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PRACTICAL GUIDE
TO ANTIMICROBIAL STEWARDSHIP IN HOSPITALS

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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]*, the Australian Hospital Stewardship Guidance produced by the Australian Commission on Safety And Quality in Healthcare *[Duguid et al., 2010]*, National Stewardship Guidance from Scotland *[Nathwani et al., 2006]*, the UK *[DOH-ARHAI, Start smart then Focus, 2011]* and, although less literature is available, from other countries whenever possible.

We hope that this booklet will inform, encourage and support health professionals wishing to pursue the implementation of antimicrobial stewardship initiatives, as well as combating antimicrobial resistance.

Prof. Dilip NATHWANI, MB; DTM&H, FRCP

Consultant Physician and Honorary Professor of Infection
Ninewells Hospital and Medical School
Dundee, Scotland, UK
dilip.nathwani@nhs.net

Dr Jacqueline SNEDDON, MRPharmS, MSc, PhD

Project Lead for Scottish Antimicrobial Prescribing Group
Healthcare Improvement Scotland
Glasgow, Scotland, UK
jacqueline.sneddon@nhs.net

Contents

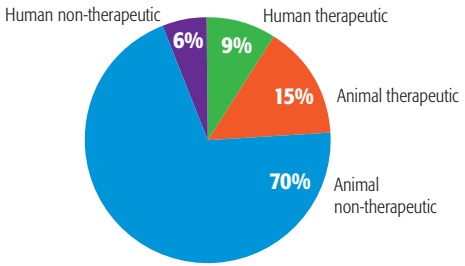
Why implement antimicrobial stewardship in hospitals?

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 misuse through use without a prescription and overuse for self-limiting infections [Figures 1 and 2] *[Hoffman et al., 2007; Wise et al., 1999; John et al., 1997]* and as predicted by Fleming in his Nobel Prize lecture, bacterial resistance has appeared and is growing fast *[www.nobelprize.org]*.

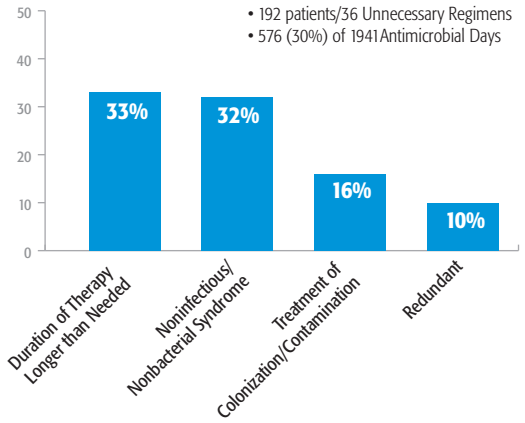
Figure 1. Current use of antibiotics in the United States.



Source: www.pewhealth.org

Today, up to 85% of antibiotics have a non-human use and up to 75% have a non-therapeutic use. Antibiotic use in hospitals and the community is common and often inappropriate [Figure 2]. In hospitals, up to 50% of antimicrobial use is inappropriate *[Dellit et al., 2007]*.

Figure 2. "Unnecessary" Antimicrobial Therapy.



Adapted from Hecker MT. et al. Arch Intern Med. 2003;162:972-978.

Antimicrobial Prescribing Facts: The 30% Rule

- **~ 30%** of all hospitalised 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 Organisation 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]*. How we address this global challenge has been the subject of much discussion and many initiatives *[Carlet et al., 2012]*.

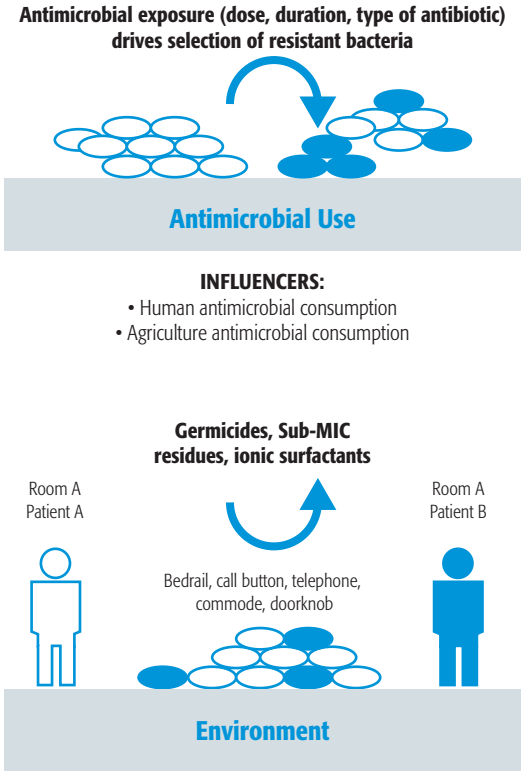
2. Combating antimicrobial resistance

To overcome the threat of antimicrobial resistance, a three-pillar approach has been advocated:

1. Optimise the use of existing antimicrobial agents
2. Prevent the transmission of drug-resistant organisms through infection control
3. Improve environmental decontamination

Figure 3 explains why antimicrobial resistance cannot be solved with single interventions alone. All 3 aspects of the "three pillars" must be addressed. To ensure this happens at a hospital level requires a strong collaboration between infection prevention, environmental decontamination and antimicrobial stewardship teams *[Moody et al., 2012]*.

Figure 3. The 3 key drivers for resistance.



Adapted from Owens RC Jr. et al. Diagn.Microbiol. and Infect. Dis. 2008; 61:110-28.

3. Defining antimicrobial stewardship

Antimicrobial stewardship [AS] is one of the key strategies to overcome resistance.

It involves the careful and responsible management of antimicrobial use.

"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*"

[Nathwani et al., 2012]

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

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

4. Goals of antimicrobial stewardship and evidence for success

The four main goals of antimicrobial stewardship are listed below with examples of evidence that stewardship programs can help achieve these goals. *[McGowan et al,. 2012; Davey P et al., (Cochrane Database), 2013]*

GOAL 1: IMPROVE PATIENT OUTCOMES

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

Table 1. Example of how appropriate antibiotics improve patient outcome and reduce healthcare costs.

