AMR has assumed greater importance in health-care settings. Preserving the efficacy of antimicrobial agents is considered a critical step in fighting communicable diseases. One of the approaches is to have evidence-based antibiotic usage policy in hospital and standard treatment guidelines for common infectious diseases. This document focuses on the mechanism to develop a practical hospital antibiotic policy and standard treatment guidelines. It also contains information on various effective strategies for implementation of standard treatment guidelines. A suggested model hospital STG for community-acquired pneumonia in adults is included.

Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines
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### List of abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ABC Calc</td>
<td>antibiotic consumption calculator</td>
</tr>
<tr>
<td>AMR</td>
<td>antimicrobial resistance</td>
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<tr>
<td>AMT</td>
<td>antimicrobial team</td>
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<tr>
<td>ARIMA</td>
<td>auto-regressive integrated moving average</td>
</tr>
<tr>
<td>ATC</td>
<td>anatomic therapeutic chemical</td>
</tr>
<tr>
<td>ATS</td>
<td>American Thoracic Society</td>
</tr>
<tr>
<td>BSAC</td>
<td>British Society for Antimicrobial Chemotherapy</td>
</tr>
<tr>
<td>CAP</td>
<td>community-acquired pneumonia</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention (Atlanta)</td>
</tr>
<tr>
<td>CLSI</td>
<td>Clinical and Laboratory Standards Institute</td>
</tr>
<tr>
<td>CWA</td>
<td>community-wide antibiograms</td>
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<tr>
<td>DDD</td>
<td>defined daily dose</td>
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<tr>
<td>EPOC</td>
<td>effective practice and organization of care</td>
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<tr>
<td>EQAS</td>
<td>External Quality Assessment Scheme</td>
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<tr>
<td>EUCAST</td>
<td>European Committee on Antimicrobial Susceptibility Testing</td>
</tr>
<tr>
<td>HAI</td>
<td>health-care associated infection</td>
</tr>
<tr>
<td>ICU</td>
<td>intensive care unit</td>
</tr>
<tr>
<td>IDSA</td>
<td>Infectious Diseases Society of America</td>
</tr>
<tr>
<td>KPC</td>
<td><em>Klebsiella pneumoniae</em> carbapenemase</td>
</tr>
<tr>
<td>MIC</td>
<td>minimum inhibitory concentration</td>
</tr>
<tr>
<td>MRSA</td>
<td>methicillin-resistant <em>Staph aureus</em></td>
</tr>
<tr>
<td>NABH</td>
<td>National Accreditation Board for Hospitals</td>
</tr>
<tr>
<td>NABL</td>
<td>National Accreditation Board for Laboratories</td>
</tr>
<tr>
<td>PDD</td>
<td>prescribed daily doses</td>
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<tr>
<td>SCA</td>
<td>Science Computing Associates</td>
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<tr>
<td>SHEA</td>
<td>Society for Healthcare Epidemiology of America</td>
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<tr>
<td>STG</td>
<td>standard treatment guidelines</td>
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<tr>
<td>STRAMA</td>
<td>Swedish Strategic Programme Against Antibiotic Resistance</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Antimicrobial resistance

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, resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, with increased numbers of infected people moving in the community. This in turn exposes the general population to the risk of contracting a resistant strain of microorganisms. When these become resistant to first-line antimicrobials, the prohibitive high cost of the second-line drugs may result in failure to treat these diseases in many individuals. Most alarming of all are the diseases caused by multidrug-resistant microbes, which are virtually non-treatable and thereby create a “post-antibiotic era” scenario.

Figure 1: Emergence of resistance and hospital cross-infections
Antimicrobial resistance in health-care associated infections (HAI)

AMR has assumed greater importance in health-care settings. The presence of compromised individuals in an environment with a variety of infectious agents which are continuously under heavy antibiotics pressure results in the emergence and spread of resistant organisms to other patients in the form of cross-infection (Fig. 1). The size of the ageing population is also on the rise, leading to an increasing number of individuals living with immunocompromised states. Such people spend more and more amounts of time in hospitals or long-term care facilities. These patients will be at risk for morbidity and mortality associated with HAI. Further, there is an association between the development of resistance in *Staphylococcus aureus*, enterococci, and Gram-negative bacilli and an increase in mortality, length of hospitalization, and the cumulative cost of health care. This attributes to inappropriate, inadequate or delayed therapy. Strategies to prevent the emergence and spread of health-care associated antimicrobial-resistant organisms are essential.

Health-care epidemiologists are still grappling with problems associated with preventing the spread of multidrug-resistant aerobic Gram-negative bacilli in health-care settings; implementing effective strategies to ensure antimicrobial stewardship; preventing the spread of multidrug-resistant *S. aureus* (MRSA) infection in health-care settings; and developing effective strategies to ensure adherence to hand hygiene standards.

An effective strategy to limit the effect of multidrug resistance must be multifaceted and must include the education of patients and physicians about appropriate drug, dose and duration, use of effective infection-control practices to prevent transmission from infected to uninfected patients, surveillance of antimicrobial resistance and antimicrobial use, and improved use of immunization. The campaigns should be undertaken to educate the public about the dangers of antimicrobial resistance and what may be done to control it.
Availability of new antimicrobial agents

The situation on the development of new antimicrobial agents is not very encouraging. Hardly any promising agents are in the pipeline for treatment of some common multidrug-resistant nosocomial organisms commonly grouped under acronym of ESKAPE:

- *Enterococcus faecium* (vancomycin-resistant enterococci-VRE).
- *Staph aureus* (methicillin-resistant *Staphylococcus aureus*-MRSA).
- *Klebsiella* and *Escherichia coli* that are producing extended spectrum beta-lactamases (ESBL) enzymes and carbapenemases.
- *Acinetobacter baumannii*.
- *Pseudomonas aeruginosa*.
- *Enterobacter sp.*

The solution to the current approaches to antimicrobial resistance is to preserve the effectiveness of the drugs presently available by antibiotic stewardship and to maximize hospital infection-control practices, to limit the spread of resistance.

