BIOMÉRIEUX

ANTIMICROBIAL STEWARDSHIP

A practical guide to implementation in hospitals

PIONEERING DIAGNOSTICS

INTRODUCTION

The objective of this booklet is to provide practical recommendations for healthcare workers in hospitals to improve the quality of antibiotic prescribing and thereby improve patient clinical outcomes.

Most of the recommendations within this booklet have been adapted from the IDSA Guidelines *[Dellit et al., 2007; Tamar F et al., 2016]*, the Australian Hospital Stewardship Guidance *[Duguid et al., 2011]*, National Stewardship Guidance from Scotland *[Nathwani et al., 2006]*, the UK *[Start smart then Focus DOH, 2011; NICE Guideline [NG15], 2015]* as well as from low and middle income countries *[Van Dijck et al., 2018; Cox et al., 2017]*.

A key component of stewardship is the availability of clinical practice guidelines to support empiric and targeted prescribing. Although a high volume of such guidance is now being produced, for example the National Treatment Guidelines for Antimicrobial Use in Infectious Diseases in India, there is consistent evidence that guidelines on empirical antibiotic use did not routinely consider local resistance patterns in their recommendations. Decision-makers should analyze and report the extent of local resistance patterns to allow better decision-making *[Elias et al., 2017]*. For this reason we have not referred to any specific clinical practice treatment guidelines.

We hope that this booklet will inform, encourage and support health professionals wishing to pursue the implementation of hospital Antimicrobial Stewardship initiatives, as well as combating antimicrobial resistance. Furthermore, we wish to highlight the importance of conducting hospital stewardship programs in tandem with stewardship in the community and other settings. The importance of stewardship in the animal setting is also recognized as in the "One Health" approach to AMR and stewardship recommended by WHO, FAO & OIE.

Prof. Dilip Nathwani
MB; DTM&H, FRCP, OBE
Consultant Physician and Honorary Professor of Infection
Director Academic Health Sciences Partnership in Tayside,
Ninewells Hospital and Medical School
Dundee, Scotland

CONTENTS

1 WHY IMPLEMENT ANTIMICROBIAL STEWARDSHIP IN HOSPITALS?

2 HOW TO IMPLEMENT AN ANTIMICROBIAL STEWARDSHIP PROGRAM?

This booklet will primarily consider appropriate use of antimicrobial stewardship in hospitals and the structures and processes to support this.

1 WHY IMPLEMENT ANTIMICROBIAL STEWARDSHIP IN HOSPITALS?

1 Antimicrobial use

Misuse and over-use of antibiotics

The last 50 years have witnessed the golden age of antibiotic discovery and their widespread use in hospital and community settings. Regarded as very effective, safe and relatively inexpensive, antibiotics have saved millions of lives. However, this has led to their overuse and misuse in the human, animal and other sectors (**Figure 1**).

Globally, between 2000 and 2010 there has been a massive rise in overall antimicrobial consumption (**Figure 2**), largely as a consequence of uncontrolled prescription or over-the-counter sales.

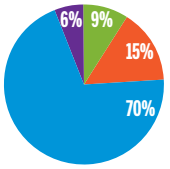
At global level, 70% of antibiotics are used for animals *[O'Neill report, 2016]*. In the US, this is 85% (Figure 1).

In hospitals, up to 50% of antimicrobial use is inappropriate *[Dellit et al., 2007]*.

More recent global data on the **quality of antimicrobial prescribing in hospitals**, undertaken using a **global point prevalence survey method** *[Global PPS-http://www.global-pps.com]* reveals significant variation in practice against commonly used metrics of the quality of prescriptions (**Figure 3**). Such real world data is beginning to provide much needed intelligence of what the problem is, the scale of the problem and ways of measuring the effectiveness of our interventions.

Figure 1: Current use of antibiotics in the United States

Adapted from www.pewhealth.org



Most antibiotics are given to animals and most of them are healthy.

Animal non-therapeutic
Animal therapeutic
Human therapeutic
Others (pesticides, etc)

Figure 2: Percentage change in antibiotic consumption per capita 2000-2010* by country

Adapted from Van Boekel TP et al. 2015. *Lancet Infect Dis.* 2014;14:742-750

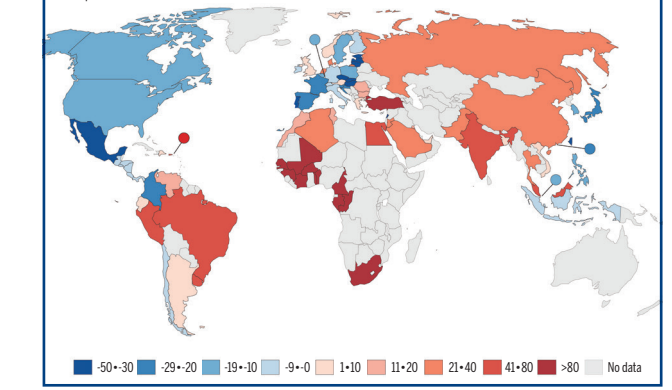
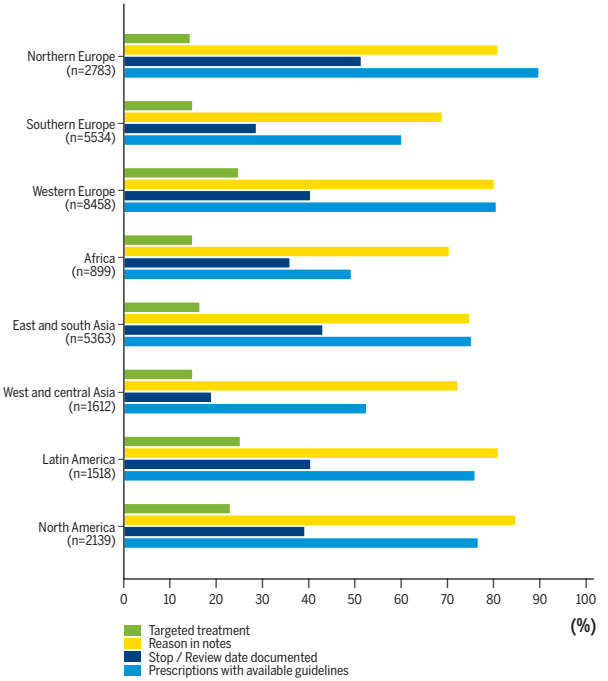


Figure 3: Overview of antimicrobial/antibiotic quality indicators for adult inpatients by region, 2015 Global Point Prevalence Survey

Adapted from Versporten A et al. *Lancet Global Health.* 2018; 6: 619-629



The 30% Rule

- ~ 30% of all hospitalized inpatients 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 pharmacy costs can be saved by antimicrobial stewardship programs

(Hoffman et al., 2007; Wise et al., 1999; John et al., 1997)

The rising threat of antimicrobial resistance

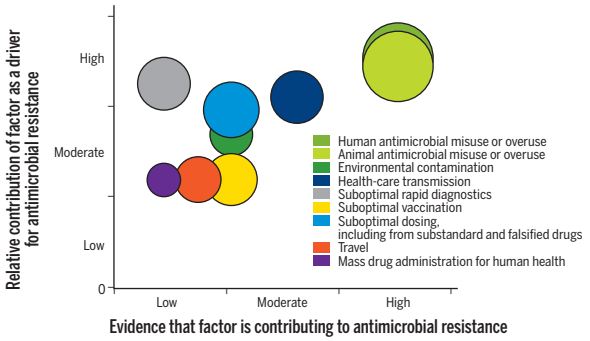
Antimicrobial resistance has been identified as a major threat by the World Health Organization *[WHO, 2012]* due to the lack of new antibiotics in the development pipeline and infections caused by multi-drug resistant pathogens becoming untreatable *[Goossens et al., 2011; Carlet et al., 2011]*. In 2015, the WHO set out the global action plan for AMR *[WHO, 2015]* and a subsequent broader stewardship framework.

2 Combating Antimicrobial Resistance

There are numerous drivers for AMR (**Figure 4**). Human antimicrobial misuse and overuse is a key driver factor, as are suboptimal dosing, lack of availability and/or under-use of rapid diagnostics or point of care tests and insufficient infection prevention and control.

Figure 4: Mechanisms and drivers of antimicrobial resistance

Adapted from Holmes AH et al. *The Lancet* 2016;387:176-187



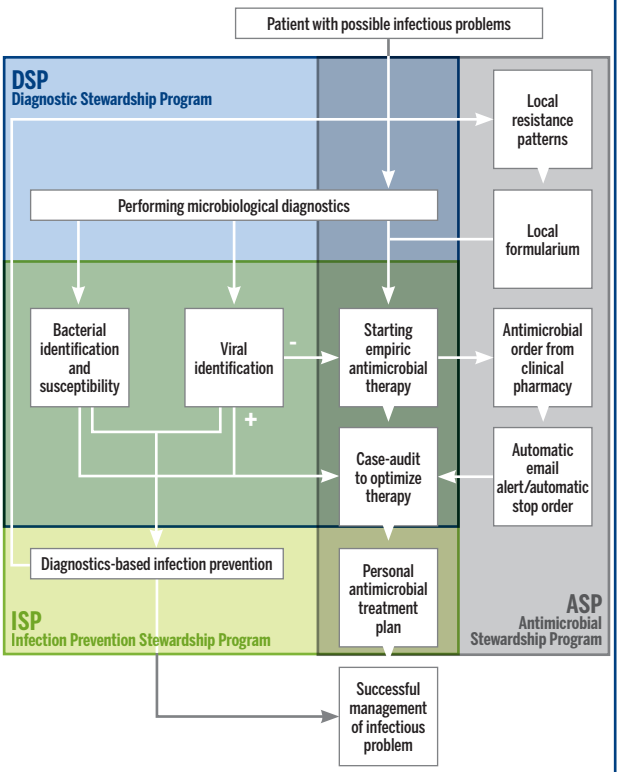
To combat AMR, a "three-pillar" approach is recommended:

1. Optimize the use of antimicrobials,
2. Prevent the transmission of drug-resistant organisms,
3. Improve environmental decontamination.

To achieve this approach, an integrated stewardship approach has been advocated, encompassing antimicrobial stewardship, diagnostic stewardship and infection control (**Figure 5**).

Figure 5: An integrated stewardship model: antimicrobial, infection prevention and diagnostic (AID)

Adapted from Dik JH et al. *Future Microbiol.* 2015; 11: 93-102



3 Defining antimicrobial stewardship

Antimicrobial stewardship (AMS) is a key strategy to overcome resistance. It involves the careful and responsible management of antimicrobial use.

Two definitions help to understand the objectives of AMS

Adapted from Nathwani D et al. 2012 *Hosp Epidemiol Infect Control*

a systems level

"Antimicrobial stewardship is an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness"

an individual/team level

"Antimicrobial stewardship:

- is an **inter-professional effort**, across the continuum of care,
- involves timely and optimal selection, dose and duration of an antimicrobial,
- for the best clinical outcome for the treatment or prevention of infection,
- with minimal toxicity to the patient,
- and minimal impact on resistance and other ecological adverse events such as *C. difficile*."

AMS can also simply be put as achieving:

> "The right antibiotic for the right patient, at the right time, with the right dose, the right route and cause the least harm to the patient and future patients."

www/cdc.gov/getsmart/healthcare/inpatient-stewardship

4 Goals of antimicrobial stewardship and evidence for success

The four main goals of antimicrobial stewardship are illustrated in **Figure 6** with examples of evidence that stewardship programs can help achieve these goals. The importance of additional balancing measures or measurement of unintended consequences is also emphasized *[Toma et al., 2017]*.

Figure 6: The goals of antimicrobial stewardship programs for patient and public health

Adapted from D. Nathwani, personal communication

IMPROVE PATIENT OUTCOMES	OPTIMIZE PATIENT SAFETY	REDUCE RESISTANCE	CONTROL HEALTHCARE COSTS

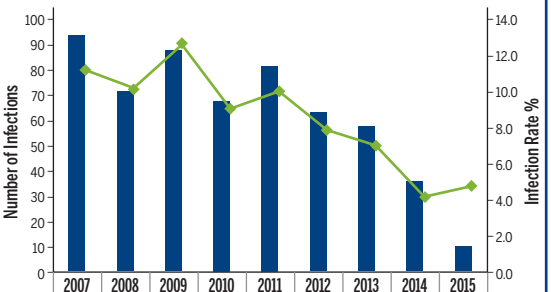
Goal 1: Improve patient outcomes

- Improve infection cure rates
- Reduce surgical infection rates
- Reduce mortality and morbidity

The prevention of surgical site infections (SSIs) remains one of the most accessible and "doable" areas of antimicrobial stewardship programs (ASPs) usually in combination with infection prevention measures. The effect of ASPs on reducing surgical site infections can be dramatic and of high impact, making SSIs a very visible "quick win" that can encourage buy-in into stewardship programs (**Figure 7**).