CHARACTERISTIC	Inappropriate Antibiotics (n=238)	Appropriate Antibiotics (n=522)
DEMOGRAPHICS		
Age, mean ± SD (yr)	57.7 ± 15.8	59.9 ± 16.5
Male	48.7%	54.2%
CHRONIC HEALTH STATE		
Immunosuppressed	32.4%	34.3%
Chronic dialysis	14.7%	7.1%
Nursing home resident	13.4%	18.2%
Coronary artery disease	11.7%	7.9%
Chronic obstructive pulmonary disease	21.6%	17.2%
Congestive heart failure	21.6%	18.1%
Malignancy	23.1%	34.1%
Diabetes mellitus	27.5%	20,1%
Charlson score, mean ± SD	4.8 ± 3.7	4.8 ± 3.7
DISEASE SEVERITY		
Acute Physiology and Chronic Health	23.2 ± 6.6	23.9 ± 6.7
EVALUATION II, MEAN ± SD		
Need for mechanical ventilation	62.6%	51.5%
Need for vasopressors	59.9%	58.0%
Organ failures, mean ± SD	2.3 ± 1.0	2.2 ± 1.1
Treatment with drotrecogin alfa (activated)	3.8%	4.4%
INFECTION CHARACTERISTICS		
Nosocomial	69.3%	48.7%
Community-acquired	5.9%	11.1%
Healthcare-associated	24.8%	40.2%
ADDITIONAL FACTORS		
Length of stay before infection (mean ± SD)	15.3 + 20.7	7.5 + 14.9
Length of stay before infection (median)	9	1
Hospital mortality	51.7%	36.4%

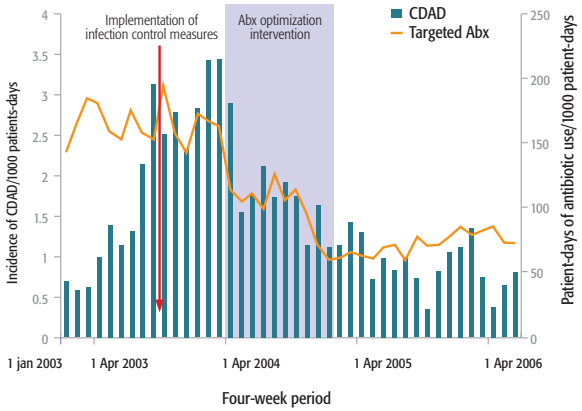
Adapted from Shorr AF. et al., Crit. Care Med. 2011;39:46-51.

GOAL 2: IMPROVE PATIENT SAFETY

(Minimize unintended consequences of antimicrobials)

- Reduce antimicrobial consumption, without increasing mortality or infection-related readmissions e.g. 22%-36% reduction in antimicrobial use *[Dellit et al., 2007].*
- Reduce *C. difficile* colonization or infection by controlling the use of "high-risk" antibiotics *[Valiquette et al,. 2007].*

Figure 4. Example of robust stewardship program with strict implementation of infection control measures leading to sustained reduction in *C. difficile* infection [CDI] cases during an epidemic.

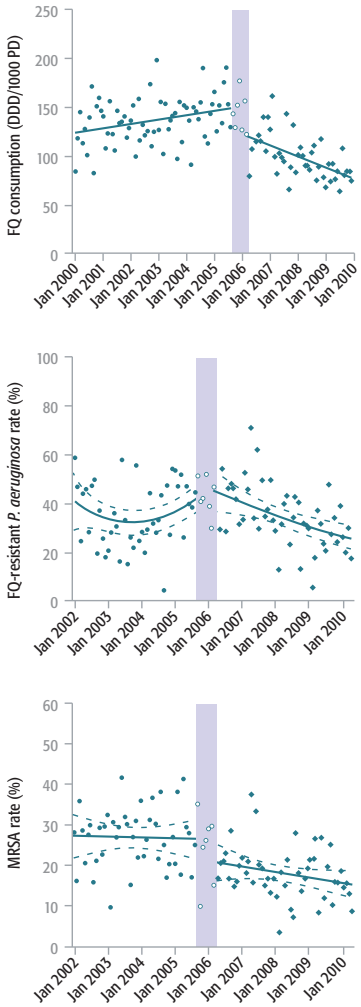


Adapted from Valiquette L et al., Clin. Infect. Dis. 2007;45:S112-121.

GOAL 3: REDUCE RESISTANCE

- Restricting relevant agents can reduce colonization or infection with Gram-positive or Gram-negative resistant bacteria.

Figure 5. Example of a reduction of fluoroquinolone use associated with decreased MRSA and fluoroquinolone-resistant *P. aeruginosa* isolation rates.



Adapted from Lafaurie et al., J. Antimicrob. Chemother. 2012;67:1010-5.

GOAL 4: REDUCE HEALTHCARE COSTS
(without adversely impacting quality of care)

- Savings achieved by reducing antibiotic costs can be greater than the cost of the intervention or program (from $200,000 to $900,000 depending on the studies) *[Dellit et al., 2007].* Such cost-effectiveness data are sparse but emerging *[Stevenson et al., 2012; Davey et al., (Cochrane Database), 2013]*.

Table 2. Example of annual savings associated with the implementation of an Antimicrobial Stewardship Program.

YEAR	METHOD A*	METHOD B**
2000[a]	158,161	229,076
2001	548,002	1,267,638
2002	806,393	1,446,883
2003	473,174	1,354,129
2004	244,160	1,555,048
2005	419,613	2,005,202
2006	983,690	2,172,756
2007	675,036	1,990,967
2008	817,503	2,557,972
2009	1,278,301	2,782,519
2010	2,175,927	3,456,373
2011[b]	1,770,827	2,406,399
Yearly average	920,070	2,064,441
Total savings	10,350,787	23,224,961

Note: data are US dollars
[a] April-December 2000
[b] January-June 2011

* Method A: Inflation rate determined using the annual US consumer price index for Medical Care Commodities.
** Method B: Inflation rate determined using an Anti-Infective Specific Index (see article).