Strategies against antimicrobial-resistant microorganisms in hospitals

Strategic objectives

- To develop a system to recognize and report trends in antimicrobial resistance within the institution.
- To develop a system to rapidly detect and report resistant microorganisms in individual patients and ensure prompt treatment.
- To assure increased adherence to basic infection control policies and procedures.
- To incorporate the detection, prevention and control of antimicrobial resistance into institutional strategic goals and provide the required resources.
To develop a plan for identifying, transferring, discharging and readmitting patients colonized with specific antimicrobial-resistant pathogens.

To establish policy and practices for rational use of antimicrobials.

Strategic approaches

- Optimizing the duration of choice and dose of empiric therapy: antimicrobial stewardship.
- Optimizing antimicrobial prophylaxis for operative procedures.
- Developing and implementing an antibiotic policy and standard treatment guidelines (STG).
- Monitoring and providing feedback regarding antibiotic resistance.
- 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.

Scope of the document

This document focuses on the mechanism to develop a practically applicable hospital antibiotic policy and standard treatment guidelines (STG). In addition, the document contains information on various effective strategies for implementation of STG. It also discusses various activities and information required for the development of the antibiogram, antibiotic policy and standard treatment guidelines, such as surveillance programmes, the cause and controlling strategies for AMR and HAI; performance measures of antibiogram, antibiotic policy and standard treatment guidelines. A model hospital STG for community-acquired pneumonia in adults is included.

The figure below (Fig.2) summarizes the process for the development of antibiotic policy as well as the standard treatment guidelines in a hospital setting.
The document elaborates all these activities.

**Guideline development process**

The WHO Regional Office for South-East Asia commissioned the Christian Medical College and Hospital, Vellore, India, to develop the first draft of the guidelines. The objectives were to provide a tool to developing countries for establishing procedures and practices for formulating hospital antibiotic policy and standard treatment guidelines which should lead to rational use of antibiotics and minimize the emergence of antimicrobial resistance. The guidelines were reviewed by several experts from Christian Medical College and Hospital, Vellore, and subsequently by Director, WHO Collaborating Centre on Antimicrobial Resistance, other experts including colleagues in the WHO Regional Office for South-East Asia and the WHO Country Office for India.

**Guidelines development team**

WHO wishes to acknowledge the support provided by various experts in drafting, reviewing and finalization of the guidelines (please see list in Annex 1).
Antibiotic policy\textsuperscript{1,2}

The primary aim of the hospital antimicrobial policy is to minimize the morbidity and mortality due to antimicrobial-resistant infection; and to preserve the effectiveness of antimicrobial agents in the treatment and prevention of communicable diseases.

Scope of hospital antibiotic policy

The antibiotic policy is essentially for prophylaxis, empirical and definitive therapy. The policy shall incorporate specific recommendations for the treatment of different high-risk/special groups such as immunocompromised hosts; hospital-associated infections and community-associated infections.

The hospital antibiotic policy shall be based upon:

- spectrum of antibiotic activity;
- pharmacokinetics/pharmacodynamics of these medicines;
- adverse effects;
- potential to select resistance;
- cost;
- special needs of individual patient groups.

\textsuperscript{1} Antibiotic versus antimicrobial agents: An antibiotic or an antimicrobial is a chemical therapeutic agent that inhibits or abolishes the growth of micro-organisms such as bacteria, fungi or protozoa. The term originally referred to an agent sourced from biological organisms; however, “antibiotic” is now used commonly to refer to substances with anti-bacterial, anti-fungal or anti-parasitical activity.

\textsuperscript{2} Policy versus guidelines: The terms policy and guideline are used interchangeably, though they mean different things. Policy should be used to refer to local, regional, or national antibiotic stewardship programmes as a whole, while guidelines should refer to specific treatment or prophylaxis recommendations for individual diseases, syndromes, etc.
It should also set the levels for prescribing antibiotics; for example, first choice antibiotics can be prescribed by all doctors while restricted choice antibiotics can only be prescribed after consulting the head of the department or the antimicrobial team (AMT) representative. Reserve antibiotics, on the other hand, are prescribed only by designated experts.

**Development of antibiotic policy**

An overview of the key elements of the hospital antibiotic policy is presented in Figure 3.

**Figure 3: Key elements of hospital antibiotic policy**

Establish a multidisciplinary antibiotic management team to draft policy

An efficient antibiotic policy in a health-care setting shall demand from the top management their full commitment as well as their total support to the development and implementation of this policy.

To develop an antibiotic policy each hospital shall establish a multidisciplinary antibiotic management team (AMT). The team’s
functions should include developing a hospital antimicrobial policy, monitoring the implementation of the antibiotic policy, receiving feedback, assessing outcome and discussing with clinicians, conducting a revision of the policy every year based on the experience of prescribers and antimicrobial susceptibility profiles, and setting audit targets.

The group developing the antibiotic policy should be a multidisciplinary group with 6–10 members with expertise and experience in different subjects (usually infectious diseases, internal medicine, surgery, pediatrics, clinical microbiology, pharmacology and hospital pharmacy). At least one member should have the skills to conduct literature and systematic reviews. There should be inputs from all stakeholders, including trainees, in order to ensure “ownership” of guidelines.

The other functions assigned to the AMT team include:
- antimicrobial dose and regimen alteration;
- streamlining and sequential therapy;
- discontinuation of antimicrobials;
- advice on and as a result of therapeutic drug monitoring;
- automatic stop orders for antimicrobial prophylaxis;
- restricted antimicrobials;
- empirical antimicrobials;
- approval of restricted antibiotics;
- assistance in interpretation of laboratory results;
- indication for use of specific antimicrobials;
- suggestion for ordering additional laboratory testing and formal educational events.

**Review available for antibiotic policies and evidences**

The available evidence-based antibiotic policy from other institutes, or the national policy if formulated, may be reviewed and, if appropriate, adapted to suit local circumstances. The advantage of adapting from national policy is that the clinical, managerial and technical skills as well as time and financial resources needed for the task are adequately available. But knowledge at the local level is unlikely to be sufficiently
Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines

broad, hence the opinion of local personnel may introduce bias into the decision-making process. However, the advantage with local guidelines is that it requires fewer resources for effective dissemination and implementation.