Figure 7: Impact of ASP on surgical site infection rates

Adapted from Frenette C et al. *Am J Inf Control.* 2016;44:977-82



	2007	2008	2009	2010	2011	2012	2013	2014	2015
# OF INFECTIONS	94	72	88	68	81	63	58	36	9
# OF PROCEDURES	838	695	703	751	819	802	831	887	192
INFECTION RATE	11.2%	10.4%	12.5%	9.1%	9.9%	7.9%	7.0%	4.1%	4.7%

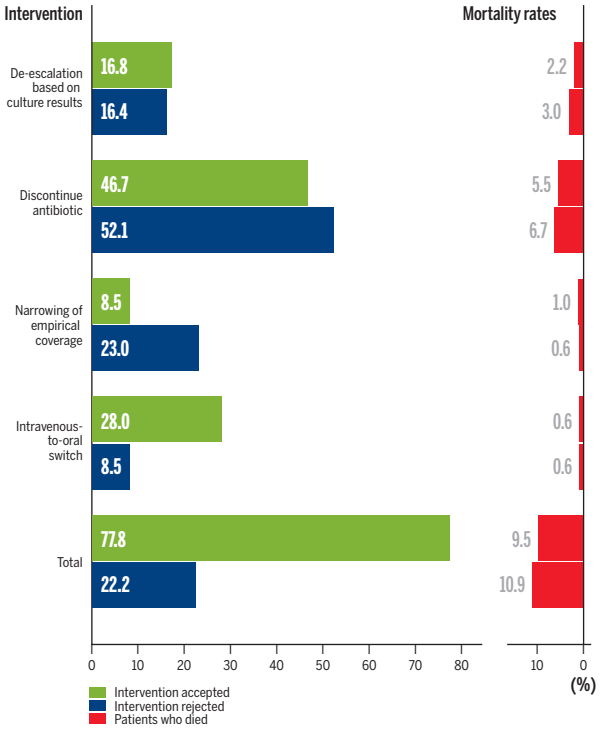
Goal 2: Optimize patient safety

(Minimize unintended consequences of antimicrobials)

Studies have shown that ASPs can effectively reduce antibiotic utilization, cost of care and even antimicrobial resistance rates, without increasing mortality. However, ASPs should avoid the perception that the goal of the program is primarily to reduce antibiotic purchases and costs, instead of focusing on improving the quality of care. To address the patient safety concern, data showing **no adverse impact on morbidity or mortality** is important for reassurance and engagement (**Figure 8**).

Figure 8: Types of ASP interventions that may impact morbidity and mortality

Adapted from Liew YX et al. *Int J Antimicrob Agents* 2012;40:55-60



- **Reduce duration of hospital stay, without increasing mortality or infection-related readmissions (Figure 8).**

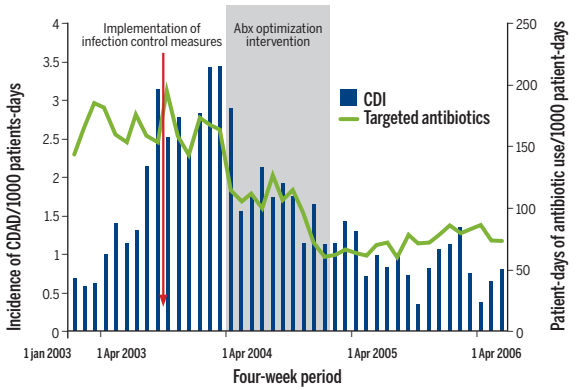
  This Singapore-based study showed that in patients whose physicians accepted suggested ASP interventions, there was:

  - shorter average length of stay (mean 19.4 days vs. 24.2 days),
  - significantly shorter hospital stay between ASP intervention and discharge (mean 10.2 days vs 16.6 days),
  - significant reduction in 14-day re-infection rates between accepted (0%) and rejected (10%) groups,
  - no difference in all-cause mortality (P = 0.191).

- **Reduce *C.difficile* colonization or infection by controlling the use of "high-risk" antibiotics (Figure 9).**

Figure 9: Example of a robust stewardship program with strict implementation of infection control measures leading to sustained reduction in *C. difficile infection* (CDI) cases during an epidemic

Adapted from Valiquette L et al. *Clin Infect Dis.* 2007;45:S112-121



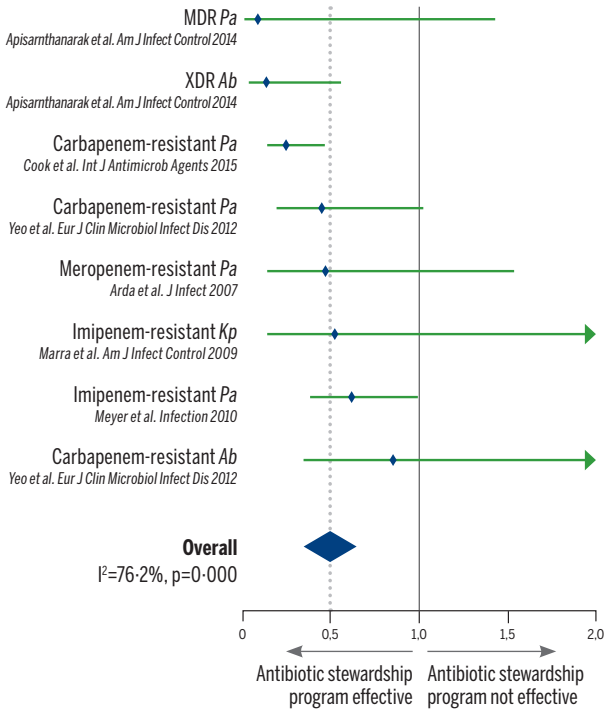
A more recent example in Scotland showed a reduction in *C. difficile* infection (CDI) applicable at a national level following restriction of high risk antibiotics that included cephalosporins, co-amoxiclav, quinolones and clindamycin *[Lawes et al, 2017]*. This illustrates the potential for massive impact of stewardship programs at nationwide levels.

Goal 3: Reduce resistance

Restricting relevant agents can reduce colonization or infection with Gram-positive or Gram-negative resistant bacteria (**Figure 10**). Numerous other examples of the effect of ASPs on multi-drug resistant Gram-negative bacteria are given in this meta-analysis *[Baur et al., 2017]*

Figure 10: Effect of ASPs on the incidence of MDR GNB

Adapted from Baur D et al. *Lancet Infect Dis.* 2017;17:990–1001 / Systematic review and meta-analysis
(Refer to source article for full references of reviewed articles)



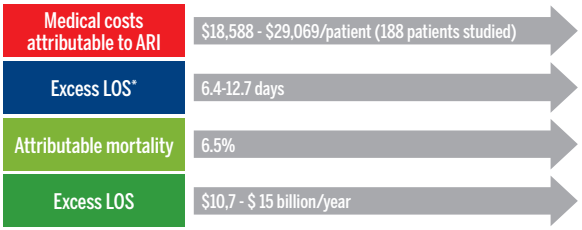
ABBREVIATIONS
GNB: Gram-negative bacteria - MDR: Multidrug-resistant - XDR: Extremely drug-resistant
Ab: *Acinetobacter baumannii* - Kp: *Klebsiella pneumoniae* - Pa: *Pseudomonas aeruginosa*

Goal 4: Control healthcare costs (without adversely impacting quality of care)

Antibiotic-resistant infections are associated with high costs (**Figure 11**).

Figure 11: The costs of antibiotic-resistant infections (ARI)

Adapted from Roberts RR et al. *Clin Infect Dis.* 2009;49:1175–1184



* LOS: length of stay

Figures 12a and 12b are examples of how stewardship programs in hospitals can deliver significant cost savings through improved antimicrobial prescribing practices.

Figure 12a: Changes in antibiotic prescribing rates

Adapted from Bao L et al. *PLoS ONE* 2015;10:e0118868

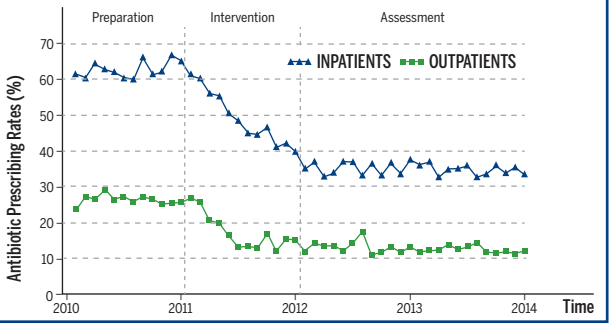
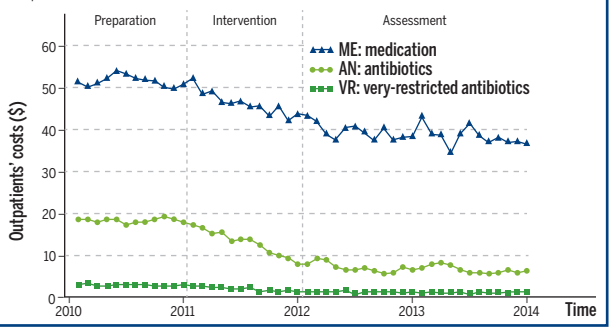


Figure 12b: Changes in outpatients' costs

Adapted from Bao L et al. *PLoS ONE* 2015;10:e0118868

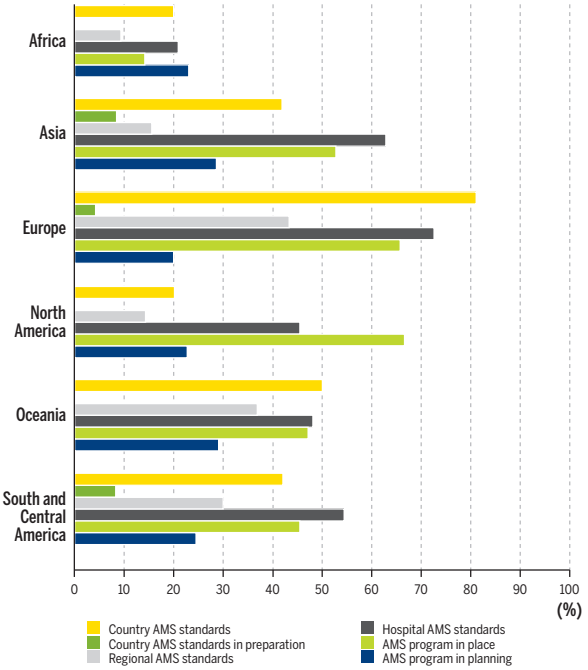


5 Implementation of Antimicrobial Stewardship Programs

A global survey has outlined the availability of stewardship programs across the continents (**Figure 13**).

Figure 13: Summary of AMS standards and programs

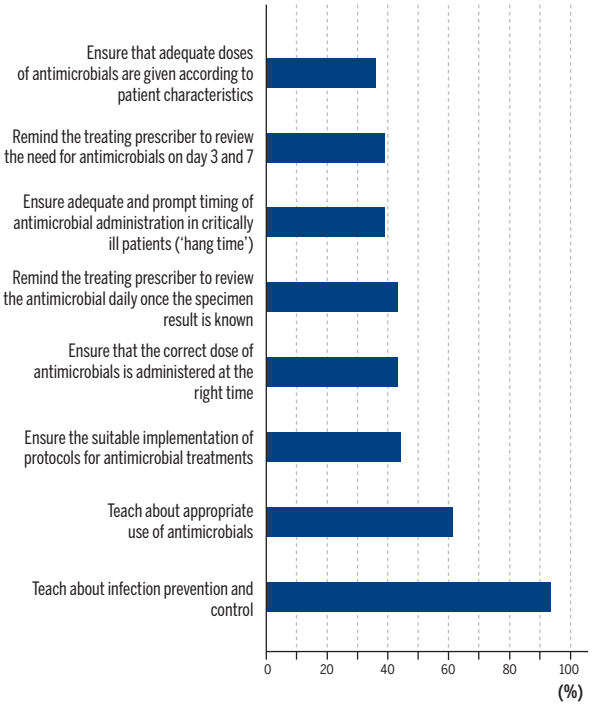
Adapted from Howard P et al. *J Antimicrobial Chemother.* 2015; 70: 1245-1255



This remains a unique global survey, although more recent continental data is emerging showing that in Africa, for example, nurses are a key part of hospital stewardship programs (**Figure 14**) *[Bulabula et al. 2018]*.