Adapted from Beardsley J et al. Inf. Control. Hosp. Epidemiol., 2012;33:398-400.

5. Implementation of Antimicrobial Stewardship Programs

A recent global survey outlined the range of stewardship activities across the continents [Table 3, Figure 6]. This survey provides some understanding about current or planned activity and barriers.

For example, depending on the continent, stewardship programs are planned in a further 20-30% of cases and funding is the most important barrier.

Table 3. Implementation of Antimicrobial Stewardship Programs worldwide

North America	67%
Europe	65%
Asia	53%
Oceania	48%
South America	46%
Africa	13%

Figure 6. Barriers to providing a planned AMS Programme.

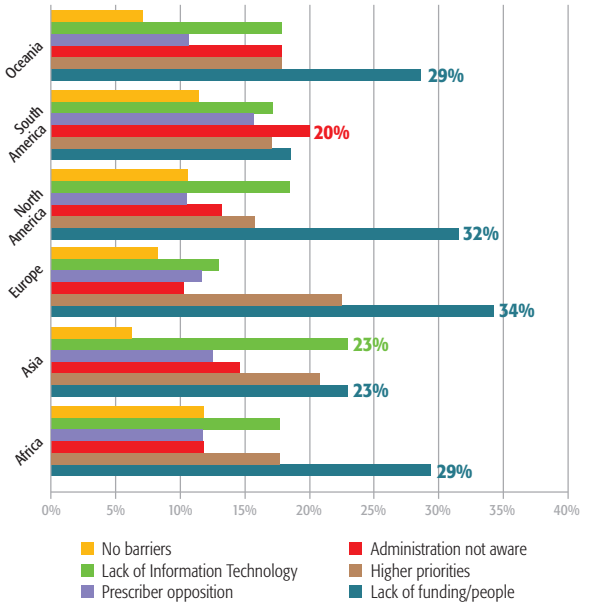
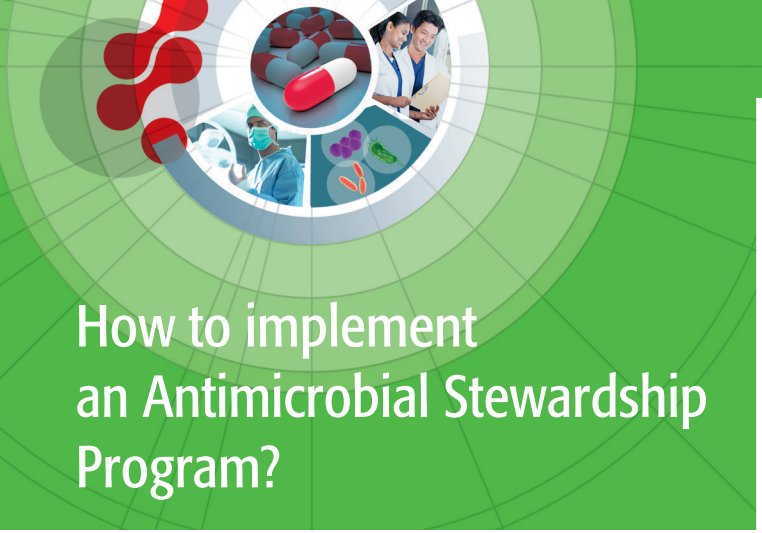


Table 3 and Figure 6 are adapted from First global survey of antimicrobial stewardship (AMS), Howard P. et al., ESCMID Study Group for Antimicrobial Policies (ESGAP) & ISC Group on Antimicrobial Stewardship ECCMID 2013, Berlin Presentation Nr. 2448.



How to implement an Antimicrobial Stewardship Program?

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

- **Analyse your situation** and what problems you want to address. There are many international guidelines available (see page 38), 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 (see Chapter 6).
- 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
- Intravenous (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 of antibiotic use**. This can be set out as a **driver diagram** (see pages 14 and 16 for more details).

Table 4. Driver Diagram Overarching Driver: Leadership and Culture.

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, as appropriate: - 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.

Adapted from www.cdc.gov/getsmart/healthcare/improve-efforts/driver-diagram/overarching-driver

3. Set up structure and organization

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

1. **Dedicated resources**, including dedicated personnel time for stewardship activities, education, and measuring/monitoring antimicrobial use.

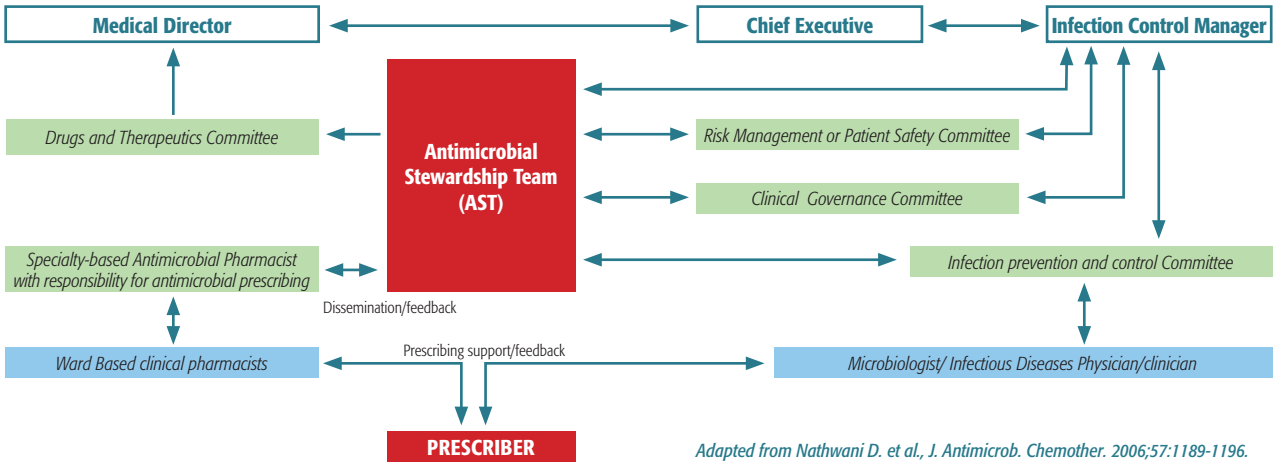
2. A **multidisciplinary AS team** [AST] with core membership of:
   - an **infectious diseases physician** (or lead doctor or physician champion)
   - a **clinical microbiologist**
   - a **clinical pharmacist** with expertise in infection.