The policy to be adapted for local needs with modifications can be chosen based on the various parameters of the antimicrobial policy. This includes how information is gathered, cost analysis done, what was the outcome expected, the method used for analysis, how the quality and strength of evidence was assessed, how recommendations were formulated, the strength of recommendations and their validation.

Draft antibiotic policy based upon available evidence

The policy should be based on a systematic review of scientific evidence which would minimize the risk of bias. The literature should be identified according to an explicit search strategy and defined inclusion criteria assessed against consistent methodological standards. In addition the search terms and period of search should be mentioned.

When robust evidence is not available a hybrid of a varying degree of evidence and expert opinion may contribute to develop antibiotic policy. However, this recommendation should be done with grading according to the strength of evidence supporting them. The grading should be validated based on study design and quality and of the consistency and clinical relevance.

Attributes of antibiotic policy

The policy should be simple, clear, clinically relevant, flexible and applicable to day-to-day practice and available in user-friendly format such as a pocket guide, web-based form, etc.

The recommended antibiotic should be effective against pathogens often seen in that locality.

- Recommendations should be provided for optimal selection, dosage, route of administration, duration, and alternatives for allergy to first-line agents; and for adjusted dosage for patients with impaired liver or renal function.
• Recommendation for prophylactic use should specify procedures for which antibiotic are needed, optimal agents, dosage, timing, route and duration of administration so that adequate antibiotic concentrations are available at the time of bacterial contamination. Prophylaxis recommendation should mainly focus on clean as well as contaminated procedures. The prophylactic dose is recommended for a short duration, free of side-effects, and should be relatively cheap. Also, the antibiotics selected for prophylaxis should not be used therapeutically; as this may lead to emergence of antimicrobial resistance.

Identification of gaps and research priorities
The Policy Group should identify evidence that is lacking and areas for further research. For example, if empiric therapy results in clinical failure, then review of cumulative antibiogram data may be needed to change the policy accordingly. For example, an elderly male patient with cystitis seen in emergency room does not respond to empiric ciprofloxacin treatment though previously the same was successful. Culture is performed and result shows *E. coli* resistant to ciprofloxacin. Then the research question would be – what percentage of urine isolates from emergency room patient are susceptible to ciprofloxacin?

Monitoring and review of policy
The Policy Group should identify sample outcome measures that would form basis for auditing both the process and outcome of the policy. For example ciprofloxacin is recommended for treatment of typhoid fever, only if MIC of ciprofloxacin is ≤0.25µg/ml. Auditing should include whether this recommendation is followed? Has ciprofloxacin MIC been determined for every *Salmonella typhi* identified? Furthermore, the audit should also monitor and evaluate the quality of antimicrobial prescriptions for right duration and dosage.

Policy should be reviewed by experienced peers who are not the members of the policy development group, but are experts in the relevant field.

Policy is not static. It is a living document. It should be reviewed at periodic intervals, updated according to current medical knowledge, clinical practice and local circumstances.
**Hospital versus national antibiotic policy**

Generally, the hospital antibiotic policy should concur or align with the national antibiotic policy except for a few changes as warranted by the local antimicrobial resistance profiles. If there is a wide variation from national to hospital, and hospital to hospital then the desired purpose is defeated i.e., to minimize the morbidity and mortality due to antimicrobial-resistant infections; to preserve the effectiveness of antimicrobial agents in the treatment and to prevent microbial infections.

**Important issues that may be addressed in the national antibiotic policy**

A national antibiotic policy should address all relevant issues for antibiotic use, both in the community and the hospital, including veterinary and agricultural use. The important issues that need to be included in the policy are as follows:

- Existing laws should be enforced to prevent non-prescription, over-the-counter sale of antibiotics.
- Guidelines for antibiotic treatment and prophylaxis should be prepared and adapted institutionally at a local level.
- Consumption of antibiotics should be monitored to estimate the national consumption of antibiotics.
- A national antimicrobial resistance surveillance system should be established and coordinated with international systems.
- A national control of infections programme including a hospital infection control programme should be implemented.
- A national institute of excellence with mandate to make recommendations on various microbiological culture and susceptibility tests and disk diffusion and minimum inhibitory concentration breakpoint interpretive criteria should be established.
- External Quality Assessment Scheme (EQAS) to ascertain the quality of laboratory results should be launched and sustained.
- Educational programmes should be elaborated for both health-care workers and the public.
- Collaboration with international organizations should be established.
- Appropriate funding should be made available by the government or any other organization.

Limitation of the national antimicrobial policy

There are limitations in using the national antimicrobial policy which include the local resistance problems which dictate different solutions and different prescribing practices within a defined geographical region and, moreover, huge economic and social differences between the different regions will demand different approaches at different levels.
The antibiotic policy shall depend heavily on surveillance of antimicrobial resistance and antibiotic consumption in any setting. Hence, it is mandatory to establish an efficient surveillance system.

Surveillance is defined as “the ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know”.

**Surveillance of antimicrobial resistance**

Antimicrobial surveillance data will help to formulate, monitor and identify the prevailing and emerging problem, which can be contained by effective strategy. Currently, the majority of surveillance programmes are laboratory-based. Very few clinical data are collected and the data obtained by most surveillance programmes are not useful to implement control and/or prevention measures. One strategy to improve the collection, collation and dissemination for effective use in the hospital/community is to integrate this function of antimicrobial resistance surveillance activities into the existing disease surveillance activities.

It is beyond the scope of this document to describe a comprehensive laboratory-based antimicrobial resistance surveillance programme. This issue is addressed in other WHO documents. However, the following four features must be considered while establishing a surveillance mechanism:
Use standards

Laboratories should use standards for reporting quantitative resistance data (e.g. minimal inhibitory concentrations or zone diameters) that will detect decreased susceptibility. This is necessary because numerical antimicrobial test results reported qualitatively (e.g., as susceptible, intermediate, or resistant) may hide an emerging resistance character in microorganisms with a small decrease in susceptibility that may still be classified as susceptible.