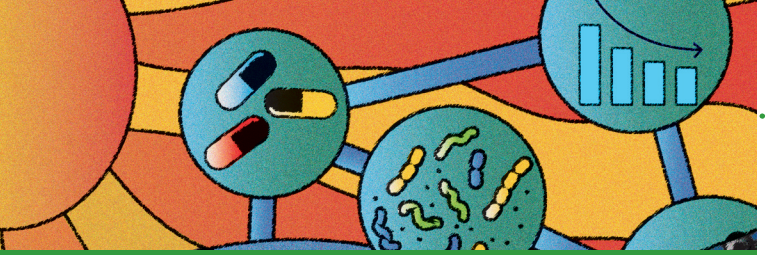
Figure 14: AMS tasks undertaken by nurses

Adapted from Bulabula ANH et al. *J Antimicrobial Chemother* 2018;73:1408–1415



A recent systematic review of antimicrobial stewardship programs in Asia illustrates emerging experience of their impact on a range of outcomes *[Lee et al. 2018]*. This meta-analysis, which reviewed 77 studies, showed that among those studies:

- 91% reported reduced antibiotic usage,
- 100% reported cost savings,
- duration of antibiotic therapy was reduced in 6 of 7 studies,
- rates of all-cause mortality and HAI were not significantly different between the intervention and control groups,
- mortality rates were significantly improved by ASPs using drug monitoring,
- HAI rates were also improved by ASPs that included infection control or hand hygiene programs.



2 HOW TO IMPLEMENT AN ANTIMICROBIAL STEWARDSHIP PROGRAM?

Antimicrobial stewardship (AMS) strategies can use different methods or techniques to support the adoption, implementation, and sustainability of a clinical program or practice.

The strategies include 'top down/bottom up,' 'push/pull,' and 'carrot/stick' tactics, and typically involve 'package' approaches. They also include methods for provider training and decision support; intervention-specific tool kits, checklists, and algorithms; formal practice protocols and guidelines; learning collaboratives, business strategies and organizational interventions (such as "plan-do-study-act" cycles) and economic, fiscal, and regulatory methods.

Although strategies depend on local needs and issues, and available expertise and other resources, there are a number of core elements that make up the basis of a good stewardship program.

In 2014, the CDC released **The Core Elements of Hospital Antibiotic Stewardship Programs** *[https://www.cdc.gov/antibiotic-use/healthcare/pdfs/core-elements.pdf]* that identifies key structural and functional aspects of effective programs.

In 2018, these core elements were adapted for a global audience and supplemented by a check list descri bing **essential and minimum standards for AMS programs in hospitals** worldwide (**Figure 15**).

Figure 15: Core elements and checklist items for global hospital AMS programs

Adapted from Pulcini C et al., *Clin Microbiol Infect*. 2019;25:20-25

CORE ELEMENT 1	
Senior hospital management leadership towards antimicrobial stewardship	This section relates to governance of the programme by hospital executives, and specifies how senior hospital management supports the antimicrobial stewardship programme
CORE ELEMENT 2	
Accountability and responsibilities	
CORE ELEMENT 3	
Available expertise on infection management	
CORE ELEMENT 4	
Education and practical training	
CORE ELEMENT 5	
Other actions aiming at responsible antimicrobial use	
CORE ELEMENT 6	
Monitoring and surveillance (on a continuous basis)	**Does your hospital monitor the quality of antimicrobial use at the unit and/or hospital wide level?** This can be done for example by undertaking point prevalence surveys or audits, assessing appropriateness of infection management and antimicrobial prescription (e.g. indication, choice and duration of antibiotic therapy in pneumonia or surgical prophylaxis according to policy/guidance)
CORE ELEMENT 7	
Reporting and feedback (on a continuous basis)	All these reports should also be shared with the hospital management leadership

Once these core elements have been identified, an 8-step process of implementation described on page 16 is one pragmatic way of implementing the stewardship program.

A program devised for hospitals in the Netherlands is also worthy of review *[http://esgap.escmid.org/wp-content/uploads/2015/ 11/SWAB_guideline_ABS_hospitals.pdf]*.

EIGHT KEY STEPS

for implementing an Antimicrobial Stewardship Program (ASP)

1. Assess the motivations
2. Ensure accountability and leadership
3. Set up structure and organization
4. Define priorities and how to measure progress and success
5. Identify effective interventions for your setting
6. Identify key measurements for improvement
7. Educate and Train
8. Communicate

1 Assess the motivations

- **Analyze your situation** and what problems you want to address. There are many international guidelines available, but you will need to adapt them to your local situation.
- Define **where you are** and **where you want to go**, with **quantitative figures**. One of the ways of obtaining these data is to measure the quantity and quality of antibiotic use, for example, **using a Point Prevalence Survey, such as the Global-PPS** (see Section 6.1.1).
- What can be implemented will depend on local needs/issues, geography, available skills/expertise and other resources.

  For example, **easier or less costly approaches** can include:
  - simple clinical algorithms,
  - prescribing guidance for treatment, surgical prophylaxis,
  - IV to oral conversion,
  - provision of microbiological support,
  - restricting availability of certain antibiotics (formulary restriction),
  - automatic therapeutic substitution,
  - IV antimicrobial batching,
  - promoting education.

[Goff et al., 2012]

2 Ensure accountability and leadership

To ensure a successful Antimicrobial Stewardship Program:

- the program should be supported by the **senior hospital management**, who are accountable for the outcomes,
- a **team of people and resources** should be allocated by the head of the organization to implement and evaluate the program,
- the ASP team members must possess **power, expertise, credibility and leadership**. These individuals need to convince managers and healthcare staff of the added value of the program.

A key component of a stewardship program is leadership and culture. This can be set out as a driver diagram (see Table 1 on page 18 for more details).

Table 1: Driver Diagram - Overarching Driver: Leadership and Culture

Adapted from:
https://www.cdc.gov/getsmart/healthcare/pdfs/Antibiotic_Stewardship_Driver_Diagram_10_30_12.pdf

SECONDARY DRIVER	KEY CHANGE CONCEPTS	SPECIFIC CHANGE IDEAS
Promote a culture of optimal antibiotic use within the facility	Engage administrative and clinical leadership to champion stewardship effort	1. Identify clinical providers as champions to be thought leaders about antibiotic stewardship. 2. Work with administrators to ensure that they understand the rationale and goals for stewardship programs and interventions and provide support (financial and non-financial). 3. Engage a physician champion and core team to enhance the focus of antimicrobial stewardship into the current process of care. 4. Bring disciplines together to improve communication and collaboration about improving antibiotic use, including: - Infection preventionists; - Hospitalists; - Intensivists; - Emergency department physicians; - Microbiologists; - Pharmacists; - Nurses; and - Infectious disease experts. 5. Consider having the multidisciplinary group perform a gap analysis of antimicrobial use at the facility to identify priority areas for improvement.

3 Set up structure and organization

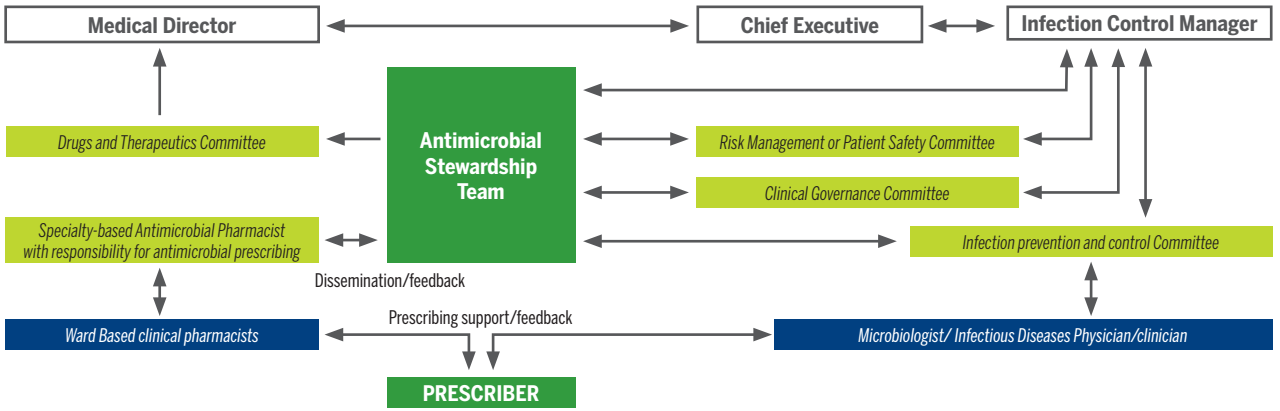
The key components of the structure and governance of the ASP are:

- **Dedicated resources**, including dedicated personnel time for stewardship activities, education, and measuring/monitoring antimicrobial use.
- **A multidisciplinary AS team** with core membership of:
  - an **infectious diseases physician** (or lead doctor or physician champion),
  - a **clinical microbiologist**,
  - a **clinical pharmacist** with expertise in infection.

  Other members could be specialist nurses, for example infection prevention or stewardship nurses, quality improvement /risk management/patient safety managers and clinicians with an interest in infection.
- **Governance** within the hospital's **quality improvement and patient safety governance** structure
- Clear lines of **accountability** between the chief executive, clinical governance, drug and therapeutics committee, and infection prevention and control committees, and the AST. **Figure 16** illustrates such an organization structure. This structure would need to be adapted to local context and available resources.

Figure 16: Model of Antimicrobial Prescribing Pathway and Organization in Acute Hospitals in Scotland

Adapted from Nathwani D. *J Antimicrob. Chemother.* 2006; 57: 1189-1196



4 Define priorities and how to measure progress and success

The objectives of the ASP and how they are going to be achieved and measured need to be agreed by all the key stakeholders and communicated clearly.

One way of doing this is to produce a **Driver Diagram** (see **Figure 17** as an example). A Driver Diagram is a logic chart with three or more levels, including:

- a goal or vision,
- the high-level factors needed to achieve this goal (called 'primary drivers'),
- specific projects and activities that would act upon these factors.

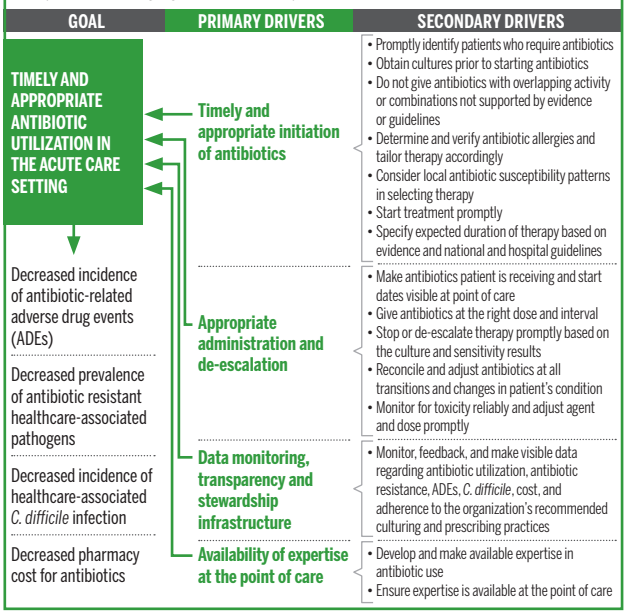
For more complex goals, each primary driver could have its own set of '**secondary drivers**' (or lower level drivers).

Driver diagrams can help an ASP team to:

- explore the factors that need to be addressed to achieve a specific overall goal,
- show how the factors are connected,
- act as a communication tool for explaining a change strategy,
- provide the basis for a measurement framework.

Figure 17: Example of a Driver Diagram for Antimicrobial Stewardship

Adapted from www.cdc.gov/getsmart/healthcareimprove-efforts/



5 Identify effective interventions for your setting

A range of stewardship interventions has been reviewed in the IDSA guidelines *[Barlam et al.2016]*.

When establishing a new stewardship program, it is best to start with the core strategies and focus on achieving and maintaining them before adding some of the supplemental strategies (Table 2).