   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.

3. **Governance** within the hospital's **quality improvement and patient safety governance** structure

4. **Clear lines of accountability** between the chief executive, clinical governance, drug and therapeutics committee, infection prevention and control committees, and the AST. Figure 7 illustrates such an organization structure.

Figure 7. Model of Antimicrobial Prescribing Pathway and Organization in Acute Hospitals in Scotland.



Adapted from Nathwani D. et al., 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**.

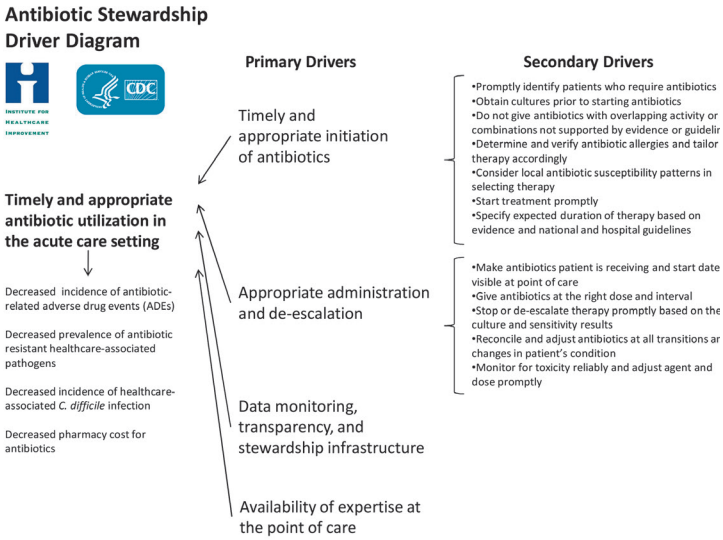
One way of doing this is to produce a **Driver Diagram**. A Driver Diagram is a logic chart with three or more levels, including:

- 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 8. Example of a Driver Diagram for Antimicrobial Stewardship Adapted from www.cdc.gov/getsmart/healthcare/improve-efforts/



5. Identify effective interventions for your setting

A range of stewardship interventions has been reviewed in the IDSA guidelines *[Dellit et al., 2007]*.

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 5. Antimicrobial Stewardship Toolkit: Quality of Evidence to support interventions.

Core Strategies	Supplemental Strategies
Formulary restrictions and preauthorization*	Streamlining / timely de-escalation of therapy*
Prospective audit with intervention and feedback*	Dose optimization*
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

Adapted from Dellit et al. Clinical Infectious Diseases 2007; 44:159-77.

* Strategies with strongest evidence and support by IDSA.

Two core ASP strategies have emerged:

- **"Front–end strategies"** where antimicrobials are made available through an approval process (formulary restrictions and preauthorization).
- **"Back-end" strategies** are where antimicrobials are reviewed after antimicrobial therapy has been initiated (prospective audit with intervention and feedback)

ADVANTAGES of FRONT-END STRATEGIES	ADVANTAGES OF BACK-END STRATEGIES
Immediate reduction in use and expenditure of restricted antibiotics	Timely de-escalation of antibiotics Reduction in inappropriate use

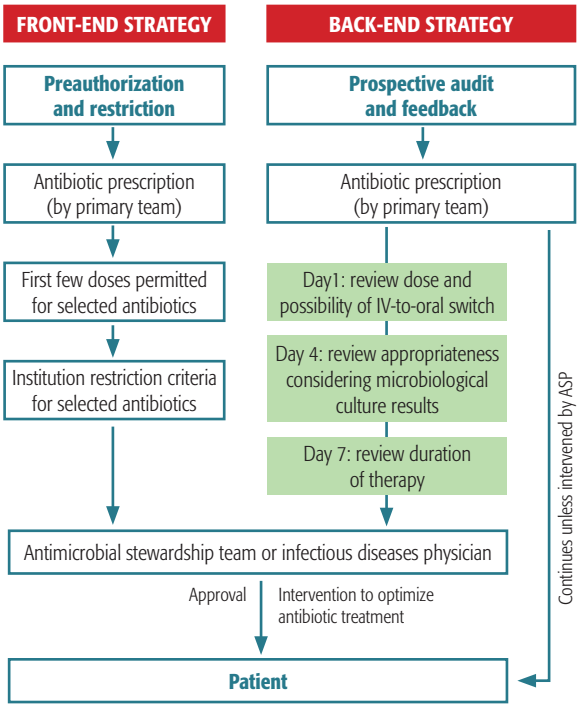
A review of back-end *versus* front-end strategies reveals that **back-end strategies**, although more labour-intensive, are:

- **More widely practiced**
- **More easily accepted** by clinicians
- Provide a **higher opportunity for educational opportunities**.

They probably provide a **more sustained impact** of improving the overall quality of antimicrobial prescribing *[Chung et al., 2013]*.

An example of such a system from Singapore is illustrated below.

Figure 9. Front- and Back-end Antimicrobial Stewardship Strategy.



Adapted from Chung GW et al. Virulence 2013; 4:1-7.

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.

