). Diagnostics must be appropriate for the individual patient, target all pathogens causing acute infections and detect colonization and/or infection. Diagnostic test should provide results in < 48 hours of admission. Molecular diagnostics and point-of-care assay (testing different biomarkers) should be considered. The use of innovative methods (next-generation sequencing) is an exciting evolving field within clinical microbiology and infection control, which is advocated as the solution for antimicrobial resistance. These diagnostic assays and next-generation diagnostics are mostly based on molecular technologies and are therefore more expensive compared with classical culture-based methodology. But they are faster, delivering results within hours.

Table 7: Goal and key considerations for diagnostic stewardship

Goal	Key question	Key considerations and potential strategies
Right test	Is the test appropriate for the clinical setting?	• Sensitivity /specificity • Predictive values • Volumes • Diagnostic yield • Laboratory feasibility • Cost • Clinical impact
Right patient	Will the clinical care of the patient be affected by the test result?	• Appropriate use criteria • Indication selection • Benchmarking Specimen rejection
Right time	Will the result be available in time to optimally affect care?	• Time to specimen receipt • Centralized vs point-of-care testing • On-demand vs batched testing • Specimen preparation time • Run time • Result reporting time

Table 8: Key antimicrobial stewardship for implementation of rapid diagnostic test

Goal	Key question	Key considerations and potential strategies
Right interpretation	Will the clinician understand the test result?	• Result report language • Selective reporting of relevant results • AS prospective audit and feedback • AS real-time decision support

Right antimicrobial	Will the clinician appropriately modify antimicrobials based on the test result?	• Clinical practice guidelines • EMR-based decision support with result reporting • AS prospective audit and feedback • AS real-time decision support
Right time	Will the clinician act upon the test result promptly?	• EMR reporting • Results called with read-back reporting • AS prospective audit and feedback • AS real-time decision support

Fig 7 : Concept within the antimicrobial, infection prevention and diagnostic stewardship model

14. Diagnostic Stewardship

Appropriate antimicrobial therapy: 5D's are essential for optimal antimicrobial therapy which includes diagnosis/indication, right drug, right dose, right duration of therapy and de-escalation to pathogen-targeted therapy.

14.1 Culture collection before antibiotic therapy

It is necessary to obtain cultures before starting antimicrobial therapy; prior antimicrobial therapy may interfere with bacterial growth. Therapy is streamlined after cultures and sensitivities are available. Delaying therapy when infectious processes are suspected is

not an option, but similarly, obtaining adequate cultures before administering antibiotics is equally important. In these situations, timing is key. Obtaining appropriate cultures before initiating antimicrobial therapy plays an important role in patient care.

The prompt identification of offending organisms will influence diagnosis, therapy, and prognosis. This will not only benefit the patient by providing more appropriate and definitive treatment, but will also help control the emergence of antibiotic resistance by minimizing the use of broad-spectrum agents.

Obtaining cultures before antibiotic use improves the chances of identifying the offending microorganism, which improves patient care. Inappropriate antibiotic use can result in prolonged hospital stays and increased costs, but it can also have adverse consequences on the patient's prognosis.

The Surviving Sepsis Campaign Guidelines reiterate that antimicrobial therapy should be reassessed once these organisms have been identified in order to more accurately direct therapy. Obtaining cultures after antimicrobial therapy has been started can cause inconclusive results because organisms that would otherwise be detected may not necessarily grow after exposure to an antibiotic agent. The administration of antimicrobials before the collection of samples may decrease blood culture yields.

To summarize, the prompt initiation of therapy is very important whenever infections are suspected. It is also important to remember to obtain cultures from patients before administering antimicrobial agents so that more appropriate treatment strategies can be tailored based on culture and sensitivity results. So remember, collect before you treat to ensure optimal patient care. Do not delay therapy by delaying cultures. Get cultures immediately.