Table 2: Antimicrobial Stewardship Toolkit: Quality of Evidence to support interventions

Adapted from Dellit TH et al. *Clin Infect Dis.* 2007; 44:159-77; Barlam TF et al. *Clin Infect Dis.* 2016; 62:51 -77

CORE STRATEGIES	SUPPLEMENTAL STRATEGIES
Formulary restrictions and preauthorization*	Streamlining / timely de-escalation of therapy*
Prospective audit with intervention and feedback*	Dose optimisation*
Multidisciplinary stewardship team*	Parenteral to oral conversion*
	Guidelines and clinical pathways*
	Antimicrobial order forms
	Education
	Computerized decision support, surveillance
	Laboratory surveillance and feedback
	Combination therapies
	Antimicrobial cycling

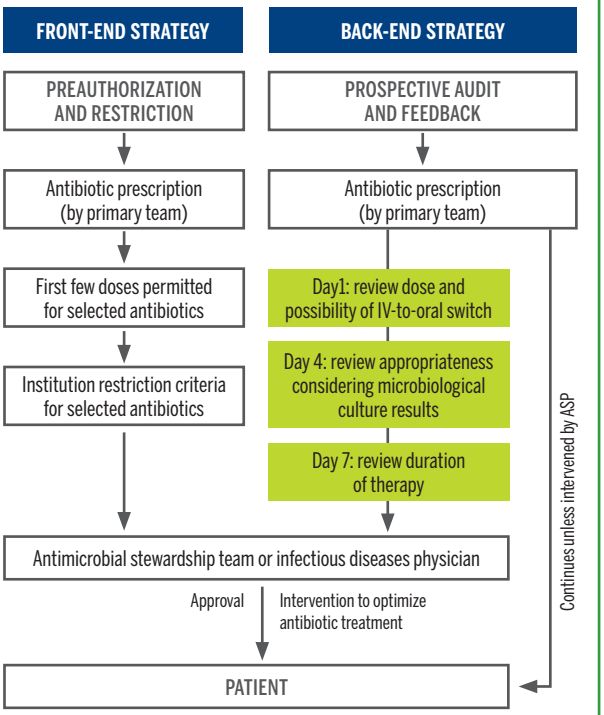
*Strategies with strongest evidence and support by IDSA

Two core ASP strategies have evolved (**Figure 18**):

FRONT–END STRATEGIES	Antimicrobials made available through an approval process (formulary restrictions and preauthorization)
BACK-END STRATEGIES	Antimicrobials reviewed after antimicrobial therapy has been initiated (prospective audit with intervention and feedback)

Figure 18: Front- and Back-end Antimicrobial Stewardship Strategies

Adapted from Chung GW et al. *Virulence* 2013;4:151-157



Some of the advantages and disadvantages of these two strategies are given in **Figure 19**.

Although more labour-intensive, **back-end strategies** are:

- **more widely practiced**,
- **more easily accepted** by clinicians as they reflect the daily decision-making process,
- provide a **higher opportunity for educational opportunities**,
- ultimately provide a **more sustained impact** of improving the overall quality of antimicrobial prescribing.

[Chung et al., 2013].

In the UK, this approach has been innovatively adapted to create a simple pragmatic approach that is aligned with the clinical teams' daily decision-making process (**Figure 20**).

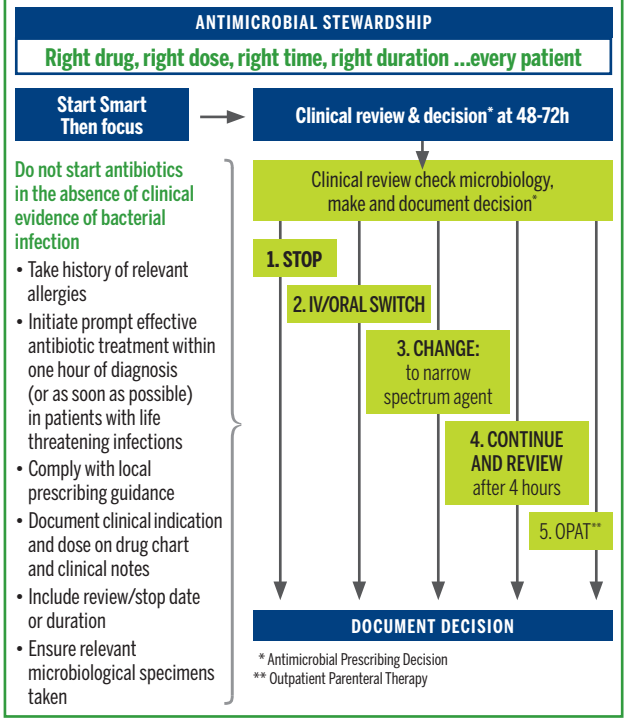
Figure 19: Advantages and Disadvantages of Pre-Authorization and Prospective Audit and Feedback

Adapted from Dellit TH et al. *Clin Infect Dis.* 2007;44:159–77; Barlam TF et al. *Clin Infect Dis.* 2016;62:51 -77

PRE-AUTHORIZATION	PROSPECTIVE AUDIT AND FEEDBACK
EXAMPLES OF ADVANTAGES	
Prevents unnecessary/ inappropriate initiation of antibiotics	Increases visibility of ASP and helps to form professional relationships
Ensures optimal empirical therapy	Maintains autonomy of prescribers
Prompts review of clinical parameters, patient history and prior cultures before initiating antimicrobial therapy	Frequency can be tailored based on resources available to the ASP
EXAMPLES OF DISADVANTAGES	
Has little effect post empirical therapy	Compliance voluntary
Loss of prescriber autonomy	Labour intensive
May delay initiation of therapy	Success is dependent on how feedback is communicated to prescribers

Figure 20: Antimicrobial Stewardship Treatment Algorithm

Adapted from Start Smart Then Focus Guidance for Antimicrobial Stewardship in hospitals (PHE, UK)



5.1 Front-end strategies

5.1.1. Antimicrobial Prescribing Policy

Hospital ASPs should include an **Antimicrobial Prescribing Policy** that is regularly reviewed and updated.

The important messages that need to be incorporated into the policy (MINDME) from Australian Stewardship Guidelines *[Duguid et al., 2010]* are illustrated in **Table 3**.

Table 3: The Golden Rules of Antimicrobial Prescribing "MINDME"

Adapted from Antibiotic Expert Group. Therapeutic guidelines: antibiotic. Version 14. Melbourne: Therapeutic Guidelines Limited; 2010

M	**microbiology guides therapy wherever possible**
I	**indications should be evidence based**
N	**narrowest spectrum required**
D	**dosage appropriate to the site and type of infection**
M	**minimise duration of therapy**
E	**ensure monotherapy in most cases**

5.1.2. Clinical guidelines or care pathways

Clinical guidelines or care pathways should take into account local microbiology and antimicrobial susceptibility patterns, as well as local resources and priorities, clinician preference/views and potential risk or unintended consequences. For guidelines to be relevant to daily practice, it is important they are updated on a regular basis and that older or outdated recommendations are removed.

The publication of national guidelines for South Africa and India for the antimicrobial treatment of infectious disease are recent examples of good practice. Furthermore, India has just published specific guidelines for Antimicrobial Stewardship Programs *[ICMR, 2018]*.

5.1.3. Formulary restrictions / approval systems

This involves determining the list of **restricted antimicrobial agents** (broad spectrum and later generation antimicrobials) and criteria for their use combined with an **approval system** which is subject to regular audit and feedback to the prescribers. It is essential that all aspects of prescribing are supported by expert advice 24 hours a day where possible.

5.2 Back-end strategies

5.2.1. Antimicrobial review methods

Antimicrobial review methods are employed post-prescription and outlined in **Table 4**. The most appropriate interventions for your institution should be chosen, according to local resources.

Table 4: Antimicrobial Review Methods

Adapted from Johannsson B et al. *Inf Control Hosp Epidemiol.* 2011;32: 367-374

TYPE OF INTERVENTION
COMMONLY USED
■ Review of indication for antibiotic and compliance with policy/guideline/formulary; note any recording of exception
■ Review of appropriateness of antibiotic choice, dose, route and planned duration; review of drug allergy, review of agents that may provide duplicative therapy (potential overlapping spectra)
■ Review of directed therapy based on culture and susceptibility test results
■ Potential for conversion from IV to oral route
■ Review requirement for therapeutic drug monitoring
■ Review any antibiotic related adverse events
LESS COMMONLY USED AND DEPENDENT ON LOCAL RESOURCES
■ Unsolicited review of specific resistant pathogens (e.g MRSA) or site of infection (e.g blood stream infections)
■ Specific review of high cost/high use/novel agents
■ Review of optimal dose (PK/PD) in relation to dose and frequency; renal adjustment, need for extended infusion, review of any potential drug interactions
■ Review of directed therapy based on microscopy or PCR or other rapid tests**
■ Review of empiric or directed therapy based on biomarkers**

**The lack of diagnosis and delay in microbiology remains a significant hurdle to good stewardship and source of high cost.

5.2.2. Audit and direct feedback to prescribers

The audit and feedback process can be managed by either the medical infection specialist or specialist pharmacist. However, depending on the intervention, specialist nurses or clinical pharmacists can also be trained to support this process.

During clinical review, a range of **point-of-care stewardship interventions** are useful to provide direct and timely **feedback to the prescriber** at the time of prescription or laboratory diagnosis, and provide an opportunity to **educate clinical staff** on appropriate prescribing.

POINT-OF-CARE INTERVENTIONS CAN INCLUDE:

- appropriate use of guidance,
- indication for antibiotic,
- choice of agent,
- route [IV vs. oral] of administration of treatment,
- timeliness of treatment,
- likelihood of on-going infection or not,
- use of diagnostic tests for investigation,
- interpretation of microbiology with a view to de-escalation,
- duration of therapy.

The types of interventions selected, how they are delivered and by whom, will be determined by local resources, need and available expertise.

Feedback on antimicrobial prescribing should be provided regularly to prescribers in the **critical care setting**, and **areas of high and/or poor quality antimicrobial use**.

One way of evaluating prescribing within a unit or hospital is through regular **point prevalence surveys** (PPS) *[Ansari et al., 2009, Seaton et al., 2007]*.

These data can be used in an audit process to provide structured feedback to prescribing teams and to define areas for improvement. Such point prevalence surveys can be used to establish baseline prescribing information and **identify priorities for quality improvement**.

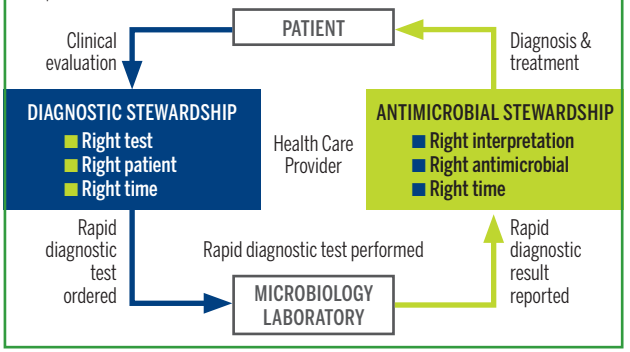
See section 6.1.1 for more details on Point Prevalence Surveys.

5.3 Role of Diagnostics in Stewardship

Diagnostic stewardship refers to the **appropriate use of laboratory testing to guide patient management**, including treatment, in order to optimize clinical outcomes and limit the spread of antimicrobial resistance. This requires a seamless partnership between clinical laboratories, pharmacists, and infectious diseases clinicians, so that appropriate tests are ordered and diagnostic information is translated into appropriate management in real time.

Figure 21: Example of diagnostic and antimicrobial stewardship in the implementation of rapid molecular disease diagnostics

Adapted from Messacar et al. *J Clin Microbiol.* 2017;55:715-723



Laboratories play a key role in antimicrobial stewardship (**Figure 21**). However, they are often not used optimally or, in many parts of the world, they do not exist or have poor capacity and capability to deal with the problem. An example of an antimicrobial stewardship program for the microbiology laboratory and how it could be achieved is described in **Figure 22**.

Figure 22: Examples of essential, achievable, and aspirational antimicrobial stewardship activities for the microbiology laboratory

Adapted from Morency-Potvin et al. *Clin Microbiol Rev.* 2017;30:381-407

ESSENTIAL	ACHIEVABLE	ASPIRATIONAL
■ Collaborate in educating local healthcare workers on microbiology issues that impact treatment and AMR ■ Optimize communication of critical results and alert systems ■ Provide annual Cumulative Antimicrobial Susceptibility Report	■ Provide comments, in collaboration with ASP team, to guide therapy on microbiology reports ■ Use rapid diagnostics, multiplex PCR and AST* for targeted critical specimen types and respiratory pathogens ■ Collaborate in audit and feedback of antimicrobial therapies when lab tests are critical (eg: *C.difficile*, bloodstream infections)	■ Participate in national/ regional surveillance systems ■ Promote appropriate use of point-of-care microbiological tests

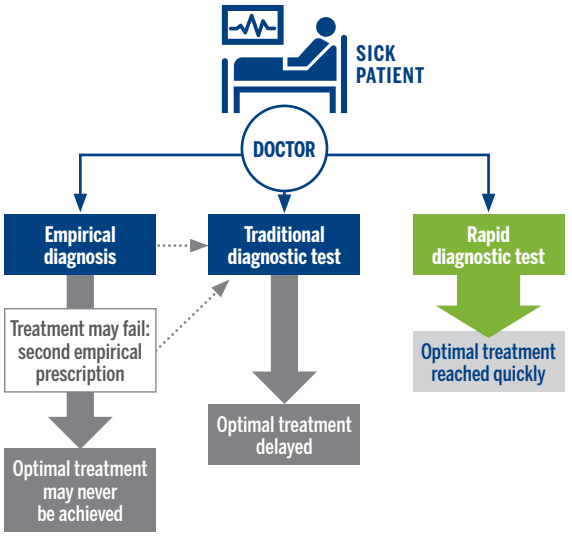
* AST: Antimicrobial Susceptibility Testing

The O'Neill report on AMR highlights the critical importance of the laboratory in reducing antimicrobial resistance and supporting prudent prescribing, as well as the role of new diagnostics and point-of-care tests *[O'Neill et al. 2015]*.