A template for a hospital antimicrobial policy prepared in the UK by the Specialist Advisory Committee on Antimicrobial Resistance *[SACAR]* and the important messages that need to be incorporated into the policy *[MINDME]* are illustrated in Tables 6 and 7 from the Australian Stewardship Guidelines *[Duguid et al., 2010]*.

Table 6. Summary of contents of the SACAR template for hospital antimicrobial policy.

TITLE PAGE
- name of policy, date, version, review date, and contact details for normal hours and out-of-hours enquiries

INTRODUCTION SECTION
- statement as to whether the guideline is mandatory or for guidance only, contents and a local procedure for microbiological samples

SUMMARY LIST OF AVAILABLE ANTIMICROBIALS
- unrestricted, restricted (approval of a specialist is required) or permitted for specific conditions

REGIMENS FOR TREATMENT OF COMMON INFECTIONS
- treatment, prophylaxis and rules for switching from intravenous to oral administration

Adapted from Specialist Advisory Committee on Antimicrobial Resistance36 (SACAR) Antimicrobial Framework. J. Antimicrob. Chemother. 2007;60:i87–i90.

Table 7. The Golden Rules of Antimicrobial Prescribing "MINDME".

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

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

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 resource and priorities, clinician preference/views and potential risk or unintended consequences.

Guidance on what **advice to give for treatment and prophylaxis** is available in the Australian Guidelines (Table 8) although this will depend on local burden and epidemiology. These guidelines and policies should ideally be supported by a program of on-going education for all relevant healthcare professionals.

Table 8. Example of the United Kingdom Specialist Advisory Committee on Antimicrobial Resistance recommended guidelines.

TREATMENT OF:

- Urinary tract infections
- Upper respiratory tract infections
- Lower respiratory tract infections (community and hospital acquired pneumonia, and exacerbations of chronic obstructive pulmonary disease)
- Soft tissue infections (injuries or bites, cellulitis, chronic ulcers and necrotising fasciitis)
- Central nervous system infections (bacterial meningitis, viral encephalitis
- Gastrointestinal infections such as food poisoning and intra-abdominal sepsis
- Genital tract infections
- Bloodstream infections
- Eye, ear, nose and throat infections
- Sepsis of unknown origin
- Specific confirmed infections; for example, treatment regimens for methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile* and tuberculosis
- Endocarditis

PROPHYLAXIS USE FOR:

- Prevention of bacterial endocarditis (which patients should receive prophylaxis)
- Endoscopic procedures (which individuals, considered at high risk, should receive prophylaxis; for example, neutropenic patients)
- Surgical procedures (recommendations for all common surgical interventions, including timing of initial dose and exceptional circumstances for repeat doses)
- Splenectomy patients (provide details of both the immunisation and antimicrobial prophylaxis requirements)

Adapted from Specialist Advisory Committee on Antimicrobial Resistance (SACAR) Antimicrobial Framework. J. Antimicrob. Chemother. 2007;60:i87–i90.

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.

5.2. BACK-END STRATEGIES

5.2.1. Antimicrobial review methods

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

Table 9. Antimicrobial Review Methods.

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

- Clinical review by AST 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 barrier to good stewardship and may be a save of high cost. See Figure 10, page 27.

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

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 investigation,
- interpretation of microbiology with a view to de-escalation or stopping therapy,
- 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. At a national level, as illustrated in an example for Scotland [Table 10], such point prevalence surveys can be used to **establish baseline prescribing information** and **identify priorities for quality improvement**. This information has contributed to the development of national **prescribing indicators**. *[Malcolm et al., 2012]*

Table 10. Overview of prescribing from baseline PPS (May 2009) and follow up PPS (September 2011).

Measure	Baseline PPS (May 2009)		Follow up PPS (Sept 2011)
	Scotland Acute Hospitals	Europe	Scotland Acute Hospitals
Number of patients surveyed	7,573	73,060	11,604
Number of patients (%) prescribed antimicrobials	2,289 (30.2%)	21,197 (29.0%)	3,728 (32.3%)
Number of patients (%) prescribed single antimicrobial	1,432 (62.6%)	14,403 (67.9%)	2,268 (60.8%) ↓ ☺
Number of prescriptions (%) for parenteral antimicrobials	1,731 (51.8%)	17,947 (60.5%)	2,147 (47.8%) ↓ ☺
Number of prescriptions (%) with indication recorded in notes	2,538 (75.9%)	22,456 (75.7%)	3,811 (86.8%) ↑ ☺
Number of prescriptions (%) compliant with local policy	1939 (81.0%)	17,223 (82.5%)	2,245 (82.8%) ↑ ☺
Number of surgical prophylaxis prescriptions (%) with duration single dose	146 (49.3%)	927 (27.0%)	287 (59.5%) ↑ ☺
Number of surgical prophylaxis prescriptions (%) with duration = 1 day	57 (19.3%)	723 (21.1%)	81 (16.8%) ↓ ☺
Number of surgical prophylaxis prescriptions (%) with duration >1 day	93 (31.4%)	1783 (51.9%)	114 (23.7%) ↓ ☺

Adapted from Malcolm W, Nathwani D, et al. Antimicrob. Resist. infect. Control. 2012;2:3.

5.2.3. Use of diagnostic tools

The role of rapid diagnostics and biomarkers in antimicrobial stewardship is recognised as a key recommendation by the IDSA.

➢ The IDSA policy statement for combating antimicrobial resistance and saving lives recommends "Greater Investment in Rapid Diagnostics R&D and Integration into Clinical Practice" as one of the key strategies. *[Dellit et al., 2007]*

Figure 10. The high cost of poor diagnosis of infection.

	Individual health	Public health	Overall impact
No treatment	Continued illness	Continued transmission	Increasing burden of disease
Lack of diagnosis			
Syndromic treatment	Mis- or over-use of antibiotics Antibiotic-related adverse events	Waste of antibiotic resources Antibiotic resistance and *C. difficile* infection	Breakdown in disease control and in spread of resistant pathogen Failure of health system to treat infection

Integration of diagnostics with other AMS 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].*

However, the availability of these interventions in resource-limited environments is likely to be a challenge to their introduction.