Generate reliable numerator

It is crucial to avoid including duplicate results since a patient may have either consecutive cultures obtained from the same body site or cultures from different body sites yielding the same organism (e.g., urine and blood culture). Therefore, only the first positive culture from the patient for each disease episode should be reported for surveillance purposes. This will be the reliable numerator for the antimicrobial resistance surveillance.

Express resistance as incidence rate

It is important to express antimicrobial resistance rates as incidence rates within a defined human population instead of using the number of isolates tested as denominators. This is imperative because the submission of microbiology specimens to the laboratory is inconsistent and varies broadly. In hospital settings, it is recommended to use the number of admissions and the number of days of hospitalization, which are particularly useful for inter- or intra-health-care facility comparison. It should be recognized that this process captures data only from patients admitted to health facility and excludes those who attend as out door patients.

Participate in external quality assessment schemes

The validity and reliability of surveillance data is deemed acceptable only when the clinical laboratories providing data for the surveillance program should have routinely participated in pertinent training and proficiency testing (external quality assessment) programmes with good performance.
The other considerations for an effective antimicrobial resistance surveillance include:

- Clinical microbiologists should be trained in health-care epidemiology.
- The choice of micro-organisms and antimicrobials to survey should be based on their relative public health importance, using criteria such as expected numbers of cases, severity of the infectious disease as measured by its mortality rate and case-fatality ratio, medical costs of such infections, and preventability.
- Microbiologists should collect not only laboratory data but also the clinical data that is often missing from surveillance reports.

A well-structured computer system with WHO (WHONET) open source software can be used for data entry and analysis ([http://www.who.int/drugresistance/whonetsoftware/en/](http://www.who.int/drugresistance/whonetsoftware/en/)). The analysis should be done at regular intervals and the results/observations should be shared within the institution, with community and collaborative study groups.

**Attributes of good surveillance systems**

The attributes of a “good surveillance system” are

- simplicity,
- flexibility,
- representativeness,
- timeliness, and
- usefulness.

A surveillance system should accurately describe the occurrence of antimicrobial resistance over time and its distribution in the population by place and person. This is a difficult task as the spectrum of micro-organisms under surveillance includes uneven distribution of pathogens and opportunistic pathogens.

The surveillance system should be flexible so that changing information can be incorporated easily and also have room for inclusion of new diseases and health conditions. An example is the capacity of an *S. aureus* surveillance system to conduct special surveillance for glycopeptide-intermediate or resistant *S. aureus*. 
The timeliness of surveillance programs should be optimal since antimicrobial resistance is rapidly evolving and delay does not augur well for efficient policy. The published data usually does not reflect the current state of antimicrobial resistance.

**Evaluation of a surveillance system**

The evaluation of the surveillance can be measured by investigating the following aspects:

- Does the system detect trends that signal changes in the occurrence of diseases?
- Does the system provide estimates of the magnitude of morbidity and mortality related to the health problem under surveillance?
- Does the system stimulate epidemiologic research and action likely to lead to control and prevention?
- Does the system identify risk factors associated with disease occurrence?
- Does the system permit assessment of the effects of control measures?
- Does the system lead to improved clinical practice by the healthcare providers who are the constituents of the surveillance system?

**Prediction of evolution of antimicrobial resistance**

To predict the short-term evolution of resistance, the behaviour of antimicrobial use, and its dynamic relationship, time-series analysis on antibiotic resistance and consumption data help to estimate the probability of susceptibility of the microorganism to every available antibiotic. This information facilitates to make recommendations about the empiric therapy, relevant to the local environment that would minimize the probability of error in the therapeutic choice.

**Surveillance of antimicrobial consumption**

It is essential to have surveillance data on antibiotic use/consumption in the hospital/community. This is an indispensable tool in the strategy to contain antimicrobial resistance. Hence it is a must that all the hospital/community should generate a valid data on antibiotic prescriptions.
and sales. The same should be made publicly available to formulate antibiotic policy and STG.

To evaluate if antibiotic prescribing is rational, data on number of prescriptions, indications, dose and duration of treatment, as well as different age groups are essential. Such data are needed in order to evaluate the impact of antibiotic prescribing on resistance, morbidity, complications, and mortality.

However, drug consumption data with varying data collection system, time periods, and units of measurements makes it difficult to compare trends in antibacterial usage between geographical regions. Further, in many developing countries, the lack of access to essential pharmaceuticals, over the counter sales, and suboptimal dosage are major problems in collecting reliable data.

Measurement of antimicrobial consumption

WHO Collaborating Centre for Drug Statistics Methodology (1999) describes unit called as defined daily dose (DDD) according to the Anatomic Therapeutic Chemical (ATC) classification system. This defined daily dose is a unit based on the average adult dose used for the main indication of the drug. To make comparisons between geographical areas possible, the number of DDDs per 1000 inhabitants and day (DID) may be calculated. This measure will be influenced by several factors, for example, the dosage and duration of treatment, which may vary between hospitals even for the same indication.

The other measure of antibiotic use is the number of antibiotic prescriptions per 1000 inhabitants per year. This measure is probably more appropriate when evaluating antibiotic use in children.

WHO commissioned five pilot projects in different countries to ascertain community-based surveillance of antimicrobial use and resistance in resource-constrained settings. The methodology followed and observations made can be seen in WHO document published in 2009.

It has been observed that instead of individual antibiotic pattern, better guidance is obtained using the cumulative antibiogram. The cumulative antibiogram (CA) represents a report which summarizes the susceptibility of commonly isolated microorganisms to usual antibiotics in a defined period of time.
Cumulative antibiogram

The surveillance for antimicrobial resistance/antibiotic consumption and preparation of an “enhanced” or cumulative antibiogram at the local level helps in clinical decision-making, design infection control interventions, and antimicrobial-resistance containment strategies.