The role that rapid diagnostic tests can play in optimizing the prescription of the most appropriate antibiotic therapy is illustrated in **Figure 23**.

Figure 23: How rapid diagnostic tests help optimize treatment

Adapted from O'Neill et al. The Review On Antimicrobial Resistance. 2015



The case study in **Figure 24** illustrates the real world impact of a rapid respiratory panel (RP) on antibiotic and resource use.

Figure 24: Effect of rapid diagnostics on duration of antimicrobial therapy (ABX) and hospital length of stay (LOS)

Adapted from File et al. *Open Forum Infect Dis.* 2017;4(Suppl 1): S628–S629

RP result for virus	Mean Duration ABX after test result	LOS after test result
Virus + (n=30)	1.6 days	3.6 days
Virus - (n=51)	4 days	4.9 days
Virus +; PCT<0.25 (n=17)	1.2 days	2.9 days
Virus +; PCT<0.25; AST* (n=10)	0.6 days	2.7 days

* Antimicrobial Stewardship Team recommendation. There was no difference in 30-day readmission rates. Of the patients with pneumonia; 11 had + RP for virus (7-HMV), 4 had co-infection with + bacteria with mean PCT of 0.62 and mean duration of ABX 6 days after test result; of the 7 with no bacterial co-infection the mean PCT was 0.12 with mean duration of ABX 0.28 days after the test result. RP: Respiratory Panel

Integration of diagnostics with other AS interventions, to provide fast **accurate identification and susceptibility testing**, will achieve **better clinical outcomes** and **timely streamlining/de-escalating of empiric broad-spectrum antibiotics** in seriously ill patients.

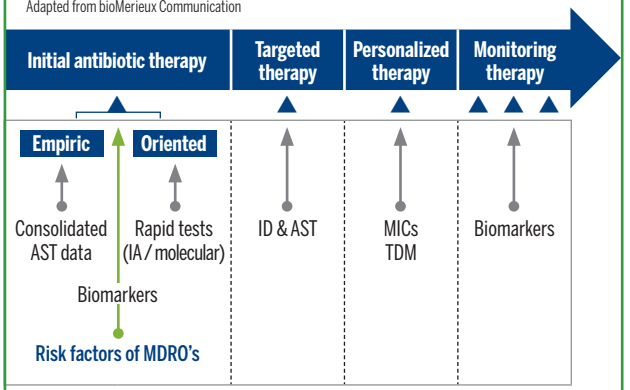
Many studies have assessed algorithms based on **procalcitonin (PCT)** as a rapid-reacting biomarker of bacterial infection for antibiotic stewardship. Recent systematic reviews showed benefits of PCT among patients with respiratory tract infection and sepsis by significantly **reducing antibiotic exposure** as well as a trend towards **reduced costs and reduced length of ICU stay** *[Schuetz et al., 2011, Agarwal et al., 2011, Heyland et al., 2011, Mann et al., 2011, Matthaiou et al., 2012]*.

Near-patient rapid tests, e.g. influenza, Strep A, can be useful to identify patients with bacterial *versus* viral infections.

Molecular diagnostics or screening tests providing a faster result play an important role in **pathogen detection in critically ill patients** which will improve antibiotic stewardship and clinical outcomes *[Afshari et al., 2012]*.

Figure 25: Role of diagnostics in supporting ASPs and appropriate antibiotic therapy

Adapted from bioMerieux Communication



ABBREVIATIONS
AST: Antimicrobial Susceptibility Testing - IA: Immuno Assay - ID: Identification - MDRO: Multi Drug Resistant Organism - MIC: Minimum Inhibitory Concentration - TDM: Therapeutic Drug Monitoring

Diagnostic tests are key components of Antimicrobial Stewardship Programs, enabling the adjustment of treatment from broad spectrum antibiotic therapy to targeted and personalized treatments (**Figure 25**).

6 Identify key measurements for improvement

> **"If you cannot measure it, you cannot improve it"**
> Lord Kelvin 1824-1907

Measurement of prescribing performance is essential to evaluate the impact of stewardship interventions on clinical practice and demonstrate benefits for patients.

Establishing what to measure, the frequency of measurement and how the data will be communicated and acted upon are also key.

In addition to the audit and feedback described in section 5.2.2, three other types of measurement are commonly used within stewardship programs:

- **surveillance** of antimicrobial use and resistance,
- **data collection** for quality improvement,
- **analysis of hospital datasets** to evaluate positive and negative consequences of interventions.

6.1 Surveillance of antimicrobial use and resistance

Monitoring trends in antimicrobial use and resistance within a hospital over several years and also identifying small changes in a single ward over a one-month period are essential to:

- **adapt empiric treatment** according to local resistance trends,
- **demonstrate changes** in practice over time,
- **identify wards** with high antimicrobial usage or use of non-policy antimicrobials and define targeted interventions required.

> **Measure improvement after implemented interventions**

Surveillance of antimicrobial use and resistance is important:

- at **hospital, local, regional, national** levels (i.e.: Strama *[http://en.strama.se], Wales [Heginbothom M and Howe R, 2012]*, Australia *[www.health.sa.gov.au/INFECTIONCONTROL]*),
- at **global level** (i.e.: ECDC: consolidation of resistance data at the European level *[EARSS.net]* with consolidation of antibiotic use *[ESAC.net]*), CDC National Antimicrobial Resistance Monitoring System *[cdc.gov/NARMS]* or Global PPS *[www.global-pps.com]*.

6.1.1. Prescription surveillance through Point Prevalence Surveys

Regular **point prevalence surveys (PPS)** can be used to evaluate prescribing within a unit or hospital *[Ansari et al., 2009, Seaton et al., 2007]*. A **new e-learning module** is also now available to provide training for those undertaking these surveys *[https://www.futurelearn.com/courses/point-prevalence-surveys]*.

These data can be used in an audit process to provide structured feedback to prescribing teams and to define areas for improvement. At a national level, as illustrated in an example for Scotland (**Table 5**), such point prevalence surveys can be used to establish baseline prescribing information and **identify priorities for quality improvement**. This information has led to the development of national **prescribing indicators** *[Malcolm et al., 2012]*.

Table 5: Overview of prescribing from baseline PPS (May 2009) and follow up PPS (September 2011) in acute hospitals in Scotland

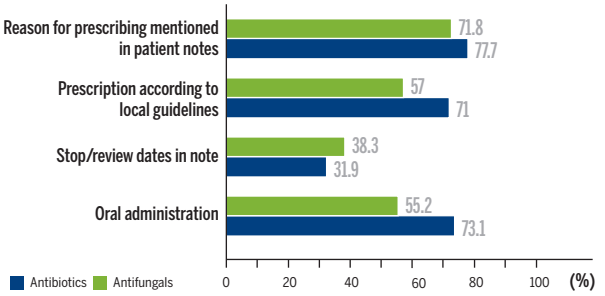
Adapted from Malcolm W et al. *Antimicrob Infect Resist Control* 2012;2:3

Measure	Baseline PPS (May 2009)	Follow up PPS (Sept 2011)
Number of patients surveyed	7,573	11,604
Number of patients (%) prescribed antimicrobials	2,289 (30.2%)	3,728 (32.3%)
Number of patients (%) prescribed single antimicrobial	1,432 (62.6%)	2,268 (60.8%) ↓ ☺
Number of prescriptions (%) for parenteral antimicrobials	1,731 (51.8%)	2,147 (47.8%) ↓ ☺
Number of prescriptions (%) with indication recorded in notes	2,538 (75.9%)	3,811 (86.8%) ↑ ☺
Number of prescriptions (%) compliant with local policy	1939 (81.0%)	2,245 (82.8%) ↑ ☺
Number of surgical prophylaxis prescriptions (%) with duration single dose	146 (49.3%)	287 (59.5%) ↑ ☺
Number of surgical prophylaxis prescriptions (%) with duration = 1 day	57 (19.3%)	81 (16.8%) ↓ ☺
Number of surgical prophylaxis prescriptions (%) with duration >1 day	93 (31.4%)	114 (23.7%) ↓ ☺

The value of these metrics has recently been illustrated at a global level. The **GLOBAL PPS** mentioned previously (see **Figure 3**) can provide not only metrics in relation to the **prescribing quality process**, but the ability to **compare variations in practice between classes of agents**. For example, in **Figure 26**, the quality of antibacterial and antifungal prescribing is compared, the latter being an important and rapidly emerging area for stewardship.

Figure 26: Global-PPS: Difference in quality of prescribing between antibacterials and antifungals

Adapted from Yusuf E et al. *J Antimicrob Chemother.* 2017;72:2906-2909



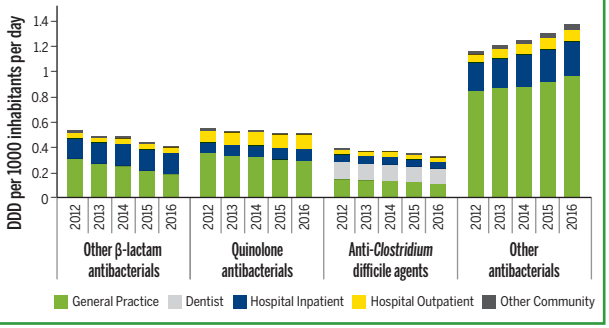
6.1.2. How is antimicrobial use data collected and analyzed?

- **Antimicrobial use at individual patient level**, using an electronic prescribing system through the Hospital Information System.
- **Data from hospital pharmacy computer systems**, showing antimicrobials delivered to each ward and used as a proxy measure for antimicrobials administered to patients.
- The measure used is **Defined Daily Dose (DDD)** which represents the average daily maintenance dose of an antimicrobial for its main indication in adults (**Figure 27**). For instance, the DDD of oral amoxicillin is 1000 mg, so a patient receiving 500 mg every 8 hours for 5 days consumes 7.5 DDDs.
- Usage data may then be divided by a **measure of hospital activity** such as number of admissions or in-patient bed days to provide more meaningful trend analysis. **In-patient bed days** is more commonly used as this data can usually be obtained earlier than admissions data.
- Other denominators are also used and their strengths and limitations have been described *[Monnet D et al., 2007; Berrington A, et al., 2010]*

Hospital level data may be transferred to a national database for further analysis.

Figure 27: Total antibiotic consumption by key antibiotic groups, expressed as DDD per 1000 inhabitants per day, England, 2012-2016

Adapted from Public Health England. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2017



ABC Calc is a simple computer tool to **measure antibiotic consumption** in hospitals. It transforms aggregated data provided by hospital pharmacies into meaningful antibiotic utilisation rates.
[http://www.escmid.org/research_projects/study_groups/esgap/abc_calc/]

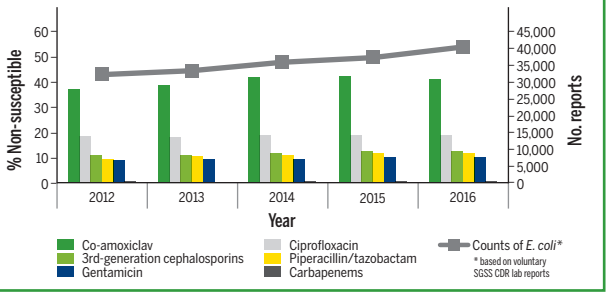
Pareto charts are another useful tool to provide an overview of **antimicrobial usage at ward level** and identify wards that have high total usage or high use of restricted antimicrobials.

6.1.3. How is antimicrobial resistance data collected and analyzed?

Resistance data is obtained from the Microbiology laboratory through computer systems. Hospital level data may then be transferred to national databases. This is illustrated by an example from England (**Figure 28**).

Figure 28: Number of bloodstream isolates of *E. coli* reported to the mandatory surveillance scheme and the proportions non-susceptible to indicated antibiotics

Adapted from Public Health England. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2017



6.2 Data collection for quality improvement

Antimicrobial stewardship is part of many **patient safety programs**. To measure the performance of these programs, data is primarily used for 3 purposes *[Solberg et al., 1997]*:

- **accountability** (e.g. targets),
- **improvement**,
- **research**.