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:

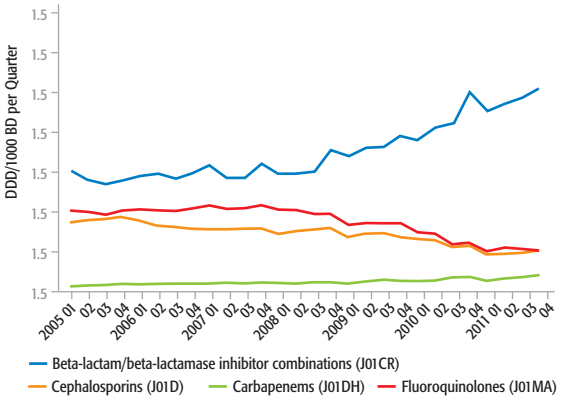
- **at hospital, local, regional, national levels** (i.e.: Strama [http://en.strama.se], Wales *[Heginbothom M and Howe R, 2012],* Australia *[www.health.sa.gov.au/INFECTIONCONTROL]*)
- and **at global level** (i.e.: ECDC: consolidation of resistance data at the European level *[EARSS.net]* with consolidation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

6.1.1. How is antimicrobial use data collected and analysed?

- **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. 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 et al., 2007; Berrington et al., 2010]*

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

Figure 11. Trends in Specific Antibacterial Group Usage for All-Wales hospitals from 2005–2011.

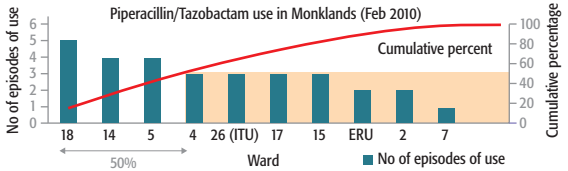


Adapted from Heginbothom M and Howe R. A Report from Public Health Wales Antimicrobial Resistance Programme Surveillance Unit. 2012.

ABC Calc is a simple computer tool to **measure antibiotic consumption** in hospitals and hospital wards. It transforms aggregated data provided by hospital pharmacies (generally as a number of packages or vials) into meaningful antibiotic utilisation rates. *[http://www.escmid.org/research_projects/study_groups/esgap/abc_calc/]*

Pareto charts are useful to provide an overview of **antimicrobial usage at ward level** and identify wards that have high total usage or high use of restricted antimicrobials. In the example below 50% of piperacillin/tazobactam use occurs within 3 wards therefore interventions to reduce use should focus on these wards.

Figure 12. Pareto chart displaying use of « restricted » antibiotics in a hospital in Lanarkshire.

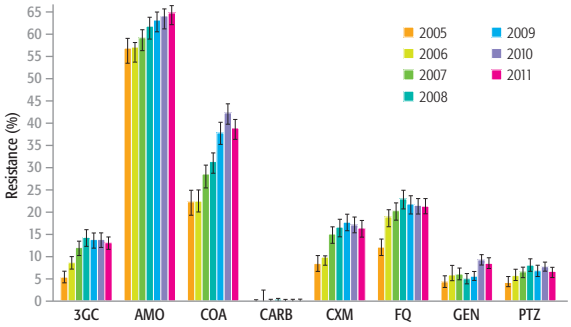


Source: Steve McCormick, Lead Antimicrobial Pharmacist, NHS Lanarkshire - presented at "Quality Improvement within Acute Medicine" Workshop organized by the Scottish Antimicrobial Prescribing Group and Society for Acute Medicine - June 2010.

6.1.2. How is antimicrobial resistance data collected and analyzed?

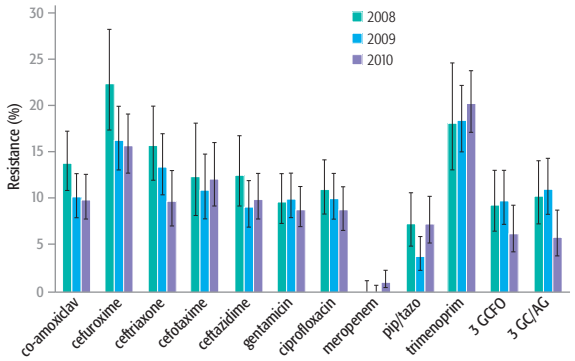
Resistance data is obtained from the Microbiology laboratory through computer systems. Hospital level data may then be transferred to national databases. Examples from two UK countries, Wales and Scotland, are shown in Figures 13 and 14.

Figure 13. All-Wales resistance rates for *E. coli bacteraemia* (2005 to 2011).



Adapted from Heginbothom et al. A Report from Public Health Wales Antimicrobial Resistance Programme Surveillance Unit. 2012.

Figure 14. Antimicrobial resistance (with 95% confidence intervals) in *K. pneumoniae* isolated from blood cultures in 2008 (n=512), 2009 (n=672) and 2010 (n=715).



Adapted from Scottish Antimicrobial Prescribing Group (SAPG), Report on Antimicrobial Use and Resistance in Humans in 2010.

At national level, resistance surveillance is particularly important to identify emerging resistance in **common pathogens** or **multi-resistant organisms** such as Gram negative bacteria which produced extended spectrum beta lactamase (ESBL) or carbapenemase enzymes.

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 (see Table 11): structural, process, outcomes and balancing (are the changes causing new problems?) *[www.abs-international.eu; Dumartin et al., 2011]*.

Table 11. AMS program measures for quality improvement.

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

PROCESS MEASURES
- **Amount of antibiotic** in DDD/100 bed days
  - 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* 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)

Adapted from Dumartin et al. J. Antimicrob. Chemother. 2011;66:1631-7; Morris et al. Inf. Control. Hosp. Epidemiol. 2012;33[3]:500-506.