Attributes of cumulative antibiogram

The major attributes of a reliable cumulative antibiogram (Fig. 4) include:

- Analyses/presentation of data regularly, at least annually.
- Inclusion of only final, verified results.
- Inclusion of only species with at least ≥ 30 isolates tested (under certain circumstances, when you don’t have >30 isolates, then combine two consecutive years’ isolates into the calculation).
- Inclusion of diagnostic (not surveillance) isolates.
- Information only on drugs routinely tested.
- Inclusion of the first isolate per patient in the period analyzed, irrespective of the body site from which the specimen was obtained or the antimicrobial susceptibility pattern.
- Calculation of the percentage susceptibility because clinicians generally avoid prescribing antimicrobials if a test result indicates intermediate susceptibility. Isolates with intermediate susceptibility should not be included in the calculation of the percentage of isolates that are susceptible.
Avoid the presentation of potentially misleading or confusing data, especially when presenting as a table and ensure all the details are provided in the accompanying footnotes.

Providing confidence intervals and statistical significance of changes in the percentage of susceptible isolates.

Utilizing statistical tools to analyze the data.

Undertaking data stratification to encourage optimal antimicrobial therapy. It is often useful to stratify results by specimens type or infection site, by nursing unit or site of care, by organism’s resistance characteristics, by clinical service or patient population.

Reviewing the cumulative antibiogram data if clinical failure occurs after empiric therapy and, if changed, the trend has to be followed.

Ensuring the quality of the cumulative antibiograms.

Comparing the cumulative antibiogram with national data. However, care must be taken to make sure that there is no variation in the drug panels of comparing antibiograms.
Antibiogram – derived radial decision trees

This type of dissemination in the hospital helps to recognize the resistance to first-line drugs indicate susceptibility to second-line drugs and as well understand the probability of encountering such organisms.

Challenges in cumulative antibiogram

Variability in culture and susceptibility ordering practices is inevitable. Usually, a significant number of the laboratory requests for the culture susceptibility from outpatient or inpatients are due to suspected infection with resistance organisms. Consequently, the number of requests received for susceptible infections are less as when compared with those for resistant cases. As a result, overcall of resistance rates are always introduced into most of the cumulative antibiograms.

Community-wide antibiograms (CWA)

Establishment of local surveillance systems improves appropriate antimicrobial use and curtailing antimicrobial resistance. To ensure that reliable data are presented consistent mechanism to generate, collect, and collate data at the local level is required that represents community prevalence of organisms.

Cumulative hospital antibiograms as a quality indicator

- Laboratories are often surveyed about their testing practices, but analysis of antibiograms may be a useful tool to measure whether laboratories are incorporating changes and updates in their testing methods.
- Analysis of antibiograms may provide useful information when deciding where to focus educational efforts.
- Increased compliance with standards and guidelines, particularly those with regard to daily verification of unusual or unlikely results, should result in decreased errors on antibiograms, and thus provide more reliable data to clinicians to guide antibiotic choice.
- Programmes that provide and explain the antimicrobial susceptibility testing standards and guidelines may encourage compliance.
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 effective STG

- The standard treatment guideline should be based on the findings of the cumulative antibiogram, antimicrobial policy, surveillance data on antimicrobial resistance and antibiotic consumption data and hospital associated infection profile of the particular hospital or community.
- If a large number of STG documents are available from different sources on the same subject, these can be compared for strengths and weaknesses in each guideline. Then a suitable guideline among the existing ones can be adapted with modifications for a desired local hospital, community/region.
- The STG should clearly specify for which disease/condition(s) they are stipulated, and also state who the intended users and the target population are, and what are the interventions and practices – such as evaluation, diagnostic studies, treatment and prevention – considered.
- The guideline developers should describe methods used to collect/select the evidence such as search of electronic databases and the number of documents sourced.
All the major recommendations should be accompanied with levels of evidence (I–III) available and grades of recommendation (strong, moderate and weak). The quality and strength of the evidence can be based on a rating scheme generally followed as listed below:

- **Level I (high):** Evidence from well-conducted, randomized controlled trials.
- **Level II (moderate):** Evidence from well-designed, controlled trials without randomization (including cohort, patient series and case-control studies). Level II studies also include any large case series in which systematic analysis of disease patterns and/or microbial aetiology was conducted, as well as reports of data on new therapies that were not collected in a randomized fashion.
- **Level III (low):** Evidence from case studies and expert opinions. In some instances, therapy recommendations come from antibiotic susceptibility data without clinical observations.

### 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.

### Development of STG

Methods used to formulate the recommendations should be declared. The strength of each recommendation is graded as “strong”, “moderate” or “weak.” Usually the guideline committee independently grades each recommendation on the basis of the evidence and also includes their expert interpretation and clinical applicability. The final grading of each
recommendation is a composite of the individual STG developer group
members’ grades. For the final document, a strong recommendation
require majority of the committee members to consider it to be strong.
The moderate or weak management recommendations are usually not
followed by the majority of the clinicians.

The description of the methods used to analyse the evidence
should be stated. This could be either a review or review of published
meta-analyses.

Also, evidence supporting the recommendations, references and
type of evidence supporting the recommendations must be mentioned,
and a formal cost analysis should be performed and included. Likewise,
if clinical algorithm(s) are useful, they could be made and included.

**Recommendations in STGs**

- Minor criteria and major criteria for the diagnosis are
  formulated and recommended for the clinical syndrome/
disease concerned.

- Recommendations are made for pathogen-directed therapy.
  Once the aetiology of the infection has been identified on the
  basis of reliable microbiological methods, antimicrobial therapy
  is directed at that pathogen.

- Decision of admission to hospital is advised on the basis of the
  severity-of-illness scores, or prognostic models. This can identify
  the level of care as outpatient, in-patient non-ICU admission
  or direct in-patient ICU admission.

- Recommendations on the empirical antimicrobial therapy
  is specified separately for outpatient treatment, inpatient
  treatment, non-ICU treatment and in-patient ICU treatment on
  considering clinical condition and presence of co-morbidities.