A range of such measures for antimicrobial stewardship programs have been proposed. They can be summarized as four types (**Table 6**): structural, process, outcomes and balancing (are the changes causing new problems?) *[www.abs-international.eu; Dumartin et al., 2011]*.

Table 6: AMS program measures for quality improvement

Adapted from Dumartin C et al. *J Antimicrob Chemother.* 2011;66:1631-7; Morris AM et al. *Inf Control Hosp Epidemiol.* 2012;33:500-506

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
  - Promoted antibiotics
  - Restricted antibiotics
- **Compliance with acute empiric guidance** (documented notes and policy compliance)
- % appropriate **de-escalation**; % appropriate switch from **IV to oral**
- Compliance with **surgical prophylaxis** (<60 min from incision, <24 hours and compliance with local policy
- Compliance with **care "bundles"** – all or nothing (3-day antibiotic review bundle, ventilator-associated pneumonia, community-acquired pneumonia, sepsis)

OUTCOME MEASURES

- *C. difficile* infection rates
- Surgical Site Infection (SSI) rates
- Surveillance of resistance
- Mortality: Standardized Mortality Rates (SMRs)

BALANCING MEASURES

- Mortality
- SSI rates
- Readmission within 30 days of discharge
- Admission to ICU
- Rate of complications
- Treatment-related toxicity (e.g. aminoglycoside-related toxicity)

A focus on outcomes data must be the key to convincing leadership, budget holders and decision makers of the value of stewardship programs. Such measures are outlined in **Table 7**.

Table 7: Examples of different outcome measures and some general remarks

Adapted from Dik J et al. *Expert Review of Anti-infective Therapy,* 2016. 14:6, 569-575

OUTCOME MEASURES	REMARKS
CLINICAL	
Mortality	Important, but less suitable for mild infections (e.g. uncomplicated UTI)
Length of Stay	General or ward-specific (e.g. ICU stay); easy to obtain, but highly sensitive to biases
Complications	Eg: IV catheter-related problems and phlebitis
Clostridium difficile	Indirect measure for antimicrobial use
Readmission rates	Due to relapse. Also consider effect of neighboring institutions
Toxicity (systemic)	Most frequently in renal function and liver
MICROBIOLOGICAL	
Resistance levels	Difficult to measure due to generally long time frame (months to years)
ANTIMICROBIAL CONSUMPTION	
Total use	Often measured in DDDs
IV/PO ratio	Of interest with an active IV-to-PO switch program
Broad/narrow ratio	Potentially relevant with regard to resistance development
FINANCIAL	**Preferably done as cost-effectiveness study**

UTI: urinary tract infection; ICU: intensive care unit; PO: per os; LOS: Length of stay; DDDs: defined daily doses; IV: intravenous.

Checklists are increasingly used to measure quality of care. A study of the use of an antibiotic checklist implemented in nine Dutch hospitals showed that use of the checklist resulted in more appropriate antibiotic use (**Table 8**).

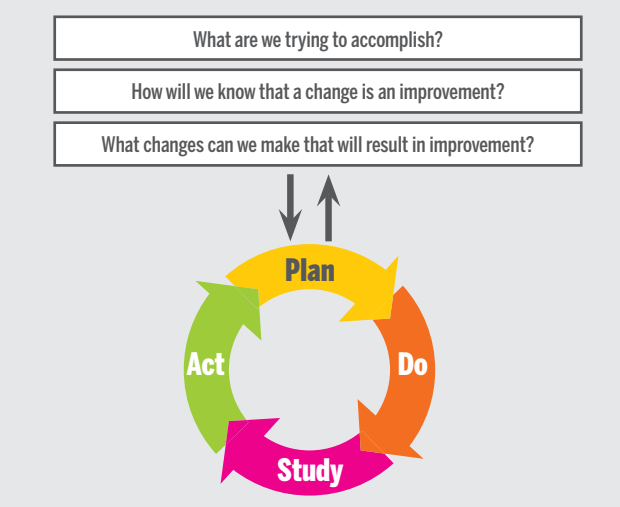
Table 8: Examples of checklist items

Adapted from van Daalen F et al., *BMC Infect Dis.* 2018;18:16

- Blood cultures
- Culture from suspected site of infection
- Guideline adherence
- Adapt dose to renal function
- Documentation of indication
- Adapt therapy when cultures become available
- IV-oral switch

6.2.1. Examples of measures for improvement

A common quality improvement methodology is the "**Plan- Do- Study- Act**" model.

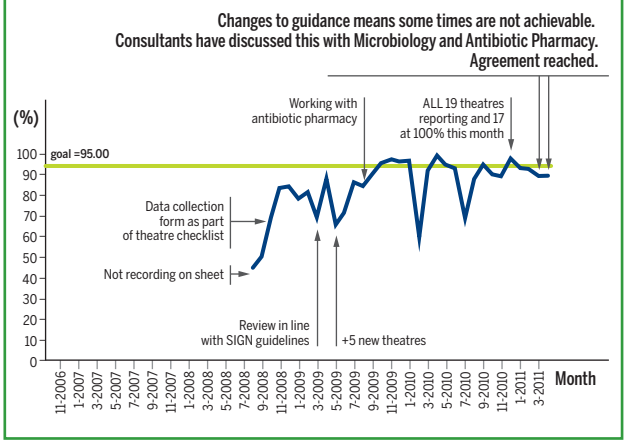


www.ihi.org/knowledge/Pages/HowtoImprove/ScienceofImprovementHowtoImprove

Quality improvement programs often use annotated run charts to display data and show the effects of changes. **Figure 29** shows an example of a run chart used to measure improvement of administration of surgical antibiotic prophylaxis on time.

Figure 29: Percent on-time administration of prophylactic antibiotics

Adapted from Scottish Patient Safety Program

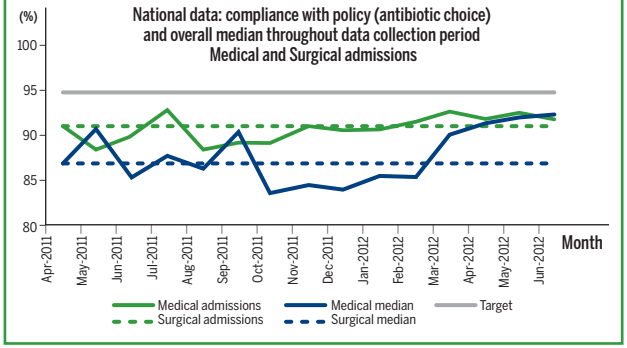


6.2.2. Example of measures used for accountability

Compliance with policy is a process measure (**Figure 30**).

Figure 30: Antibiotic choice compliant with policy

Adapted from Empirical Prescribing Indicator Report April 2011 – June 2012. Scottish Antimicrobial Prescribing Group August 2012



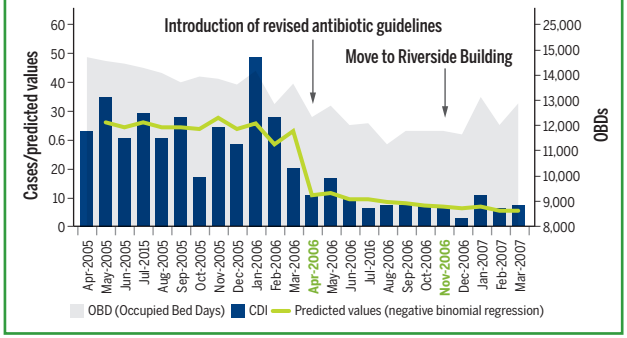
6.3 Analysis of hospital datasets

Linkage of hospital datasets such as hospital admissions, laboratory data and patient outcomes allows measurement of the **impact of stewardship interventions** on patient **morbidity and mortality**.

This provides information about effects of antimicrobial interventions on clinical outcome. **Figure 31** shows how restriction of cephalosporins and fluoroquinolones has resulted in reduced *Clostridium difficile* rates by linking antimicrobial usage data and microbiology data *[Talpaert et al., 2011, Vernaz et al., 2009, Mamoon et al., 2012]*.

Figure 31: New cases of CDI and the number of OBDs before and after the introduction of revised antibiotic guidelines

Adapted from Talpaert MJ et al. *J Antimicrobial Chemother.* 2011; 66: 2168-2174



7 Educate and Train

Education is a key component of any Antimicrobial Stewardship Program. It should include healthcare professionals from all care settings, as well as patients and the public.

By increasing people's knowledge and understanding of how antimicrobials should be used to treat common infections and why inappropriate use may lead to resistance and loss of effective treatments, we can protect this valuable resource for future generations.

7.1 Who should receive education?

Prescribers and other healthcare staff with modules adapted to their background including:

- undergraduate curriculum,
- internship,
- professional training for new staff,
- continuing professional development for all prescribers,
- postgraduate education.

The content of education should be adapted to each profession and include:

- basic knowledge of infection management,
- basic microbiology,
- importance of prudent prescribing in tackling antimicrobial resistance,
- best practices for prescribing to support safe and effective prescribing, administration and monitoring of antimicrobial therapy.

The training is usually delivered by the **antimicrobial management team** and should include competency assessment. In 2014, the first national antimicrobial prescribing and stewardship competences were developed in the UK, and their implementation was an important contribution to the delivery of the UK 5 year Antimicrobial Resistance Strategy *[Ashiru-Oredope et al., 2014]*. The Stewardship Competency Framework for all healthcare professionals has also been developed by WHO *[https://www.who.int/hrh/resources/WHO-HIS-HWF-AMR-2018.1/en/]* and advocates the principles shown in **Table 9** *[Ashiru-Oredope et al., 2014]*.

Table 9: The Stewardship Competency Framework

Adapted from Ashiru-Oredope D et al. *J Antimicrob Chemother* 2014; 69: 2886-8

This consists of five dimensions, each of which includes statements that describe the activity and outcomes that prescribers should be able to demonstrate:

- Infection prevention and control
- Antimicrobial resistance and antimicrobials
- The prescribing of antimicrobials
- Antimicrobial stewardship
- Monitoring and learning

Educating patients and the general public about hygiene and antibiotic use is also important, and may indirectly support hospital education efforts. National and regional public health campaigns, including education aimed at parents and children, have had a variable level of success *[Huttner et al., 2010]*.

Some examples of public awareness campaigns:

- www.e-bug.eu
- www.ecdc.europa.eu/en/eaad
- www.cdc.gov/getsmart

7.2 How to design an education program?

Programs should take into account local recommendations for antimicrobial stewardship, if available. If not, they could be inspired by international policies (see section on "Additional Resources", page 48) but adapted as required. **Table 10** shows educational measures to improve antibiotic use in hospitals.

Table 10: Main antimicrobial stewardship strategies recommended to improve antibiotic use at the hospital level

Adapted from Pulcini C and Gyssens IC. *Virulence* 2013;4:192–202

PASSIVE EDUCATIONAL MEASURES

- Developing/updating local antibiotic guidelines, clinical pathways or algorithms
- Face to face educational sessions, workshops, local conferences

ACTIVE INTERVENTIONS

- Clinical rounds discussing clinical cases, morbidity & mortality meetings, significant event analysis/reviews
- Prospective audit with intervention and feedback
- Reassessment of antibiotic prescriptions, with streamlining and de-escalation
- Academic detailing, educational outreach visits
- E-learning resources used as individual or group activities can compliment traditional learning methods, as a "blended learning" approach (see page 49).

An **evaluation process** should be included in the education program to measure attendance, understanding and assimilation, using regular training assessment tools such as attendance forms, completion certificates, questionnaires, tests etc.

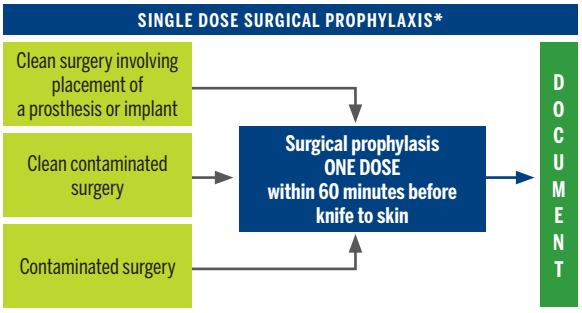
8 Communicate

Communication is a key component of the success of an ASP.

Clear, simple communication should show the vision and the benefits of the program, with core clinical messages.

Communicating to prescribers what the program recommends them to do is one of the essential implementation steps to successful stewardship. This requires a **simple messaging approach** that has identified key processes where stewardship interventions are required to be considered and actioned, such as the "**Start Smart-Then Focus**" approach developed in the UK. **Figure 32** identifies the process for delivering effective surgical prophylaxis.