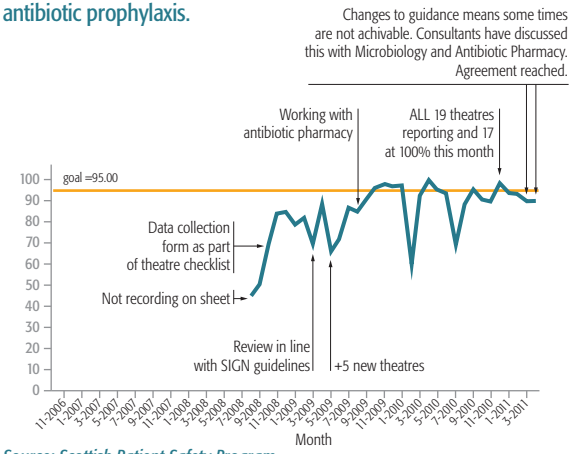
6.2.1. Examples of measures for improvement

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 15 shows an example of a run chart used to measure improvement of administration of surgical antibiotic prophylaxis on time.

Figure 15. Improvement in administration of on-time surgical antibiotic prophylaxis.



Source: Scottish Patient Safety Program.

6.2.2. Examples of measures used for accountability e.g. targets

Compliance with policy is a process measure.

Figure 16.a. Indication documented in patient's notes.

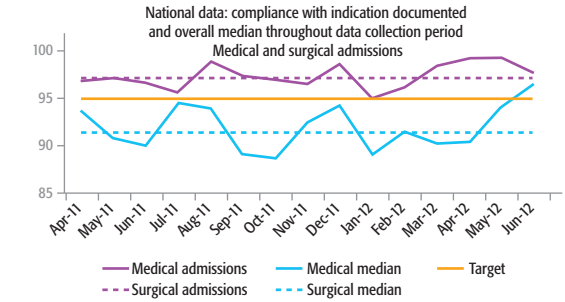
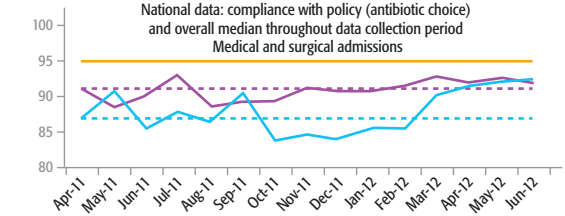


Figure 16.b. Antibiotic choice compliant with policy.



Note: non-zero y-axes.

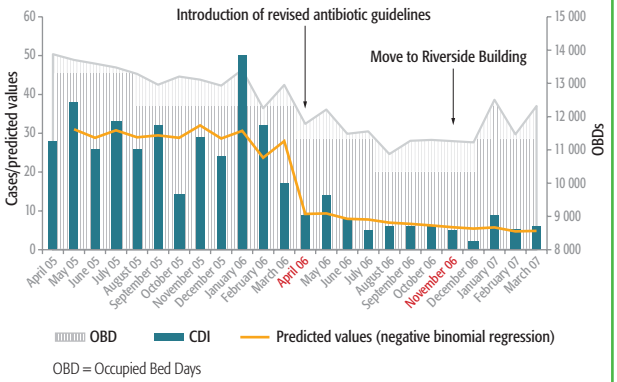
Source: Empirical Prescribing Indicator Report April 2011 – June 2012. Scottish Antimicrobial Prescribing Group August 2012.

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, i.e. 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].*

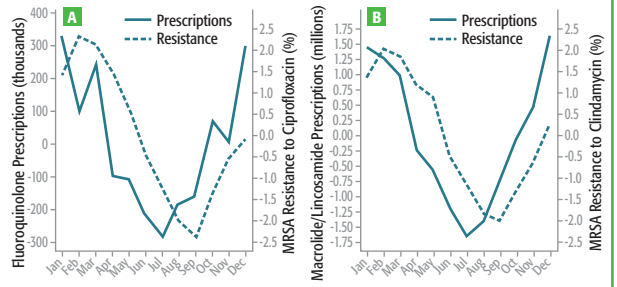
Figure 17. New cases of CDI and the number of OBDs before and after the introduction of revised antibiotic guidelines.



OBD = Occupied Bed Days

Adapted from Talpaert et al., J. Antimicrob. Chemother. 2011;66:2168-74.

Figure 18. Correlation between antibiotic use and resistance.



Seasonal pattern of antibiotic prescriptions and MRSA, showing 1-month lag.
A Mean monthly seasonal variation for quinolone prescription and MRSA isolates resistant to ciprofloxacin calculated by seasonal-trend decomposition procedures based on LOESS (STL) method.
B Mean monthly seasonal variation for macrolide and licosamide prescription and MRSA resistant to clindamycin calculated by STL method. Prescription data source: IMS Health, Xponent, 1999-2007. Resistance data source: The surveillance Network Database-USA (Focus Diagnostics, Hendon, VA). Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus.*

Adapted from Sun L, et al. Clin. Infect. Dis. 2012;55:687-94.

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, this valuable resource can be protected for future generations.

7.1. WHO SHOULD RECEIVE EDUCATION IN HOSPITALS?

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 may include competency assessment.

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 SHOULD AN EDUCATION PROGRAM BE DESIGNED?

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 38).

Educational measures recommended in the literature to improve antibiotic use in hospitals are shown in Table 12.

Table 12. Main antimicrobial stewardship strategies recommended in the international literature to improve antibiotic use at the hospital level.

PASSIVE EDUCATIONAL MEASURES
• Developing/updating local antibiotic guidelines
• Educational sessions, workshops, local conferences
ACTIVE INTERVENTIONS
• Clinical rounds discussing cases
• Prospective audit with intervention and feedback
• Reassessment of antibiotic prescriptions, with streamlining and de-escalation of therapy
• Academic detailing, educational outreach visits

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

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.