- In addition to the constellation of suggestive clinical features,
  the STG should include suggestion for diagnostic testing of the
  disease condition such as chest radiograph or other imaging
  technique, microbiological/pathological, haematological and
  biochemistry data/values. The recommendation should focus on
  the investigation for specific pathogens that would significantly
  alter standard (empirical) management decisions.
Recommendations are generally made for a class of antibiotics rather than a specific drug, unless outcome data clearly favours a specific drug. Since overall efficacy remains good for many classes of agents, the more potent drugs are given preference because of their benefit in decreasing the risk of selection for antibiotic resistance. Other factors for consideration of specific antimicrobials include pharmacokinetics/pharmacodynamics, compliance, safety and cost.

Early treatment (within 48 hours of the onset of symptoms) with appropriate antimicrobials is recommended whereas for patients admitted through the emergency department, the first antibiotic dose should be administered while still in that department.

Recommendations on the duration of therapy for patients with infection should lay emphasis that therapy should continue for a minimum of 48 to 72 hours after the patient becomes afebrile and should have no more than one or two syndrome associated signs of clinical instability before discontinuation of therapy.

Recommendation on the criteria for clinical stability should be in place. Usually this can be the minimum expected temperature; heart rate; respiratory rate; systolic blood pressure and arterial oxygen saturation.

Recommendation on switch from intravenous to oral therapy can be made when the patient is haemodynamically stable and improving clinically, is fully conscious, and able to ingest oral medications.

Recommendation on the use of antimicrobials should take into account the use of antimicrobials within the previous three months (in which case an alternative from a different class should be selected). In case the individual is from a geographical region that has a high rate (>25%) of resistant organisms reported or where high-level minimal inhibitory concentration (MIC) is observed then, the use of alternative agents is mandatory.

Recommendation on patient discharge can be suggested as soon as they are clinically stable, and have no other active medical problems.
The locally adapted guideline should offer suggestions about the epidemiology and/or risk factors for alternative or specific additional antibiotics for the treatment.

Suggestion for the management of “non-responding infections” can be outlined. Non-responding infection is defined as an inadequate clinical response despite adequate antibiotic treatment.

**Monitoring the quality of antimicrobial prescriptions**

Even with the use of STGs, one needs to monitor their application. Monitoring should be done to ascertain the following:

- Is the clinical picture compatible with an infection? Is there an indication for treatment with antibiotics?
- Is the choice of the antimicrobial drug adequate?
  - Efficacy: Is the (suspected) agent active?
  - Toxicity/allergy: Is there a less toxic alternative?
  - Cost: Is there a less costly alternative at equal efficacy and toxicity?
  - Broadness of spectrum: Is the spectrum unnecessarily broad?
- Is the duration of treatment appropriate?
  - Too long/too short?
- Is the dosage correct?
  - Dose/interval/mode of administration
- Is the timing appropriate?
  - Too early/too late?

**Validation of STG**

Guideline validation should be done by the internal peer review process. The STG is 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.
Strategies for promoting rational antibiotic prescribing

Apart from conventional methods of communication, effective strategies are found to be aimed at appropriate practices for prescribing antibiotics by changing physician behaviour such as education outreach (academic detailing with interactive sessions) and use of computer information systems and computer checks that can facilitate changes. Reminders to health-care workers have to be used sparingly; otherwise too frequent reminders will be ignored. Computer checks can be programmed into a hospital information system (HIS) to provide reminders, warnings and other suggestions to facilitate appropriate ordering of therapeutic and preventive treatments. Educational outreach is another effective strategy. For example, in academic detailing, there is a one-on-one dialog and the exchange tends to be interactive rather than didactic. In the interaction, the provider being detailed can discuss the matter with the academic detailer until the provider understands the issue.

Barrier-oriented interventions

Barrier-oriented interventions are critical and must be tended to specific local barriers. The possible local barriers would be disagreement among experts, availability of alternative practices, inapplicability of guidelines to certain patient subgroups, patient refusal to comply, institutional inertia, vested interests, ineffective continuing medical education, and uncertainty about when and how to apply evidence-based medicine measures. The other barriers identified by Cabana et al in 1999 are listed in the table shown below.
A checklist should be used to assure that the right thing is done at the right time in the right place. This checklist is warranted because medical care has become complicated enough that one physician cannot remember everything that has to be done for a particular problem. A checklist for important interventions including use of antibiotics, therefore, should be helpful.
Finally, the most generally effective strategy to consider is multifaceted interventions. Multiple strategies are likely to be more successful than one.

**Prescription auditing**

Prescription auditing is an indispensable and effective tool to monitor antimicrobial prescription practices. If properly done, it can help treating physicians to improve their antimicrobial prescription skills and help an organisation to adhere to, monitor and improve compliance to antibiotic policy.

Prescription auditing can be done by a team of physician, infectious diseases specialists, clinical microbiologists and pharmacologists depending on their availability in an organization. The health-care settings that lack hospital information management systems (HIMS) or other form of computerization can also do the auditing by formulation of clear policy and procedures. An example of the prescription auditing method is described below (Figure 5).
Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines

**Figure 5. Example of prescription auditing structure and process**

1. Formulate antibiotic policy and implement the policy by creating awareness and training of the treating physicians about the policy.

2. Form prescription auditing team consisting of treating physicians, microbiologists, infectious diseases specialists, pharmacologists as per resources in an organisation.

3. Identify indicator antimicrobials which are generally costlier antimicrobials or newer antimicrobials.

4. Design an auditing form, which include patient details, diagnosis, date of start and discontinuation of antibiotic, doses and an indication to initiate the antimicrobial therapy.

5. Critical review of patient records and policies in the organisation.

6. Compilation and analysis of data.

7. Presentation of the data to the hospital infection control committee and treating physicians.
A model standard treatment guideline for community-acquired pneumonia at the hospital level

Purpose
This document is developed for diagnosis, management and treatment of community acquired pneumonia (CAP).

Intended use
This STG is intended to be used for adults in critical care, emergency medicine, family practice, infectious diseases, internal medicine and pulmonary medicine. However, these guidelines should be modified as per the need in CAP occurring in immuno-compromised patients, transplant recipients, high-dose corticosteroid recipients and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients.