14.2 Use of Early Diagnostic kits for promoting specific antimicrobial

Effective antimicrobial stewardship is closely linked with the ability to make correct diagnoses. Speed of diagnostic testing is also a key factor in effective antimicrobial stewardship. Key goals of antimicrobial stewardship can be achieved through faster and more accurate diagnostic testing, reducing time to appropriate

antibiotics, reducing unnecessary use of antibiotics, and informing decisions regarding antibiotic de-escalation or discontinuation.

Novel diagnostic approaches currently include culture-independent rapid technologies, some of which may be developed for point-of–care use in settings such as emergency departments, intensive care units, and outpatient clinics.

Nucleic acid amplification tests (NAATs)

NAATs based on real-time polymerase chain reaction using probes, can detect and quantify known genetic sequences to identify multiple pathogens simultaneously and key resistance genes or determinants, directly from patient specimens or from positive blood culture bottles. For example, for diagnosing tuberculosis (TB), the WHO recommends the use of the Xpert MTB/RIF assay (Cepheid), which integrates sputum sample processing and PCR testing into a single self-enclosed test unit that can simultaneously detect TB and rifampicin resistance within 2 hours. The rapid, automated BioFire Film Array blood culture identification panels (bioMérieux), for instance, use multiplex PCR to enable the simultaneous identification of gram-positive and gram-negative bacteria, viruses, yeast, parasites, and selected AMR genes (mecA, vanA/B, and blaKPC).

Mass spectrometry (MS)

This methodology uses lasers to ionize and accelerate bacterial and fungal molecules, which separate according to the mass-to-charge ratio, yielding a distinct signal that can be used to identify pathogens to the species level (using a database of characterized organisms for comparison) and resistance determinants or biomarkers expressed by resistant pathogens. Commercial MALDI-TOF MS systems, such as Vitek MS (bioMérieux) and Biotyper (Bruker), are used for rapid identification of a broad range of bacteria from positive blood cultures. A related culture-independent technology, PCR/electrospray ionization–mass spectrometry (eg, the IRIDICA bacterial bloodstream infection assay system, Abbott Laboratories), can provide molecular detection of sepsis-related pathogens directly from patients' blood samples in less than 8 hours.

Peptide nucleic acid fluorescence in situ hybridization (PNA-FISH)

PNA-FISH, a cytogenetic methodology uses fluorescent probes that bind to complementary genetic sequences in bacterial pathogens, detectable via fluorescence microscopy. PNA-FISH was one of the first commercially available rapid diagnostic testing methodologies and has been modified to enable pathogen identification results in less than an hour. PNA-FISH technology can also be used in conjunction with other technologies. For example, the Accelerate Pheno system (Accelerate Diagnostics), an automated test system for identifying gram-negative bacteria and antimicrobial susceptibility from positive blood cultures, combines PNA-FISH and gel electrofiltration with automated microscopy for analyzing bacterial growth rates and extrapolating MIC values.

Whole-genome sequencing (WGS)

WGS, combined with informatics tools, can detect all potential pathogens directly from patient samples. WGS can also provide data on AMR by identifying known resistance genes, but it does not provide information on whether the genes are expressed as phenotypic resistance. It can also provide information on slow-growing or difficult-to-culture organisms including viruses, bacteria, yeast, fungi and parasites. WGS has been used to identify pathogens where all other diagnostic methods have failed and can be particularly useful in hospital infection control surveillance programs and community outbreak investigations.

14.3 Role of biomarkers in AMSP

Rapid diagnostic testing (RDT), contributes to a reduction in antibiotic use. RDT allows for rapid identification of group A streptococcus, methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile*, and extended spectrum beta-lactamase (ESBL) and carbapenemase-producing organisms. Poor diagnosis may result in nosocomial outbreak of multi-drug resistant infection and spread of resistant pathogens (Fig 5). Molecular microbiology assists in rapid identification of pathogen and resistance mechanism without conventional culture. Many rapid diagnostic tools are now FDA cleared for clinical use. In 2016, IDSA guidelines for ASP recommend rapid diagnostic testing in addition to conventional microbiology methods for blood culture. Larger academic hospitals that evaluated the utility of rapid diagnostics in improving patient

outcomes had ASP programs with designated ID trained physicians and pharmacists that implemented and maintained their rapid diagnostic with ASP intervention protocol. Improved clinical outcome would be appreciated with the earliest tailoring of therapy, reconcile conflicts associated with empiric therapy and avoid antibiotic agents causing collateral damage. Rapid diagnostic tests are "game changing" for patient care, provide new opportunity for stewardship program and enhance function of clinical microbiology laboratories.

Clinicians can also utilize serum markers in order to decide whether antibiotics ought to be prescribed in a given patient. C-Reactive protein (CRP) is an acute-phase reactant, and CRP level measurements are frequently used to aid in the diagnosis of bacterial infections.

Procalcitonin (PCT) is a hormone that has emerged as a promising marker for the diagnosis of bacterial infections and may be used to support clinical decision making for the initiation and discontinuation of antibiotic therapy. It has been shown that PCT level is highly sensitive and very specific than the CRP level for differentiating bacterial from either viral or non-infective causes of inflammation. Studies have demonstrated that higher levels of PCT are found in severe bacterial infections than in viral infections and nonspecific inflammatory diseases. A Cochrane systematic review and meta-analysis of 4221 patients with acute respiratory infections have shown that measuring PCT is effective in reducing antibiotic exposure and that PCT guidance was not associated with increased mortality or treatment failure in any clinical setting. In addition, randomized controlled trials have demonstrated the feasibility of using PCT in settings ranging from primary care to emergency departments, hospital wards and intensive care units. Further validation of the use of PCT in all age groups and in patients with a variety of comorbidities such as immune compromise will be informative for clinicians.

Rapid diagnostic tests for distinguishing between viral and bacterial infection greatly facilitate the decision of whether or not to prescribe antibiotics. With the advent of new rapid diagnostics, time frame can be reduced dramatically. For example, the introduction of molecular technique utilizing PCR can dramatically reduce reporting time from several days to few hours. The reliable point of care test (POCTs) with rapid diagnostic technique

promotes rapid identification of resistant infections. It has been estimated that, use of POCTs having at least 95% sensitivity and 85 % specificity to identify febrile cases could save more than 1,50,000 lives annually and markedly reduce over treatment.

There is a general consensus that antibiotic resistance development and dissemination can be curtailed by limiting antibiotic use, discouraging misuse and reducing the burden of infectious diseases. Kumar and colleagues demonstrated the critical nature of timely antibiotic administration in patient with septic shock each hour of delay resulting in the 7.6 % decrease in survival. Traditional microbiological methods remain sub optimal in providing rapid identification and susceptibility testing. The need for rapid result is evident and current rapid molecular identification methods can provide results within minutes to few hours. This includes several commercially available rapid molecular assays for organism detection:

- PCR for identification and AMR
- Nano particle pro technology (Verigene blood culture system)
- Fluorescent in-situ hybridization (peptide nucleic acid)
- Matrix assisted laser desorption/ionization – time of flight mass spectrometry
- Procalcitonin as a sepsis biomarker
- The use of these diagnostic tools on patient care is an area of great interest, they can be best applied to stewardship effect.
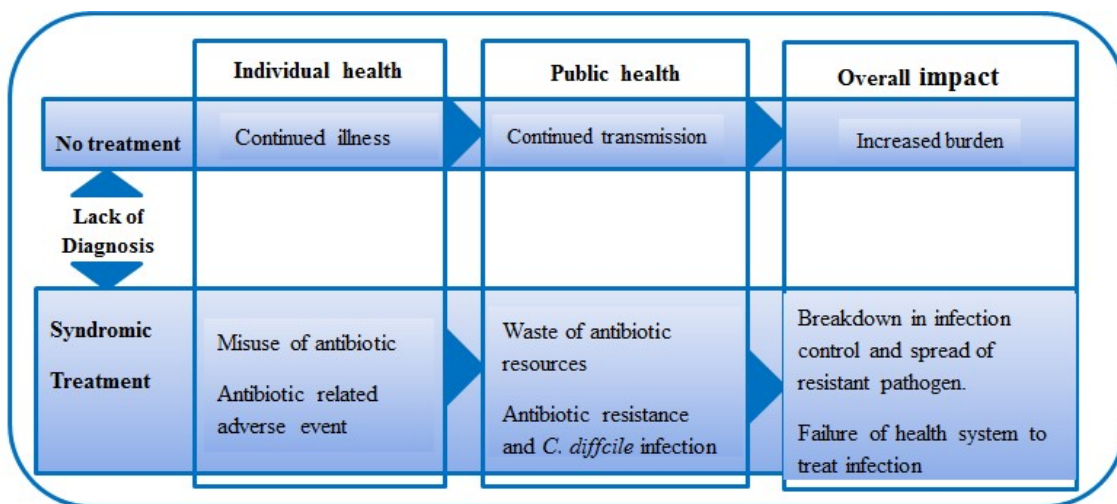
	Individual health	Public health	Overall impact
No treatment	Continued illness	Continued transmission	Increased burden
Lack of Diagnosis			
Syndromic Treatment	Misuse of antibiotic Antibiotic related adverse event	Waste of antibiotic resources Antibiotic resistance and *C. diffcile* infection	Breakdown in infection control and spread of resistant pathogen. Failure of health system to treat infection

Fig 5 : The high cost of poor diagnosis infection

15. ASM program measures for quality improvement

Structural indicators

- Availability of multi-disciplinary antimicrobial stewardship team
- Availability of guidelines for empiric treatment and surgical prophylaxis
- Provision of education in the last 2 years

Process measures

- Amount of antibiotic in DDD/100 bed days
- Compliance with acute empiric guidance
- Percentage of appropriate de-escalation
- Percentage of appropriate switch from IV to oral
- Compliance with surgical prophylaxis
- Compliance with care bundles

Outcome measures

- *C. difficile* rates
- Surgical site infection
- Surveillance of resistance
- Mortality

Balancing measures

- Mortality
- SSI rates
- Re-admission within 30 days of discharge
- Admission to ICU
- Rate of complications
- Treatment-related toxicity

16. Recent recommendations

- Antimicrobial stewardship should be monitored in ambulatory healthcare settings.

- Education about antimicrobial resistance and antimicrobial stewardship must be accomplished.

- Antimicrobial use data should be collected and readily available for both inpatient and outpatient settings.

- Research on antimicrobial stewardship is needed and should be funded by the appropriate federal agencies

17. Goal and Targets of the AMSP and the future vision

AMSP is a coordinated, quality improvement strategy designed to encourage the appropriate use of antimicrobial agents to optimize clinical outcomes while minimizing collateral antimicrobial effects. Collateral effects are primarily AMR but also include any other adverse antimicrobial event. AMS promotes prudent, effective prescribing through optimization of antimicrobial selection, dosage, duration of treatment, and route of administration.

An AMS programme is one empowered by an organization to deliver AMSP on its behalf. It comprises both clinical leadership in prescribing and corporate responsibility for prescribing practice, including strategy, surveillance of antimicrobial use, and education relating to antimicrobial therapy. Availability of prescribing and resistance data and an understanding of prescribing culture and practice are fundamental to inform interventions, guidance, and educational activities. Traditionally AMSPs have focused on hospital-based prescribing, where the use of broad-spectrum antibiotics is most prevalent and infections most severe.

An AMSP should:

1. Deliver the national antibiotic agenda locally, optimize antibiotic prescribing, and with infection prevention control teams contribute towards reduction in antibiotic resistance and healthcare-associated infections.

2. Receive support from clinical and managerial leadership who are accountable for the AMSP outcomes.

3. Develop and implement appropriate educational packages for all healthcare professionals to improve knowledge of antibiotics and to support the AMSP interventions.

4. Promote adherence to recommended good antibiotic prescribing practices.

5. Develop and survey standard datasets of antibiotic usage and antimicrobial resistance.

6. Audit and feedback the results of any new intervention and interpreted surveillance data to key stakeholders.

7. Assess adherence to antibiotic guidelines and progress towards national antibiotic targets through the introduction of performance indications.

Have flexibility to respond acutely to emerging challenges including collaborating during HCAI outbreaks where antibiotic prescribing may be implicated.

18. Expected threat if AMSP is not rigidly practiced

Antibiotic resistance is the crisis that is precipitating the current push for AMSP. The impact of antimicrobial resistance is high. The Centers for Disease Control and Prevention (CDC) estimates that each year in the United States, at least 2 million people acquire serious infections with bacteria that are resistant to 1 or more of the antibiotics designed to treat those infections. At least 23 000 people die each year as a direct result of these antibiotic-resistant infections. Many more die from other conditions that were complicated by an antibiotic-resistant infection. Antibiotic-resistant infections add considerable and avoidable costs to the already over-burdened healthcare system. In most cases, antibiotic-resistant infections require prolonged and/or costlier treatments, extend hospital stays, necessitate additional healthcare encounters, increased morbidity, and result in greater disability and death compared with infections that are easily treatable with antibiotics. Therefore, it is essential to follow the AMSP to avoid the above mentioned threats. The most awaiting threat of AMSP includes non-acceptance of physicians strictly restricting to institution specific guidelines or national antibiotic guidelines based on local antibiogram. Implementation of AMSP is time-consuming and

extensively labour intensive. In addition, de-escalation, redundant therapy, source controlled based debridement could be challenging in the successful implementation of AMSP. Non-compliance to AMS recommended antibiotic stop date among physicians would an additional challenge in implementing AMSP institutions.

19. Inappropriate disposal of leftover antibiotics: Risk to environment and man

India is one of the major countries that holds fifth place in global pharmaceutical market and has been ranked third place in terms of volume. When antibiotics are no longer needed, they should be disposed off promptly. Proper drug disposal is important because it helps protect human health and our environment. Unwanted drugs should not be flushed down the drain and it has a strong impact on the environment. A showed the presence of antibiotics such as metronidazole, sulfamethoxazole, ofloxacin, norfloxacin, tinidazolein the range of 1.4 to 236.6 μg-1 was documented in hospital effluents in Ujjain district, India.

It is important to avoid releases of antibiotics that can reach the ecosystem. Antibiotic waste must be treated differently depending on its stability .An unused medicine can be returned to the pharmacy for safe collection and disposal by incineration. Anti-infective drugs are encapsulated to delay release to the environment and avoid high concentrations. Anti-infective drugs should not be discarded in an untreated form. Generally, they are unstable and are best incinerated, and if that is not possible encapsulated or inertized. Liquid anti-infective drugs may be diluted in water, left for two weeks and disposed to the sewer.

It is important to have a good drug management system:

- Estimation of drugs based on health service utilization data and standard treatment regimens
- A well-functioning stock inventory control system, ß Practicing First Expiry First Out (FEFO) and First In First Out (FIFO) for drugs stocked
- Coordination with health institutions
- Negotiation with suppliers for the possible return of drugs that are about to expire.

Handling/storage

Antibiotics to be deposited for combustion must be treated as hazardous waste. Solutions containing antibiotics are collected in plastic drums and treated as hazardous waste.

Disposal Methods

Hazardous Waste: Encapsulation and Landfill

It should be immobilized or encapsulated prior to disposal into landfill as per the encapsulation method below

i) Return to donor or manufacturer

Wherever practical the possibility of returning unusable drugs for safe disposal by the manufacturer should be explored.

ii) Waste immobilization: encapsulation

Encapsulation involves immobilizing the pharmaceuticals in a solid block within a plastic or steel drum. They are filled to 75% capacity with solid and semi-solid pharmaceuticals, and the remaining space is filled by pouring in a medium such as cement or cement/lime mixture, plastic foam or bituminous sand. For ease and speed of filling, the drum lids should be cut open and bent back. Once the drums are filled to 75% capacity, the mixture of lime, cement and water in the proportions 15:15:5 (by weight) is added and the drum filled to capacity. Steel drum lids should then be bent back and sealed, ideally by seam or spot welding. The sealed drums should be placed at the base of a landfill and covered with fresh municipal solid waste. For ease of movement, the drums may be placed on pallets which can then be put on a pallet transporter.

iii) Incineration of hazardous pharmaceutical waste

The incinerators should be set according to the environment control strategies of the National Environment Commission (NEC). Of the available methods, incineration is more effective and optimal for safe disposal. The incinerators should have the following specifications:

Type	rotary kiln incinerators
Chambers	Two
Minimum Temperature	1100 degree Celsius
Capacity Range	Depending on the waste generated data

Wastes with high heavy-metal content (e.g. lead, cadmium, mercury) should not be incinerated as it will cause emission of toxic metals into the atmosphere. Hazardous pharmaceutical wastes, including wastes containing more than 1 % halogenated compounds, should be incinerated in rotary kiln incinerators with a minimum temperature of 1100 °C.

20. Initiative of ICMR / Govt of India in efforts of AMSP

To respond national AMR crisis in India, the Indian Council of Medical Research (ICMR), New Delhi, India, initiated the Anti- Microbial Resistance Surveillance and Research Network (AMRSN) across the country in 2013 with the purpose of rationalizing AMSP in India. This initiative was in line with the recommendations of Chennai Declaration which coincided with the global initiatives to combat antimicrobial resistance. Surveillance of six pathogenic groups was initiated by constituting 6 nodal centres and 20 regional centres. One of the key objectives of the network was to use evidence to guide treatment strategies thereby rationalising antimicrobial use. Having achieved greater success in its first phase, the network is now moving to the accelerated phase, for the next 5 years, wherein the focus would be on in improving diagnostic stewardship and infection control.

Moving on from phenotypic characterisation and realising the importance of monitoring MICs for better therapeutic outcomes, the network emphasises on the determination of carbapenem MIC and micro broth dilution based MIC determination for colistin isolates, irrespective of the anatomical sites. This would be coupled with molecular characterisation of ESKAPE pathogens to formulate appropriate empirical treatment guideline addressing appropriate indication for newly available βL/βLI drugs. Necessary trainings have been conducted and will continue to form part of capacity building efforts to train the regional labs for technical competency for the complete

molecular characterisation of the MDR pathogens. In the next phase of ICMR AMR programme, the impetus would be on moving towards in-depth understanding of molecular mechanisms of resistance, clonality and transmission dynamics. Necessary steps have been initiated towards a revision of Standard Operating Protocol of laboratory diagnosis, next edition of standard treatment guidelines based on current evidence, and expanding the activities under the hospital infection control and AMSPs being undertaken by the network hospitals.

Establishment of surveillance network was followed by launching a nationwide antimicrobial stewardship programme (AMSP). Hospital based programmes dedicated to improving antibiotic use, commonly referred to as AMSP have been found helpful in improving the quality of patient care and safety through increased infection cure rates, reducing treatment failures, and increasing the frequency of correct prescribing for therapy and prophylaxis. Under the Antibiotic Stewardship, Prevention of Infection and Control (ASPIC) programme of ICMR, microbiologists, pharmacologists and physicians were trained.

Implementation of an effective AMSP requires a multidisciplinary approach involving a variety of experts. It is recommended that the core team should include a clinical pharmacist and a physician trained in infectious diseases, a clinical microbiologist, an informatics specialist, a hospital epidemiologist, and an infection control specialist. In a survey of hospitals with stewardship programmes, clinical pharmacists and infectious diseases physicians are the most common element of the team. The ICMR set up a Steering Committee for guiding AMSP in the country in 2013. Treatment guidelines for important clinical infections and hospital infection control (HIC) guidelines are prepared. On the recommendation of the AMSP steering committee, a survey was carried out on existing AMSP practices in the country to gauge ground realities and plug the loop holes and strengthen AMSP.

Regulation of antibiotics and its misuse in settings outside of health-care continues to be a cause of serious worry. ICMR is working with the relevant stakeholders and respective departments of the government of India to reduce the colistin use in therapy and altogether ban its use as a growth promoter in livestock and poultry. To this

effect, a collaborative effort has been initiated with FAO and NEIVDI to establish AMR network for susceptibility testing and molecular characterisation of veterinary pathogens. For the same, a program on integrated surveillance has been initiated.

Unlike in the past, there is now plenty of evidence available from the country, which throw light on not only trends and patterns but allows us to monitor the MICs and mechanisms of resistance from key locations. The challenge in the years ahead would be to expand this capacity to other health-care institutions and also use this evidence to create a national treatment strategy to prevent abuse and misuse of antimicrobials as part of the antimicrobial stewardship effort.

Table 2: Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Strength of recommendation	A - Good evidence			B - Moderate evidence			C - Poor evidence		
Quality of evidence	I*	II*	III*	I*	II*	III*	I*	II*	III*
Prospective audit with intervention and feedback	physician/pharmacist - reduced inappropriate use of antimicrobials	-	-	-	-	-	-	-	-
Formulary restriction and pre-authorisation	-	Immediate and significant reduction in antimicrobial use and cost	-	-	Nosocomial outbreak of infection, Shifting to an alternative agent results in increased resistance	Monitoring overall trend in antimicrobial use	-	-	-
Education	-	-	Enhance the acceptance of stewardship strategies	-	Education without active intervention – marginal effect in changing antimicrobial prescribing practice	-	-	-	-
Guidelines and clinical pathways	Local resistance pattern improve antimicrobial utilization	-	Education & feedback on antimicrobial use & patient outcome	-	-	-	-	-	-
Antimicrobial cycling		-	-	-	-	-	-	Reducing AMR over long period of time	
Antimicrobial order forms	-	-	-	-	Implementation of practice guidelines				
Combination therapy	-	Increase the coverage against MDR pathogens	-	-	-	-	-	Prevent emergence of resistance	
Streamlining/de-escalation of therapy		Culture result & elimination of combination therapy							
Dose optimization	-	PK/PD of drug, patient characteristics, causative organism, site of infection							
Parental to oral conversion	Decrease length of hospital stay and health care cost		Excellent bioavailability, decrease hospital stay & healthcare cost						
Healthcare information technology			Electronic medical records	Computer physician order entry, Clinical decision support					
Computer based surveillance				Tracking of AST pattern, Identification of nosocomial infection					
Clinical microbiology laboratory			Optimize individual AMR management, Surveillance of MDR outbreak						
Recommendations									
Core members of antimicrobial stewardship team		Physician & clinical pharmacist	Clinical microbiologist, Infection control professional						
Collaboration			Stewardship team,HICC,medicalstaff,local providers						
Hospital administrative support			Track antimicrobial use on an ongoing basis						

*I - Evidence from1 properly randomized, controlled trial

*II - Evidence from1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from 11 center); from multiple time-series; or from dramatic results from uncontrolled experiments

*III - Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

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Compiled by:

Dr. V. Balaji
Professor and Head
Department of Clinical Microbiology
Christian Medical College, Vellore, TN

Dr. Priscilla Rupali
Professor
Department of Infectious Diseases,
Christian Medical College, Vellore, TN

Dr. Kamini Walia
Scientist F and Program officer AMR
Division of ECD, ICMR, New Delhi

Dr. V C Ohri
Consultant AMR, ICMR, New Delhi

Reviewed by:

Dr. V Ramasubramanian,
Consultant,
Apollo Hospitals,
Chennai, TN

Dr. Ramgopalkrishnan,
Consultant
Apollo Hospitals,
Chennai, TN

Dr. Y K Gupta
Professor
All India Institute Medical Sciences
New Delhi