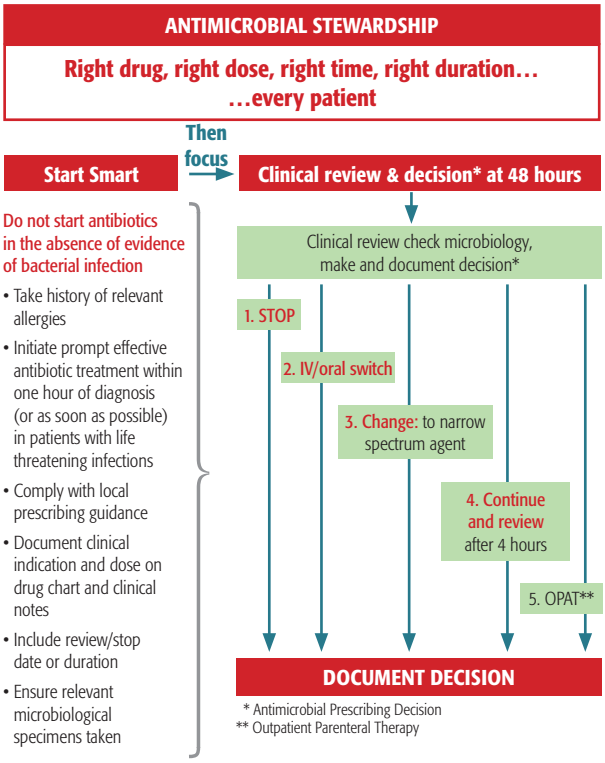
8. Communicate

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**.

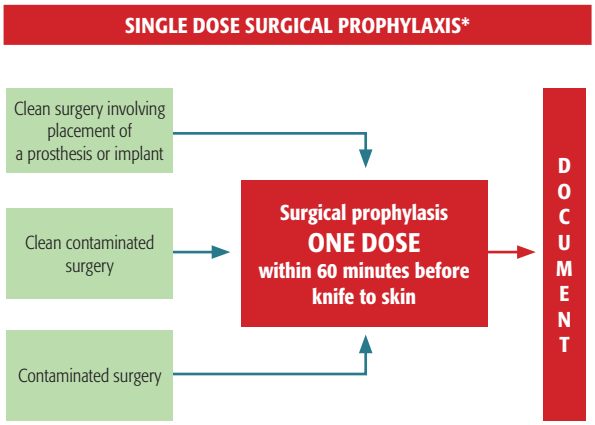
The **"Start Smart - Then Focus"** approach in the UK is a good example of such an approach [Figures 19 and 20].

Figure 19. Start Smart … Then Focus approach.



Figures 19 and 20 are adapted from 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) November 2011.

Figure 20. 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 approach is to identify and communicate to prescribers specific situations where antibiotics should be withheld and guidance in relation to the duration of antibiotic use, which is often an area of misuse (Table 13, page 36).

The importance of **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 teams, web-ex conferences, etc. are all important in promoting learning about prudent prescribing.

Table 13. Specific Situations where Antibiotics should be withheld

- Respiratory tract syndromes
  - 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

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

Table 14. Practice Guideline Recommendations regarding duration of therapy

• Community-acquired pneumonia (CAP)	5 days
• Health care-acquired pneumonia	8 days
• Skin and Soft Tissue Infections (SSTI)	5 days
• Urinary Tract Infections (UTI)	
- Cystitis	3-5 days [a]
- Pyelonephritis	5-14 days [a]
- Catheter associated	7 days [b]
• *S. aureus* bacteremia	
- Low risk of complications,	2 weeks
- High risk of complications	4-6 weeks
• Intra-abdominal infection	4-7 days
• Surgical antibiotic prophylaxis,	1 dose [c]

[a] Depending on antibiotic
[b] Prolonged to 10-14 days for delayed response
[c] Up to 24h, witout exception

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

THE KEYS TO SUCCESS

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

- Establish a **clear aim/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

Global Resources for implementing and measuring the impact of hospital Antimicrobial Stewardship Programs

AFRICA

Antimicrobial Stewardship and Infection Control African Network : www.ischemo.org/index.php/sections/isc-wg-antimicrobial-stewardship-and-infection-control-african-network

Best Care…Always! (BCA) campaign supporting South(ern) African healthcare organisations: www.bestcare.org.za/Antibiotic+Stewardship

South African Antibiotic Stewardship Programme : www.fidssa.co.za/A_SAASP_Home.asp

Suleman F, Meyer H. Antibiotic resistance in South Africa: your country needs you! S. Afr. Pharm. J. 2012;79:44-46.

ASIA-PACIFIC

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Ghafur A, Mathai D, Muruganathan A, *et al.* "The Chennai Declaration" Recommendations of "A roadmap- to tackle the challenge of antimicrobial resistance" - A joint meeting of medical societies of India. Indian Journal of Cancer 2013;49.

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Cooke J, Alexander K, Charani E, *et al.* Antimicrobial stewardship: an evidence-based, antimicrobial self-assessment toolkit (ASAT) for acute hospitals. J. Antimicrob. Chemother. 2010;65:2669-2673.

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ESCMID Study Group for Antibiotic Policies (ESGAP): www.escmid.org/index.php?id=140

Guidance for antimicrobial stewardship in hospitals (England) ARHAI Antimicrobial Stewardship ; http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_131181.pdf

Guidelines for Antimicrobial Stewardship in Hospitals in Ireland. SARI Hospital Antimicrobial Stewardship Working Group http://www.hpsc.ie/hpsc/A-Z/MicrobiologyAntimicrobialResistance/InfectionControlandHAI/Guidelines/File,4116,en.pdf

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US

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CDC: http://www.cdc.gov/getsmart/healthcare/

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Drew RH, White R, MacDougall C, *et al.* Insights from the Society of Infectious Diseases Pharmacists on antimicrobial stewardship guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Pharmacotherapy 2009;29:593-607.

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