The suggested reading references are considered along with the microbiology culture susceptibility data (antibiogram) for the previous five years for developing the hospital-based STG for CAP. The quality and strength of the evidence should be followed as stated in the adult CAP guidelines.

Among the recommended antibiotics (empirical or pathogen-specific therapy) included are crystalline penicillin, macrolides, doxycycline, fluoroquinolones, beta-lactam plus beta lactam and carbapenem based on the severity of illness and the causative microorganisms often seen in this region.

1 This STG is suggestive and health facilities need to modify it to suit their needs, match with local epidemiological data and antibiotic usage policies.
Standard treatment guideline for community acquired pneumonia

1 **Suspect** if patient (not been hospitalized in the previous two weeks; not immunocompromised) has any combination of the following:
   (a) Symptoms: fever, cough (with or without expectoration), pleuritic chest pain, dyspnoea.
   (b) Signs: Temp >38 °C, tachypnoea, tachycardia, impaired percussion notes, bronchial breath sounds, crackles, altered VF/VR.

2 **Check oxygen saturation** (SpO2) by pulse oximetry; **start oxygen** if SpO2 <90%.

3 **Confirm** with chest X-ray (to be done as soon as possible).

4 **Severity assessment** based on CURB-65 score
   (a) 6 point score (range 0 - 5)
   (b) Gives one point each for:
      (i) Confusion (abbreviated mental test score ≤ 8 or new disorientation in person, place, or time)
      (ii) Urea >42 mg/dL
      (iii) Respiratory rate ≥ 30/min
      (iv) Low Blood pressure (SBP < 90 mm Hg or DBP ≤ 60 mm Hg)
      (v) Age ≥ 65 years
   (c) Interpretation
      (i) CURB-65 score 0 or 1: low risk of death
      (ii) CURB-65 score 2: moderate risk of death
      (iii) CURB-65 score ≥3: high risk of death

5 **Laboratory tests**
   (a) Complete blood counts
   (b) Urea, creatinine
   (c) Antibiogram (only if CURB 65 score ≥2)
   (d) Blood culture x 2 (only if CURB 65 score ≥2)
(e) Sputum Gram stain & culture (optional)
   (i) Only if CURB 65 score ≥2 & patient can expectorate.
   (ii) Specimen (expectorated sputum) should be transported promptly to the laboratory.

6 Setting of care
(a) CURB-65 score 0 or 1: outpatient
(b) CURB-65 score 2: inpatient (ward)
(c) CURB-65 score ≥3: inpatient (M-ICU)

7 Antibiotic management
All patients should receive the first dose of antibiotics as soon as the diagnosis of CAP is confirmed
(a) CURB-65 score 0 or 1
   (i) Preferred: Amoxicillin 500 mg orally every 8 hours x 5 - 7 days
   (ii) Alternatives:
        (1) Levofloxacin 750 mg orally once a day x 5 - 7 days
        (2) Azithromycin 500 mg orally once a day x 3 days
(b) Doxycycline 100 mg orally twice a day x 7 days CURB-65 score ≥2
(c) Preferred: Crystalline penicillin 20 L units intravenous every 4 hours x 7 days CURB-65 score ≥3
   (i) Preferred: Piperacillin-Tazobactam 4.5 G intravenous every 8 hours + Azithromycin 500 mg intravenous once a day x 7 – 14 days
   (ii) Alternatives:
        (1) Crystalline penicillin 20 L units intravenous every 4 hours + Azithromycin 500 mg intravenous once a day x 7 – 14 days
        (2) Ertapenem 1 G intravenous once a day + Azithromycin 500 mg intravenous once a day x 7 – 14 days

* Change to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 hours, and there is no contraindication to the oral route.
* Modify antibiotic regimen based on results of culture and susceptibility reports.
Other recommendations included in the hospital STG for CAP are:

- If patient is critical with signs of infection admitted through the emergency department, the first antibiotic of choice should be recommended for administration while still in the emergency room.

- Once the aetiology of CAP has been identified and susceptibility reports are available the antimicrobial therapy should be either continued or altered according to the susceptibility report.

- Patients with CAP should be treated for a minimum of five days. Patient should be afebrile for at least 48 to 72 hours, and should have no more than 1 CAP-associated sign of clinical instability before discontinuation of therapy.

- When patient is haemodynamically stable and improving clinically (temperature <37.8 degrees C, heart rate <100 beats/min, respiratory rate <24 breaths/min, systolic blood pressure >90 mm Hg, arterial oxygen saturation >90% or pO2 >60 mm Hg and full conscious), able to take oral medications, then a switch from intravenous to oral therapy is recommended.

- Patients should be discharged as soon as they are clinically stable. At discharge, patient should have no other active medical problems, and have a safe environment for continued care.

- Failure to respond to initial therapy should raise questions of diagnosis, treatment adherence, and antimicrobial resistance.

- Polysaccharide pneumococcal (23-valent) may be given either at hospital discharge or during outpatient treatment.

- Smoking cessation and alcohol abstaining should be advised for patients in whom such habits contributed to the illness.

- Educating the patient regarding the hygiene measures, including the use of hand hygiene and masks or tissues for patients with cough, should be used to reduce the spread of respiratory infections.
STG performance measures to improve/track outcome in the hospital

- Antibiotics should be administered within four hours of admission to the health-care facility.
- Only the recommended antibiotics should be used and not others.
- Blood cultures, if drawn, should be drawn before antibiotics are given.
- The patients should receive advice or administered pneumococcal vaccine before discharge.
Good antimicrobial stewardship involves selecting an appropriate drug and optimizing its dose and duration to cure an infection while minimizing toxicity and conditions for selection of resistant bacterial strains.

**Benefits of prescribing against non-prescribing of antibiotics**

The clinical syndromes should be carefully assessed based on the benefits of prescribing against non-prescribing of antibiotics as outlined below:

- Patient cure/improvement against failure/mortality.
- Development of resistance in pathogens infecting the patient.
- Risk for spread of resistance.
- Suppression of normal flora.
- Development of resistance in normal flora.
- Risk for super infection.