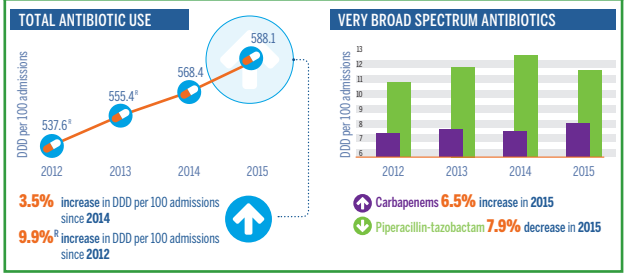
Figure 32: Start Smart ... Then Focus approach



* A repeat dose dose of prophylaxis may be required for prolonged procedures or where there is significant blood loss. A treatment course of antibiotics may also need to be given (in addition to appropriate prophylaxis) in cases of dirty surgery or infected wounds. The appropriate use and choice of antibiotics should be discussed with infection specialists for each case.

Another key communication tool that improves the effectiveness of conveying key messages is data visualization. Using infographic or other visual aids can be a compelling means of communicating data (**Figure 33**).

Figure 33: Examples of infographics on Antibiotic Use



Finally, it is important to keep messages for clinical practice simple. For example, the **10 point principles approach** below is easy to assimilate into practice and is relevant to the whole team looking after a patient with infection on antibiotics (**Table 11**).

Table 11: Ten key points for the appropriate use of antibiotics in hospitalized patients

Adapted from Levy et al. *Int J Antimicrob Agents*. 2016; 48: 239-46

1. Get microbiological samples before antibiotic administration and carefully interpret results: if no clinical signs of infection, colonization rarely requires antimicrobial treatment.
2. Only treat significant bacterial infections.
3. When indicated, start empirical antibiotic treatment, according to site of infection, risk factors for MDR bacteria, and local microbiology/susceptibility patterns.
4. Prescribe drugs at optimal dose, administration mode and length of time.
5. Use antibiotic combinations only when current evidence suggests some benefit.
6. Avoid antibiotics with a higher likelihood of promoting drug resistance or hospital-acquired infections.
7. Remove all infected devices.
8. Always try to de-escalate antibiotic treatment according to clinical situation and microbiological results; switch to oral route as soon as possible.
9. Stop antibiotics as soon as a significant bacterial infection is unlikely.
10. Set up local teams with an infectious diseases specialist, clinical microbiologist, hospital pharmacist, infection control practitioner or hospital epidemiologist; comply with antibiotic policies/guidelines.

Another approach is to identify and communicate to prescribers specific situations where antibiotics should be withheld (**Table 12**) and guidance in relation to the duration of antibiotic use, which is often an area of misuse (**Table 13**).

Communicating, sharing and learning from data is also important.

Face-to-face meetings with prescribers, where there is an opportunity for reflection about their prescribing practices, or attending **multi-disciplinary team web-ex conferences**, etc. are all important in promoting learning about prudent prescribing.

Table 12: Specific Situations where Antibiotics should be withheld

Adapted from Wlodaver CG et al., *Infect Dis Clin Pract.* 2012;20:12-17

RESPIRATORY TRACT INFECTIONS

- Viral pharyngitis
- Viral rhinosinusitis
- Viral bronchitis
- Noninfectious cardiopulmonary disorders misdiagnosed as pneumonia

ACUTE OTITIS MEDIA (AOM) (for selected cases, refer to article)

- Skin and Soft Tissue Infections (SSTI)
  - Subcutaneous abscesses (for selected cases, refer to article)
  - Lower extremity stasis dermatitis

ASYMPTOMATIC BACTERIURIA AND PYURIA, INCLUDING CATHETERIZED PATIENTS

MICROBIAL COLONIZATION AND CULTURE CONTAMINATION

LOW-GRADE FEVER

Recently, as shown in **Table 13**, the move towards **safely and effectively reducing duration of treatment**, an important antimicrobial stewardship goal, is gaining pace *[Spellberg, 2016]*, as is the whole concept of **completing courses of therapy** *[Llewelyn, 2017]*. The **use of diagnostic tests, including biomarkers**, will further support the move towards a more precise approach to duration of antimicrobial therapy.

Table 13: Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

Adapted from Spellberg B. *JAMA Intern Med.* 2016; 176:1254-1255

TREATMENT DURATION IN DAYS	SHORT	LONG
Community-acquired pneumonia	**3-5**	7-10
Nosocomial pneumonia	**≤8**	10-15
Pyelonephritis	**5-7**	10-14
Intraabdominal infection	**4**	10
Acute exacerbation of chronic bronchitis and COPD*	**≤5**	≥7
Acute bacterial sinusitis	**5**	10
Cellulitis	**5-6**	10
Chronic osteomyelitis	**42**	84

* COPD: chronic obstructive pulmonary disease

THE KEYS TO SUCCESS

A number of interventions are key to the success of a hospital-based Antimicrobial Stewardship Program.

- Establish **clear aims/vision** that is shared by all the stakeholders and that conveys a sense of urgency. **Stewardship should be a patient safety priority.**
- Seek **management support**, accountability and secure funding.
- Assemble a strong coalition including a **multi-professional antimicrobial stewardship team** with a strong influential clinical leader.
- Establish **effective communication structures** within your hospital.
- Start with core **evidence-based stewardship interventions** depending on local needs, geography and resources and **plan measurement** to demonstrate their impact.
- Ensure all healthcare staff are aware of the importance of stewardship. Empower them to act and support with **education** using a range of effective strategies.
- Ensure **early or short term wins** and then consolidate success/gains while progressing with more change or innovation.

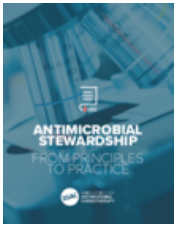
ADDITIONAL RESOURCES

KEY EVIDENCE-BASED PUBLICATIONS ON ANTIMICROBIAL STEWARDSHIP

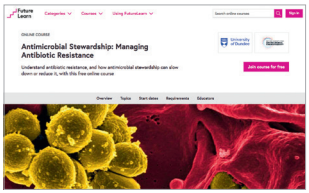
- Baur D, et al. **Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis.** *Lancet Infectious Diseases* 2017; 17:990-1001
- Davey P, et al. **Interventions to improve antibiotic prescribing practices for hospital inpatients.** *Cochrane Database of Systematic Reviews* 2017;(2): CD003543
- Davey P, et al. **Interventions to improve antibiotic prescribing practices for hospital inpatients.** *Cochrane Database of Systematic Reviews* 2013;(4): CD003543
- Dellit TH, et al. **Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship.** *Clinical Infectious Diseases* 2007;44:159-77
- Dik J-WH, et al. **Financial evaluations of antibiotic stewardship programs—a systematic review.** *Frontiers in microbiology* 2015:6:317
- Feazel LM, et al. **Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis.** *Journal of Antimicrobial Chemotherapy* 2014;69:1748–1754
- Feazel, LM, Malhotra, A, Perencevich, EN, Kaboli, P, Diekema, DJ, and Schweizer, ML. **Effect of antibiotic stewardship programs on *Clostridium difficile* incidence: a systematic review and meta-analysis.** *J Antimicrob Chemother.* 2014; 69: 1748–1754
- Karanika S, et al. **Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs.** *Antimicrobial Agents and Chemotherapy* 2016;60:4840–4852
- Schuts EC, et al. **Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis.** *Lancet Infectious Diseases* 2016;16:847-56
- Van Dijck C, et al. **Antibiotic stewardship interventions in hospitals in low-and middle-income countries: a systematic review.** *Bulletin World Health Organization* 2018; 6(4):266–280

USEFUL RESOURCES FOR EDUCATION AND TRAINING IN ANTIMICROBIAL STEWARDSHIP

- **WHO on-line course - Antimicrobial stewardship: a competency- based approach.**
  Access: https://openwho.org/courses/AMR-competency
- **CDC on-line course: Antibiotic Stewardship**
  Access: https://www.train.org/cdctrain/course/1075730/compilation



- **Ebook- Antimicrobial Stewardship: From Principles to Practice. British Society for Antimicrobial Chemotherapy [BSAC]**
  Access: http://bsac.org.uk/antimicrobial-stewardship-from-principles- to-practice-e-book/



- **Massive Open Online Course on Antimicrobial Stewardship.**
  Available in English, Mandarin, Spanish, and Russian.
  BSAC with University of Dundee and FutureLearn
  Access: https://www.futurelearn.com/courses/antimicrobial-stewardship
  New on-line Stewardship module for Africa
  Access: https://www.futurelearn.com/courses/antimicrobial-stewardship-for-africa
- **Antimicrobial Stewardship (AMS), Volume 2, 1st Edition.**
  Access: https://www.elsevier.com/books/antimicrobial-stewardship/pulcini/978-0-12-810477-4
- **CIDRAP web-based resource:** Antimicrobial stewardship project with emphasis on news, commentary, webinars, podcasts
  Access: http://www.cidrap.umn.edu/asp

- **Global Point Prevalence Survey led by the University of Antwerp**
  Access: http://www.global-pps.com

REFERENCES

- Afshari A, Schrenzel J, Ieven M, Harbarth S. **Bench-to-bedside review: Rapid molecular diagnostics for bloodstream infection--a new frontier?** *Critical care (London, England).* 2012;16(3):222.
- Agarwal R, Schwartz DN. **Procalcitonin to guide duration of antimicrobial therapy in intensive care units: a systematic review.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2011;53(4):379-387.
- Aldeyab MA, Kearney MP, Scott MG, et al. **An evaluation of the impact of antibiotic stewardship on reducing the use of high-risk antibiotics and its effect on the incidence of *Clostridium difficile* infection in hospital settings.** *The Journal of antimicrobial chemotherapy.* 2012;67(12):2988-2996.
- Ansari F, Erntell M, Goossens H, Davey P. **The European surveillance of antimicrobial consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2009;49(10):1496-1504.
- Ashiru-Oredope D, Cookson B, Fry C. **Developing the first national antimicrobial prescribing and stewardship competences.** *The Journal of antimicrobial chemotherapy.* 2014;69(11):2886-2888.
- Barlam TF, Cosgrove SE, Abbo LM, et al. **Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2016;62(10):e51-77.
- Bao L, Peng R, Wang Y, et al. **Significant reduction of antibiotic consumption and patients' costs after an action plan in China, 2010-2014.** *PloS one.* 2015;10(3):e0118868.
- Baur D, Gladstone BP, Burkert F, et al. **Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis.** *The Lancet Infectious diseases.* 2017;17(9):990-1001.
- Berrington A. **Antimicrobial prescribing in hospitals: be careful what you measure.** *The Journal of antimicrobial chemotherapy.* 2010;65(1):163-168.
- Bulabula ANH, Jenkins A, Mehtar S, Nathwani D. **Education and management of antimicrobials amongst nurses in Africa-a situation analysis: an Infection Control Africa Network (ICAN)/ BSAC online survey.** *The Journal of antimicrobial chemotherapy.* 2018;73(5):1408-1415.
- Carlet J, Collignon P, Goldmann D, et al. **Society's failure to protect a precious resource: antibiotics.** *Lancet (London, England).* 2011;378(9788):369-371.
- Chung GW, Wu JE, Yeo CL, Chan D, Hsu LY. **Antimicrobial stewardship: a review of prospective audit and feedback systems and an objective evaluation of outcomes.** *Virulence.* 2013;4(2):151-157.
- Cox JA, Vlieghe E, Mendelson M, et al. **Antibiotic stewardship in low- and middle-income countries: the same but different?** *Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases.* 2017;23(11):812-818.
- Davey P, Marwick CA, Scott CL, et al. **Interventions to improve antibiotic prescribing practices for hospital inpatients.** *The Cochrane database of systematic reviews.* 2017;2:Cd003543.
- Davey P, Brown E, Charani E, et al. **Interventions to improve antibiotic prescribing practices for hospital inpatients.** *The Cochrane database of systematic reviews.* 2013(4):Cd003543.
- Dellit TH, Owens RC, McGowan JE Jr, *et al.* **Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship.** *Clin. Infect. Dis.* 2007;44:159-77.
- Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI). **ANTIMICROBIAL STEWARDSHIP: "START SMART - THEN FOCUS" Guidance for antimicrobial stewardship in hospitals** (England). 2011.
- Dik JW, Hendrix R, Poelman R, et al. **Measuring the impact of antimicrobial stewardship programs.** *Expert review of anti-infective therapy.*2016;14(6):569-575.
- Duguid M, Cruickshank M (eds) **Antimicrobial stewardship in Australian hospitals. Australian Commission on Safety and Quality in Health Care.** Sydney. 2010.
- Dumartin C, Rogues AM, Amadeo B, et al. **Antibiotic usage in south-western French hospitals: trends and association with antibiotic stewardship measures.** *The Journal of antimicrobial chemotherapy.* 2011;66(7):1631-1637.
- Elias C, Moja L, Mertz D, Loeb M, Forte G, Magrini N. **Guideline recommendations and antimicrobial resistance: the need for a change.** *BMJ open.* 2017;7(7):e016264.
- **ESPAUR (English Surveillance Programme for Antimicrobial Utilisation and Resistance) Report** Public Health England. 2017
- Feazel LM, Malhotra A, Perencevich EN, Kaboli P, Diekema DJ, Schweizer ML. **Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis.** *The Journal of antimicrobial chemotherapy.* 2014;69(7):1748-1754.
- File TM, Politis P, Tan MJ, Kallstrom G. **Effect of Rapid Molecular Diagnostic Testing and Antimicrobial Stewardship on Antimicrobial Therapy of Respiratory Infections.** *Open Forum Infect Dis.* 2017;4(Suppl 1):S628–S629.
- Frenette C, Sperlea D, Tesolin J, Patterson C, Thirion DJ. **Influence of a 5-year serial infection control and antibiotic stewardship intervention on cardiac surgical site infections**. *American journal of infection control.* 2016;44(9):977-982.
- Goff DA, Bauer KA, Reed EE, Stevenson KB, Taylor JJ, West JE. **Is the "low-hanging fruit" worth picking for antimicrobial stewardship programs?** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2012;55(4):587-592.
- Goossens H. **Expert-proposed European strategies to monitor and control infection, antibiotic use, and resistance in health-care facilities.** *The Lancet Infectious diseases.* 2011;11(5):338-340.
- Heginbothom M and Howe R. **Antibacterial Resistance and Usage in Wales 2005-2011. A Report from Public Health Wales Antimicrobial Resistance Programme Surveillance Unit.** 2012.
- Heyland DK, Johnson AP, Reynolds SC, Muscedere J. **Procalcitonin for reduced antibiotic exposure in the critical care setting: a systematic review and an economic evaluation.** *Critical care medicine.* 2011;39(7):1792-1799.
- Hoffman JM, Shah ND, Vermeulen LC, et al. **Projecting future drug expenditures - 2007.** *American journal of health-system pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists.* 2007;64(3):298-314.
- Holmes AH, Moore LS, Sundsfjord A, et al. **Understanding the mechanisms and drivers of antimicrobial resistance.** *Lancet (London, England).* 2016;387(10014):176-187.
- Howard P, Pulcini C, Levy Hara G, et al. **An international cross-sectional survey of antimicrobial stewardship programmes in hospitals.** *The Journal of antimicrobial chemotherapy.* 2015; 70(4):1245-1255.
- Huttner B, Goossens H, Verheij T, Harbarth S. **Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries.** *The Lancet Infectious diseases.* 2010;10(1):17-31.
- Indian Council of Medical Research (ICMR) **Antimicrobial Stewardship Program Guideline**. 2018
- Johannsson B, Beekmann SE, Srinivasan A, Hersh AL, Laxminarayan R, Polgreen PM. **Improving antimicrobial stewardship: the evolution of programmatic strategies and barriers.** *Infection control and hospital epidemiology.* 2011;32(4):367-374.
- John JF, Jr., Fishman NO. **Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospital.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 1997;24(3):471-485.
- Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. **Systematic Review and Meta-analysis of Clinical and Economic Outcomes from the Implementation of Hospital-Based Antimicrobial Stewardship Programs.** *Antimicrobial agents and chemotherapy.* 2016;60(8):4840-4852.

- Lawes T, Lopez-Lozano JM, Nebot CA, et al. **Effect of a national 4C antibiotic stewardship intervention on the clinical and molecular epidemiology of *Clostridium difficile* infections in a region of Scotland: a non-linear time-series analysis.** *The Lancet Infectious diseases.* 2017;17(2):194-206.
- Lee CF, Cowling BJ, Feng S, et al. **Impact of antibiotic stewardship programmes in Asia: a systematic review and meta-analysis.** *The Journal of antimicrobial chemotherapy.* 2018;73(4):844-851.
- Levy HG, *et al.* **Ten key points for the appropriate use of antibiotics in hospitalised patients: a consensus from the Antimicrobial Stewardship and Resistance Working Groups of the International Society of Chemotherapy.** *Int J Antimicrob Agents*. 2016;48(3):239-46.
- Llewelyn MJ, Fitzpatrick JM, Darwin E, et al. **The antibiotic course has had its day.** *BMJ (Clinical research ed).* 2017;358:j3418.
- Liew YX, Lee W, Loh JC, et al. **Impact of an antimicrobial stewardship programme on patient safety in Singapore General Hospital.** *International journal of antimicrobial agents.* 2012; 40(1):55-60.
- Malcolm W, Nathwani D, Davey P, et al. **From intermittent antibiotic point prevalence surveys to quality improvement: experience in Scottish hospitals.** *Antimicrobial resistance and infection control.* 2013;2(1):3.
- Mann EA, Wood GL, Wade CE. **Use of procalcitonin for the detection of sepsis in the critically ill burn patient: a systematic review of the literature.** *Burns: journal of the International Society for Burn Injuries.* 2011;37(4):549-558.
- Matthaiou DK, Ntani G, Kontogiorgi M, Poulakou G, Armaganidis A, Dimopoulos G. **An ESICM systematic review and meta-analysis of procalcitonin-guided antibiotic therapy algorithms in adult critically ill patients**. *Intensive care medicine.* 2012;38(6):940-949.
- Messacar K, Parker SK, Todd JK, Dominguez SR. **Implementation of Rapid Molecular Infectious Disease Diagnostics: the Role of Diagnostic and Antimicrobial Stewardship**. *Journal of clinical microbiology.* 2017;55(3):715-723.
- Monnet DL. M**easuring antimicrobial use: the way forward.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2007;44(5):671-673.
- Morency-Potvin P, Schwartz DN, Weinstein RA. **Antimicrobial Stewardship: How the Microbiology Laboratory Can Right the Ship.** *Clinical microbiology reviews.* 2017;30(1):381-407.
- Morris AM, Brener S, Dresser L, et al. **Use of a structured panel process to define quality metrics for antimicrobial stewardship programs**. *Infection control and hospital epidemiology.* 2012;33(5):500-506.
- Nathwani D. **Antimicrobial prescribing policy and practice in Scotland: recommendations for good antimicrobial practice in acute hospitals.** *The Journal of antimicrobial chemotherapy.* 2006;57(6):1189-1196.
- Nathwani D. **Antimicrobial stewardship.** In: *Hospital epidemiology and infection Control*; Ed: C.Glen Mayhall; 4th Edition, Philadelphia, Lippincott, Williams and Wilkins, 2012.
- NICE Guideline [NG15], **Antimicrobial stewardship: Systems and Processes for effective antimicrobial medicine use.** 2015 [https://www.nice.org.uk/guidance/ng15]
- O'Neill Report: **Rapid Diagnostics: Stopping Unnecessary Use Of Antibiotics.** *The Review On Antimicrobial Resistance* 2015
- Pulcini C, Gyssens IC. **How to educate prescribers in antimicrobial stewardship practices.** *Virulence.* 2013;4(2):192-202.
- Pulcini C, Binda F, Lamkang AS, et al. **Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach.** *Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases.* 2019;25:20-25.
- Roberts RR, Hota B, Ahmad I, et al. **Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2009; 49(8):1175-1184.
- **SACAR (Specialist Advisory Committee on Antimicrobial Resistance) Antimicrobial Framework.** *Journal of Antimicrobial Chemotherapy* 2007;60,Suppl. 1, i87–i90.
- Schuetz P, Chiappa V, Briel M, Greenwald JL. P**rocalcitonin algorithms for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms.** *Archives of internal medicine.* 2011;171(15):1322-1331.
- Schuts EC, Hulscher M, Mouton JW, et al. **Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis.** *The Lancet Infectious diseases.* 2016; 16(7):847-856.
- Seaton RA, Nathwani D, Burton P, et al. P**oint prevalence survey of antibiotic use in Scottish hospitals utilising the Glasgow Antimicrobial Audit Tool (GAAT).** *International journal of antimicrobial agents.* 2007;29(6):693-699.
- Solberg LI, Mosser G, McDonald S. **The three faces of performance measurement: improvement, accountability, and research.** *The Joint Commission journal on quality improvement.* 1997; 23(3):135-147.
- Spellberg B. **The New Antibiotic Mantra-"Shorter Is Better".** *JAMA internal medicine.* 2016; 176(9):1254-1255.
- Sun L, Klein EY, Laxminarayan R. **Seasonality and temporal correlation between community antibiotic use and resistance in the United States.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2012;55(5):687-694.
- Talpaert MJ, Gopal Rao G, Cooper BS, Wade P. **Impact of guidelines and enhanced antibiotic stewardship on reducing broad-spectrum antibiotic usage and its effect on incidence of *Clostridium difficile* infection.** *The Journal of antimicrobial chemotherapy.* 2011;66(9):2168-2174.
- Toma M, Davey PG, Marwick CA, Guthrie B. **A framework for ensuring a balanced accounting of the impact of antimicrobial stewardship interventions.** *The Journal of antimicrobial chemotherapy.* 2017;72(12):3223-3231.
- Valiquette L, Cossette B, Garant MP, Diab H, Pepin J. **Impact of a reduction in the use of high-risk antibiotics on the course of an epidemic of *Clostridium difficile*-associated disease caused by the hypervirulent NAP1/027 strain.** *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.* 2007;45 Suppl 2:S112-121.
- Van Boeckel TP, Gandra S, Ashok A, et al. **Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data.** *The Lancet Infectious diseases.* 2014;14(8): 742-750.
- Van Daalen FV, Hulscher M, Minderhoud C, Prins JM, Geerlings SE. **The antibiotic checklist: an observational study of the discrepancy between reported and actually performed checklist items.** *BMC infectious diseases.* 2018;18(1):16.
- Van Dijck C, Vlieghe E, Cox JA. A**ntibiotic stewardship interventions in hospitals in low-and middle-income countries: a systematic review.** *Bulletin of the World Health Organization.* 2018;96(4):266-280.
- Venkatesh S, et al. **National Treatment Guidelines for Antimicrobial Stewardship in Infectious Diseases in India.** Version 1.0 *National Centre For Disease Control* 2016
- Versporten A, Zarb P, Caniaux I, et al. **Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey.** *The Lancet Global health.* 2018;6(6):e619-e629.
- Vernaz N, Hill K, Leggeat S, et al. **Temporal effects of antibiotic use and *Clostridium difficile* infections.** *The Journal of antimicrobial chemotherapy.* 2009;63(6):1272-1275.
- **WHO competency framework for health workers' education and training on antimicrobial resistance.** Geneva: World Health Organization; 2018 (WHO/HIS/HWF/AMR/2018.1). Licence: CC BY-NC-SA 3.0 IGO.
- Wise R, Hart T, Cars O, et al. **Antimicrobial resistance. Is a major threat to public health.** *BMJ (Clinical research ed).* 1998;317(7159):609-610.
- Wlodaver CG, May C. **Antibiotic stewardship: using clinical guidelines to control antibiotic overuse and deter microbial adaptation.** *Infect Dis Clin Pract.* 2012;20:12-17.
- Yusuf E, Versporten A, Goossens H. **Is there any difference in quality of prescribing between antibacterials and antifungals? Results from the first global point prevalence study (Global PPS) of antimicrobial consumption and resistance from 53 countries.** *The Journal of antimicrobial chemotherapy.* 2017;72(10):2906-2909.

bioMérieux
In vitro diagnostics serving public health

A major player in *in vitro* diagnostics for more than 50 years, bioMérieux has always been driven by a pioneering spirit and unrelenting commitment to improve public health worldwide.

Our diagnostic solutions bring high medical value to healthcare professionals, providing them with the most relevant and reliable information, as quickly as possible, to support treatment decisions and better patient care.

bioMérieux's mission entails a commitment to support medical education, by promoting access to diagnostic knowledge for as many people as possible. Focusing on the medical value of diagnostics, our collection of educational booklets aims to raise awareness of the essential role that diagnostic test results play in healthcare decisions.

Other educational booklets are available.
Consult your local bioMérieux representative.

The information in this booklet is for educational purposes only and is not intended to be exhaustive. It is not intended to be a substitute for professional medical advice. Always consult a medical director, physician, or other qualified health provider regarding processes and/or protocols for diagnosis and treatment of a medical condition. bioMérieux assumes no responsibility or liability for any diagnosis established or treatment prescribed by the physician.

bioMérieux S.A. • 69280 Marcy l'Étoile • France
Tel.: + 33 (0)4 78 87 20 00 • Fax: +33 (0)4 78 87 20 90
www.biomerieux.com