The other relevant issues to be considered are:

- *In vitro* susceptibility.
- Antibiotic spectrum and need for combination therapy.
- Antibiotic activity: bactericidal / bacteriostatic.
- Site of infection and achievable antibiotic concentration.
- Dosage and pharmacodynamic principles.
Dosing and host factors like weight, immunosuppression, hepatic/renal failure.

Cost-effective ratio.

Drug interactions and poor absorptions.

Further, this can be effectively assisted by instituting various regulations such as formula restriction, automatic stop-order, prior approval programmes, therapeutic substitution, streamlining and antibiotic cycling, etc.

Maximizing clinical outcomes and minimizing selection of resistant organisms

What should be done

- Appropriate empirical antimicrobial therapy, with right dose, for right duration and at right time.
  - Delayed therapy or modifying the initial antimicrobial therapy does not improve the outcome.
  - Multidrug-resistance organism predisposes for inappropriate therapy.
- Early and accurate identification of the pathogen and susceptibility.
- Combination or monotherapy chosen on the basis of the pathogen identified.
- Deescalation of initial broad spectrum therapy after definitive diagnosis (generally based on microbiology reports).

What should not be done

- Treat non-infectious or nonbacterial syndrome.
- Treat colonization or contamination.
- Treat longer than necessary.
- Fail to make adjustment in a timely manner.
- Prescribe antibiotic with spectrum of activity not indicated.
Antimicrobial stewardship, hand hygiene and STG

Hand hygiene compliance rates of 10%-40% have been observed in even the best of the units in the developed countries. Acceptability of such compliance rates and justifications of intense antimicrobial usage under the umbrella of “empirical therapy” has underscore the importance of increasing hand hygiene compliance efforts. In recent years, adoption by WHO of hand hygiene as the first global challenge and the availability of robust hand hygiene compliance monitoring tools has led to an increase in hand hygiene compliance. Uniformity in monitoring hand hygiene compliance through these tools has also provided comparability and credibility to the hand hygiene compliance figures. Improved hand hygiene compliance has also led to decline in “empirical antimicrobial therapy” in such units.

MRSA can be contained by active surveillance culture, admission culture, isolation, decolonization and decontamination. Scandinavian countries and the Netherlands effectively practices the “admission screening” for MRSA, but nowhere outside these countries is this implemented routinely. Although the importance of such activities is well known it is yet to be appreciated fully.

Antibiotic use as a cause of hospital infection

Third-generation cephalosporins and quinolones are implicated as a risk factor for increased MRSA / gram negative bacilli colonization and infection. There is also ample evidence that MRSA incidence rates declined following implementation and monitoring of antibiotic policies that reduced use of cephalosporins and quinolones. Similarly, reports of VRE incidence rates declined following implementation of antibiotic policies that reduced use of vancomycin and Clostridium difficile following reduced use of clindamycin.

Studies had demonstrated the concept of ‘squeezing the balloon’ whereby reduction in use of one drug is reflected by increasing use of another.
Pitfalls of practising according to the guidelines

The antibiotic stewardship achieves only “uniformity of prescribing” with adherence to policies, guidelines and formularies. Paradoxically this may actually be at times harmful, as the best defence against resistance is probably “diversity of prescribing”.

The other important issue is difficulty in reducing overall antibiotic use, as modern medical developments seem to have no end to the immunosuppression of the patient.

The earlier guidelines from the British and American Thoracic Societies for treatment of community-acquired pneumonia (CAP) resulted in over-use of cephalosporins, quinolones and macrolides triggering MRSA outbreaks. Though the guidelines are evidence-based, the antibiotic recommendations are definitely not and leaning heavily to combination therapy in trying to cover all etiological agents.
Further reading


(5) European Surveillance of Antimicrobial Consumption, 2003, Results of the ESAC retrospective data collection (http://www.ESAC.ua.ac.be).


(14) Gould IM. Controversies in infection: infection control or antibiotic stewardship to control healthcare-acquired infection? Journal of Hospital Infection, 2009, 73, 386-391

(15) Keuleyan E, Gould IM. Key issues in developing antibiotic policies: from an institutional level to Europe-wide. European Study Group on Antibiotic Policy (ESGAP), Subgroup III. Clin Microbiol Infect, 2001, 7(Suppl. 6), 16-21.


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(22) Taylor GM. An audit of the implementation of guidelines to reduce wound infection following caesarean section. Health Bull. (Edinb), 2000, 58, 38-44.


Annex 1

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Annex 2

Technical resources

Evidence based practice in infection control
http://www.nric.org.uk/integratedcrd.nsf/f0dd6212a5876e448025755c003f5d33/7a183d3ae5edfb478025702300504a1d?OpenDocument

Prudent antibiotics user website
http://www.pause-online.org.uk/

Alliance for prudent use of antibiotics
http://www.tufts.edu/med/apua/

National prescribing center
http://www.npc.co.uk/

Academy of infection management
http://www.infectionacademy.org/

Do bugs need drugs – community education
http://www.dobugsneeddrugs.org/

WHONet WHO Software for antimicrobial resistance surveillance
http://www.who.int/drugresistance/whonetsoftware

Antibiotic consumption calculator

- Antibiotic consumption calculator (ABC calc) is a simple computer tool utilizing the ATC/DDD system to measure antibiotic consumption at both hospital and ward level as DDD/100 beds. ABC calc is freely available as a Microsoft Excel® file and modified annually to incorporate any changes made to the ATC / DDD system. This can be downloaded from European study group on antibiotic policies (ESGAP) page on the ESCMID. http://www.escmid.org/research_projects/study_groups/esgap/

AMR has assumed greater importance in health-care settings. Preserving the efficacy of antimicrobial agents is considered a critical step in fighting communicable diseases. One of the approaches is to have evidence-based antibiotic usage policy in hospital and standard treatment guidelines for common infectious diseases. This document focuses on the mechanism to develop a practical hospital antibiotic policy and standard treatment guidelines. It also contains information on various effective strategies for implementation of standard treatment guidelines. A suggested model hospital STG for community-acquired pneumonia in adults is included.

Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines